Edelweiss Applied Science and Technology
ISSN: 2576-8484
Vol. 8, No. 6, 2679-2695
2024
Publisher: Learning Gate
DOI: 10.55214/25768484.v8i6.2531

Ecotoxicological effects of pharmaceutical preparations and the possibility of removing them through phytoremediation: A review

Ruaa M. Abdul – Jabbar[1*], Batool M. Al-Adily[2], Nuha F. Kadhim[3]
[1,2,3]Department of Biology, Collage of Science, University of Babylon, Iraq; ruaabdulabbar@yahoo.com (R.M.A.J.) batoolldily22@yahoo.com (B.M.A.A.) nuhaadhim@yahoo.com (N.F.K.)

Abstract: From several decades, there was a significant increase in the production of pharmaceuticals due to their widespread use for both animal and human health. However, these pharmaceuticals also release large amounts of waste into the water environment, where they have been found at levels of ng/l to mg/l in wastewater and surface water. Additionally, because pharmaceuticals initially have biological effects such endocrine disruption, they may have a multitude of adverse effects. Hospitals are indicated or thought to be a significant and extremely variable source that is typically released into sewers immediately, without any kind of preparation. even if they only make up a minor portion of the influents of sewage treatment plants' overall effluent volume. One of the primary sources of pharmaceuticals that are present in every area of the environment is the hospitals. These medications were transferred to wastewater treatment plants (WWTPs), which lack the necessary equipment to effectively handle these kinds of substances. Pharmaceutical contamination of water is regarded as a growing pollution issue in developed nations as these pollutants and micropollutants have been introduced into drinking water sources. In order to raise awareness among physicians, patients, and pharmaceutical manufacturers that pharmaceutical materials may have side effects outside of the patient, certain countries have implemented a classification system for pharmaceutical drugs based on their propensity to accumulate in surface water and interfere with aquatic life. This program is assessed by yearly tests of pharmaceuticals in sewage treatment effluents. The results indicate the presence of numerous types of medicines, including trimethoprim, sulfamethoxazole, and metronidazole, in all analyzed sewer treatment plant effluents. The manufacturing and consumption of pharmaceuticals appear to have an impact on their presence in wastewater.

Keywords: *Pharmaceuticals, Phytoremediation, Water pollution.*

1. Introduction

Active Pharmaceutical Ingredients are substances that have detrimental impacts on human health, are mainly existing of aquatic systems, demonstrate deleterious effects on different organisms, and are active pharmacologically.[1] Pharmaceuticals do not all have the same physical, chemical, structural or biological characteristics and can't be categorized as a class of homogenous substances like PAHs, CFCs or PCBs.[2]

The majority of medications are polar and were created to have a particular purpose in a target organism, they are differing from typical commercial chemical substances in a variety of ways such as their polymorphism, multiple ionization sites, and complex chemical structures [3]. Pharmaceutical pollutants also differing from most other contaminants .[4]

As a group, pharmaceuticals have incredibly varied chemical structures, which is essential for treating a variety of biological illnesses. According to [5]. comparable compounds can be categorized based on their therapeutic effects and chemical structure (or method of action) or physiological class.

* Correspondence: ruaa11789@gmail.com

Several methods can be used to provide pharmaceutical items to patients: topical application, inhalation, rectally, parenteral (directly in to the blood stream), i.e., intravenously, enteral (orally) via tablet capsules or liquids and so on [6].

Once the drug enters the body of a living being, whether a human or an animal, it will go through many processes known as ADME (absorption, distribution, metabolism, and excretion through secretion), these important processes are known as pharmacokinetic properties, and pharmaceutical preparations show a clear effect on the organism. The organism achieves the goal for which it was designed, which is usually still, not every time, this is done through a specific enzyme or targeted receptor. These procedures are called pharmacokinetics. Pharmacodynamics can also affect the bioavailability of the drug in the environment, inside or outside the human or animal body, once it is excreted. [7].

Metabolism of drug is divided into two stages, which are usually experienced by all substances, the liver is usually the site of catabolic phase I processes which include reactions like oxidation, hydroxylation, reduction and hydrolysis and entail the incorporating of a new emerging or preexisting functional group where the combination of glucuronic acid sulphate, acetyl, or amino acids is added to molecules in phase II anabolic processes [6].

The original chemical or its metabolites can disposal by excretion through in the form of bile or urine. certain substances are completely eliminated from body in their original form [7]. The liver does not metabolize the beta-blocker nadolol, which is eliminated entirely through the urine, on the other hand, the majority of the analgesic carbamazepine molecule is eliminated as conjugated and hydroxylated metabolites, with only 3% of the parent form being eliminated unaltered [8]. The biological processes mentioned above eliminate the pharmacological activity of many substances, some medications, meanwhile, retain some biological activity, this may be the case for substances that are not completely absorbed or those that are delivered topically [9].

Additionally, during sewage treatment operations, excreted conjugated metabolites may undergo deconjugation [10]. It has been suggestions that this process may cause some pharmaceutically inactive compounds to revert to active state [11].

2. The Sources and Entry Ways for Pharmaceutical Wastes in to Aquatic Environment

Pharmaceuticals discharge from sewage treatment facilities (STFs) is the main way that they enter the aquatic ecosystem. This is due to the fact that a significant amount of medication that patients ingest passes through their bodies unaltered and ends out in wastewater via urine [12]. Elimination rates change based on the substance, dosage and individual ,examples include the antibiotic amoxicillin, of which 80–90% is eliminated unaltered, and the β-blocker nadolol, which isn't subject to metabolism by the body at all[13].Because the majority of STFs in use today are not built to handle these kinds of materials, they are thought to be the primary source of newly discovered pollutants, since sewage effluents have a high concentration of pharmaceuticals and their metabolites, they can evade removal in STPs and find their entrances into the aquatic environment [14].

STPs are essential to the division of pharmaceuticals into two exposure paths linked to the solid and aquatic phases, as well as to their future release into the environment, the specific compound's level of polarity affects how the phases are partitioned, less polar or nonpolar pharmaceuticals are expected to end up in sludge material and subsequently terrestrial ecosystems, while polar pharmaceuticals are anticipated to stay mostly in watery environments, medications make up the majority of the load entering aquatic ecosystems, yet many of them are polar, a biodegradable and not volatile, thus these features preventing them from being sedimented or subjected to biological treatment in STPs[1].

Additionally, during times of high effluent turbidity, materials with poor solubility capacity can avoid STFs because of colloid-facilitated movement, low-solubility substances may also skip the STPs as a result of overflow brought on by technical issues, floods, or excessive influent loads [15]. Hospital wastewater also an important source of pharmaceutical compounds which include A broad spectrum of newly discovered contaminants hazardous materials such detergents, metabolites, pathogenic microbes, radionuclides, solvents, heavy metals, and pharmaceutical residues, steroid hormones, personal care and disinfectants which are bioactive and harmful to both humans and aquatic life, however, hospitals and municipal effluents are a main source of pharmaceutical contamination in different types of environment, also hospital wastewater contain different and complex compounds of pharmaceutical substances which cannot elimination by typical treatment techniques, as a result pharmaceutical residues will reach to the ground water, drinking water and surface water with different concentration range from between ng/l and mg/l [16,17 ,18].

On the other hand, the use of water after treatment for these purposes of irrigating agricultural areas constitutes an important source of pollution. where In dry areas of the US and other nations, the use of STP wastewater for irrigating public spaces and crops is growing, this method has the apparent advantage of lessening the demand on water supplies, however, there is a chance that pollutants in treated wastewater could seep into drinking water supplies found in groundwater or into aquatic habitats through irrigation runoff [1,19].Veterinary prescription drugs also consider as source of pollution where Following drug administration to an animal, the drug may undergo metabolism, leading to the excretion of a mixture of the initial chemical substance and its metabolites in the feces and urine, veterinary medications have two ways of release within environment: directly, by treating animals on pasture, for example, or indirectly, by applying animal dung, which contains excreted products, to land, once on land, the medications can seep into groundwater or travel via overland flow and drainage waters to surface waters[20]. Also, Fish farming is becoming a more significant source of pharmaceuticals in many aquatic environments. where They are added to feed as supplements in aquaculture are dumped straight into the water [21]. add to that Improper handling of leftover and expired medications .In fact, patients dont consuming their prescribed drugs completely, and some of these unused are kept in homes [22]. Also, medicines are often prescribed irrationally and this leads to storing more medicines which cause more harms to people and the environment, expired medicines are often disposed of in wastewater or regular garbage bins and when they reach drinking water or drains, it poses a grave risk to natural flora and fauna[23].Pharmaceuticals can also enter the environment by way of waste effluents from industrial operations, discarded medication, and unintentional spills that occur during production or distribution, there are three further ways to get rid of the sewage sludge: incineration, landfilling, and sea disposal, landfills are most frequently used for disposing of solid waste, however, a large number of the disposal places are open-air dumps without leachate-collection systems or protective barriers, posing a risk to the adjacent groundwater quality[12].

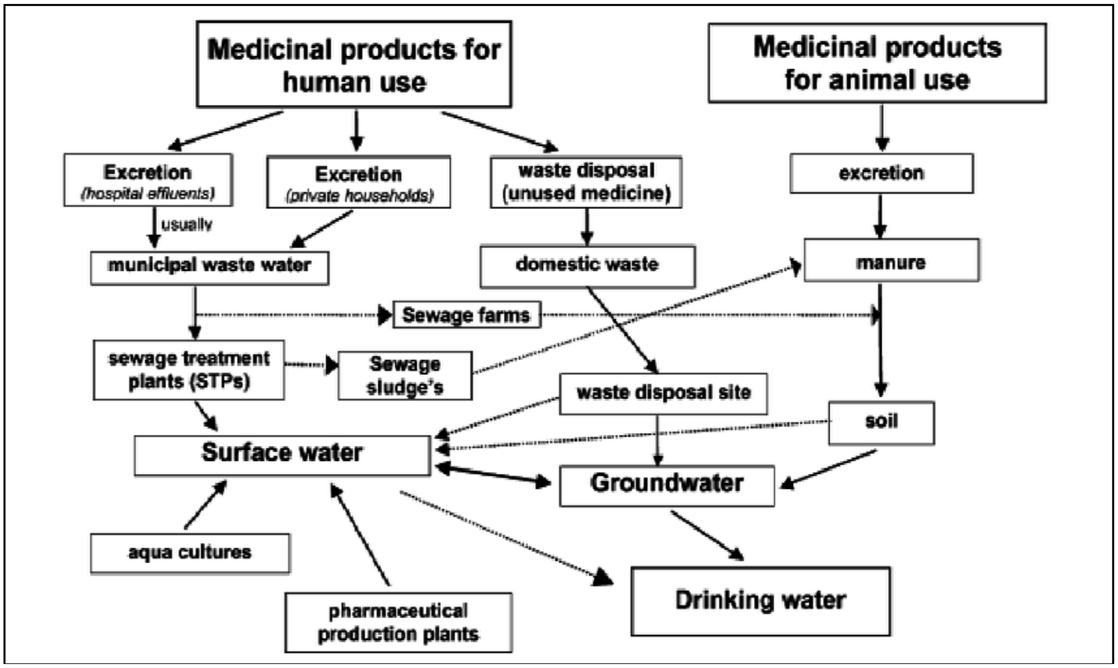

Figure 1.
Principal suppliers and routes via which drugs and pharmaceutical goods enter the aquatic environment (Heberer *et al*, 2002).

3. Fate of Pharmaceuticals in Aquatic Environments

Many drugs submit structural changes in both human and animal bodies prior eliminations from the bodies resulting in metabolites, and this change is rarely completed, i.e., usually a certain share of the original compound (the pharmaceutical ingredients) is taken out jointly with the metabolites, drugs are first undergone transformations in the body of animal or human after take up after that. They undergo partial metabolism to produce soluble forms and more polar whether it is pharmacologically active or not by a different of conjugative and oxidative enzymes (sulfoconjugation, conjugation of glucuronide, amino acid conjugation, acetylation, methylation and glutathione conjugation) These transformations make their elimination easily through feces and urine [24,25].

During their treat in wastewater treatment plants other transformation pathways occur, in addition, by biodegradation and physicochemical reactions. During secondary treatment, pharmaceutical substances and their metabolites undergo transformations [26]. In the aquatic environment another main transformation route involves biodegradation by different species of microorganisms [26,27]. In addition, under special environmental conditions such as biodegradation, photocatalysis, ozonation so, Pharmaceuticals could be easily transformed into smaller products. However, the nature of the transformed products (TPs) sometimes be more toxicity or stable whencompair with their initial compounds or vague [28].

Pharmaceuticals, can naturally attenuate through a variety of conversions and interactions [29,30]. Dilution is the first stage in tracing levels in water bodies [31]. Reaction products might be more or less hazardous and occasionally more stable than the parent substances, three main environmental fates for pharmaceuticals can occur through biotic (aerobic and anaerobic) and abiotic (chemical) interactions [32,33].

Water and carbon dioxide are the products of complete mineralization are firstly happens when take aspirin [34]. Second, they can be kept in WWTP sludge or bound in environmental matrices while keeping the same molecular structures as before, this is most frequently seen with drugs that are lipophilic and challenging to break down, Transformation into more hydrophilic molecules that endure

ISSN: 2576-8484
Vol. 8, No. 6: 2679-2695, 2024
DOI: 10.55214/25768484.v8i6.2531

is a third potential outcome. These hydrophilic compounds end up in receiving water bodies after going via facilities for treating wastewater [35].

4. Pharmaceuticals' Transformation Routes in Aquatic Environments

4.1. Hydrolysis

Significant non-biotic route to remove many pharmaceuticals is hydrolysis [36]. Although several functional groups in pharmaceuticals are hydrolyzable, the most often detected ones are amides and esters [37]. However, a large number of medications exhibit significant hydrolytic stability and are quite persistent in the environment [38]. There are many factors effect on hydrolysis, as the pH rises or falls, the rate of hydrolysis increases, also Temperature, flow rate and variations in light intensity all affect half-lives [39].

4.2. Biodegradation

One common and important route for the elimination of pharmaceuticals is microbial breakdown [40]. Fungi and bacteria both have a role in this biodegradation process where several byproducts are produced during microbial degradations .

it is possible to increase the success of biodegradation, although this is largely dependent on the sludge retention hydraulic period, and although the majority of antibiotics eventually biodegrade, the process usually takes a while [41,42]. Tetracycline degradation, for instance, was little in activated sludge [43]. In marine sediments, oxytetracycline, ampicillin, thiamphenicol and doxycycline underwent notable degradation but josamycin largely did not, this demonstrates that either the antibiotic cannot be broken down by josamycin-resistant bacteria or other antibiotics in the sediments prevent josamycin-resistant bacteria from growing [44]. Penicillin and other βlactam antibiotics can be biodegraded by bacterial β-lactamases [45]. The biodegradation of bezafrate, diazepam, oseltamivir, valsartan and atenolol each produces a number of transition products [46]. Antibiotics containing fluoroquinolones barely biodegrade in sediments or aquatic systems [47]. In an 84-day incubation period, less than 0.01% of the ciprofloxacin was mineralized in a water- soil-plant system [48].

4.3. Photodegradation

Surface waters primarily use both direct and indirect photo degradations as the abiotic means of removing medicines and their metabolites, pharmaceutical UV adsorption can cause photo degradation directly, or hydroxyl radical reactions might do it indirectly, these radicals are produced independently by sunlight reacting with inorganic materials or photosensitizers like humic acid [49,50].

The photodegradation products may exhibit varying degrees of toxicity in comparison to their parent medicines, compared to carbamazepine, the products of photodegradation from carbamazepine are more hazardous, for example, Acridine, is a highly mutagenic and carcinogenic photodegradation product of carbamazepine [51]. A multitude of environmental conditions influence the photodegradation of pharmaceuticals which include depth of the water body, plants and their shading properties, dissolved organic content, suspended particle matter, ions, seasonal variations in temperature and sunshine, and so on [52,30].

The photodegradation products may exhibit varying degrees of toxicity in comparison to their parent medicines, compared to carbamazepine, the products of photodegradation from carbamazepine are more hazardous, As an example, the photodegradation of carbamazepine produces acridine, which is extremely carcinogenic and mutagenic [45]. But many popular medications, including trimethoprim, carbamazepine, ibuprofen, and caffeine, have modest (30% approx) photodegradability [53].

4.4. Sorption

Pharmaceuticals are extracted from the aqueous phase by sorption on to organic materials, suspended particles, sludge, clays and soils. Nonetheless, the majority of medications are located distant from the line, indicating that the sorption process involves mechanisms other than hydrophobic interactions [54]. Tetracyclines are extracted from aqueous solutions by complexing with divalent calcium and magnesium cations [55].

The existence of Cu(II) ions caused increasing in thesorption of Tetracycline on sediments and soils [56]. The increased sorption of tetracycline on sediments and soils (at pH less than 5) could be a result of surface-bridging by adsorption and complexation of Cu^{+2}. Drugs having planar aromatic compounds can intercalate into clay minerals with ease [45]. In addition, ciprofloxacin exhibits very high sorption to activated sludge and sediments compared to its Kow value [57,58]. Tetracycline and hydrous oxides and humic acids have strong interactions that impact both their appearance in the water as well in the sorption [59]. The fallowing shape summarized all above routs which may occur on pharmaceuticals.

4.5. Reactions in Chemicals (oxidation and reduction)

The destiny of pharmaceuticals in any environment is influenced by a number of chemical interactions in addition to biological and physical properties. Redox reactions, which involve oxidation and reduction, are some of the most significant chemical processes. Loss of electrons during oxidation usually leads to the creation of more polar and may be more soluble in water compounds. Reduction, on the other hand, entails the acquisition of electrons and frequently results in less polar and maybe less water-soluble compounds [61]. It is challenging to forecast the drug's effects and their fate in environment due to the intricacy of these transformation processes. Moreover, these procedures can result in the creation of transformation products that might be more dangerous or persistent than the original substances [60].

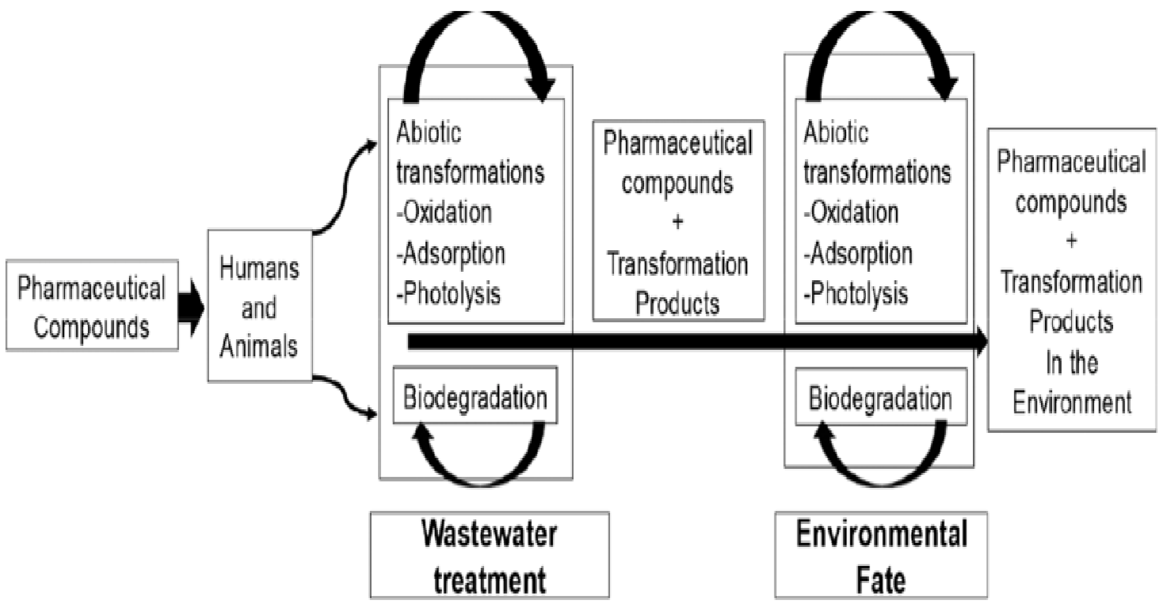

Figure 2.
Transformation ways of pharmaceutical materials in the environment.

There are two ways that pharmaceutical actives affect aquatic ecosystems:
1. According to the pharmaceutical effluent's composition.
2. According to toxic effects on aquatic life.
According to the pharmaceutical effluent's composition. They including:

- High concentration of organic materials (acetone, alcohol)
- Depletion of oxygen

ISSN: 2576-8484
Vol. 8, No. 6: 2679-2695, 2024
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Because rivers have systems for self-purification, lakes are more vulnerable to pollution than rivers. There are minimal to no consequences from the tiny amounts of wastewater that are discharged, and they might even be beneficial as sources of organic contaminants that support the nutrient supply of rivers for aquatic life. Large-scale deposits of these pollutants have the potential to harm the ecosystem as a whole by lowering the The amount of oxygen in water and reducing the quantity of light available for photosynthesis [62,63].

4.6. Algal blooms, (Eutrophications)

When a water body is overly enriched in compounds of nitrogen and phosphate , it becomes eutrophic, which accelerates the growth of algae and plants, organic substances found in pharmaceutical effluents, such as acetone and alcohols, are employed as denaturants in denatured alcohol and as solvents [64].

4.7. Antibiotic Resistance;

4.7.1. Compounds That Are Poisonous and Inhibiting (Antibiotics).

Antibiotic resistance rises as a result of pharmaceutical wastewater discharge [65]. The rise in resistant bacteria is caused by pharmaceutical pollutants; nevertheless, the rising usage and administration of antimicrobial medications has also led to an increase in pharmaceuticals in freshwater, which has had negative impacts on human health When active components from pharmaceuticals are released into waterways, they affect naturally occurring bacteria and cause medication resistance. When drug-resistant bacteria are discharged into wastewater, they may transmit genes as a result of continuous exposure to antimicrobial agents [66].

4.8. Fish With Hormonal and Hematological Abnormalities

Progestins, glucocorticoids, estrogen, and steroids have all been discovered at aquatic environment, even though in trace quantities. Fish that are continuously exposed to synthetic estrogen have had hormonal and endocrine disturbance [67]. As a result, fish exposed to these effluents that are male have become more feminine. In this scenario, intersex and poor reproduction start to manifest in the male fish [68]. Researchers have demonstrated that male and juvenile fish are less likely to reproduce when exposed to steroidal estrogen (EE 2). Additional instances include the feminization of male fish exposed to estrogen, which has the potential to seriously disturb fish populations, even at lower quantities, the anxiety medication oxybenzepam can have a substantial negative impact on fish behavior and food consumption rates in aquatic environments [69].

Moreover the hematological and hormonal harm that pharmaceuticals do to fish, it has also been shown that pharmaceutical byproducts cause these waterbodies to lose oxygen. In an aquatic biocoenosis, the presence of resistant molecules causes the oxygen levels to droph. the accumulation of suspended particles prevents algae and cyanobacteria, which provide food for the ecosystem, from receiving sunlight. The ecosystem's typical flora and wildlife are impacted by this, organic substances that degrade slowly and their resistant molecules. immunological reactions in aquatic animals being disturbed, these pollution groups are known as carcinogenic or immunotoxic [70].

- Immune response disruption in aquatic animals ;
- Slow biodegradable chemical compounds and their resistant polymers .

These pollution groups are known as carcinogenic or immunotoxic. They are to blame for the harm done to fish's intrinsic and acquired immunity, after prolonged exposure, they have been shown to impact fish's lymphocyte proliferation and macrophage activity [71]. Studies on immunotoxicological assessment have shown that suppression of innate responses by xenobiotics may have a greater impact on pathogen resistance than suppression resulting from acquired immune responses [72].

4.9. Surfactant-Containing Soaps And Detergents

Amphiphilic monomers with hydrophobic heads and hydrophilic tails are known as surfactants. Residuals from surfactants are found in many types of environmental components, such as soils and water, and end up in wastewater either because they are not treated at all or are treated partially as a result of inadequate use of one treatment process [73]. Owing to their distinct functional characteristics, surfactants are widely used in the pharmaceutical and chemical industries for a variety of purposes. These include boosting the physical and chemical compositions of medications, improving processing, Stimulating the solubility of the drug and improving its stability, as well as stabilizing the consistency of semi-solid preparations [74].

4.10. Predicted on the Detrimental Impacts on Water Life

4.10.1. Microorganisms

Ibuprofen is an anti-inflammatory analgesic that is taken orally to treat rheumatic and musculoskeletal pain, according to, this highlights potential antibacterial actions against harmful fungus and bacteria. Furthermore, it was concluded that methicillin-resistant staphylococcus aureus (MRSA) might grow on ibuprofen [69,75].

4.11. Phytoplankton

There have been reports that phytoplankton development is distorted by pharmaceutical residues. Streptomycin inhibited the growth of blue-green algal species at doses range is 0.05 to 0.93 mg/L, according to a report by, similar findings were made for Scenedesmus obliquus and Chlorella vulgaris, which both grew opulently at 0.66 mg/L streptomycin concentrations [76,75].

4.12. Plants

Different species respond differently to oxytetracycline and chlortetracycline [77]. When grown on clay-loam soils, pinto beans were shown to be the most sensitive plant species by researchers. Additionally, Daphnia magna straus was utilized to document the low toxicity of erythromycin and lincomycin, which are employed as feed additives in industrial agriculture [78].

4.13. Invertebrates, Or Amphipods

In a brief study, [79] examined the detrimental effects of pharmaceutical wastes released into the water on marine amphipods, or Amphitoe valida. The study indicated that the adverse effects dramatically expanded with the length of exposure to waste concentrations. When Amphitoe valida were exposed to remnants from pharmaceuticals over 1%, their survival rates are shown to be lesser than those control. The three pharmaceutical compounds were taken up by aquatic invertebrates (water louse, damselfly larvae, and ramshorn snails), and it was also determined that these actives had a tendency to bioaccumulate among these species [80]. When pharmaceutical waste concentrations are raised more one ppm, Temora turbinata, a calanoid copepod, has been shown to cause weak egg development, abnormal growth patterns, and decreased adult size [81].

5. Traditional Methods for Eliminating Pharmaceutical Wastewater

More work I s required to improve water consumption efficiency and wastewater treatment efficiency since research in the past few years has concentrated on the growing prevalence and detrimental effects of hazardous chemicals in aquatic environments [82]. Traditional techniques used in treating wastewater, which include physical, chemical and biological approaches are frequently using for removing hazardous chemicals that present in wastewater ,the kind of pollution and the method employed determine how effective the removal of pollutants[52].Ion exchange, neutralization, calcination, precipitation, and reduction are the chemical reactions that are most frequently utilized,on the other hand, physical treatments consist of sedimentation, stream stripping, evaporation, reverse osmosis, filtration, flocculation, dialysis, and electrodialysis, waste stabilization, microbial culture biodegradation, activated sludge, aerated lagoons, and anaerobic digestion are examples of biological treatments for contaminated water [83]. While most physical mechanisms change pharmaceuticals from a liquid to a solid phase, biological and chemical methods chemically modify the drugs to create new metabolites or breakdown products [84]. While most physical mechanisms change pharmaceuticals from a liquid to a solid phase, biological and chemical methods chemically modify the drugs to create new metabolites or breakdown products[84,85 ,86].

5.1. Phytoremediation for Eliminating Pharmaceutical Wastewater
5.1.1. Mechanisms of Aquatic Plants to Treat Wastewater

Phytoremediation is the preferred biological technique for removing pharmaceutical chemicals from aquatic settings. This is primarily because it can combat the threat of antibiotic resistance in opportunistic and pathogenic microorganisms [87]. A type of biological treatment known as phytoremediation breaks down or transforms environmental contaminants by utilizing plants and microbial communities associated with them [88,89]. It is an economical and environmentally sound method of cleaning contaminated soils and wastewater. The idea behind the method is called bioaccumulation or bioretention, in which pollutants from the water or sediment are absorbed, accumulated, or retained by the plants [90,91]. Subsequently, the contaminants are stored, broken down, or metabolized by the plants, which lowers their environmental concentrations [92,93].

Phytoremediation follows different mechanisms such as Phytoextraction, also known as phytoaccumulation, involves the intake of heavy metals in the plant roots and then their transfer into an above-ground-level component of the plant, such as shoots [95,94].

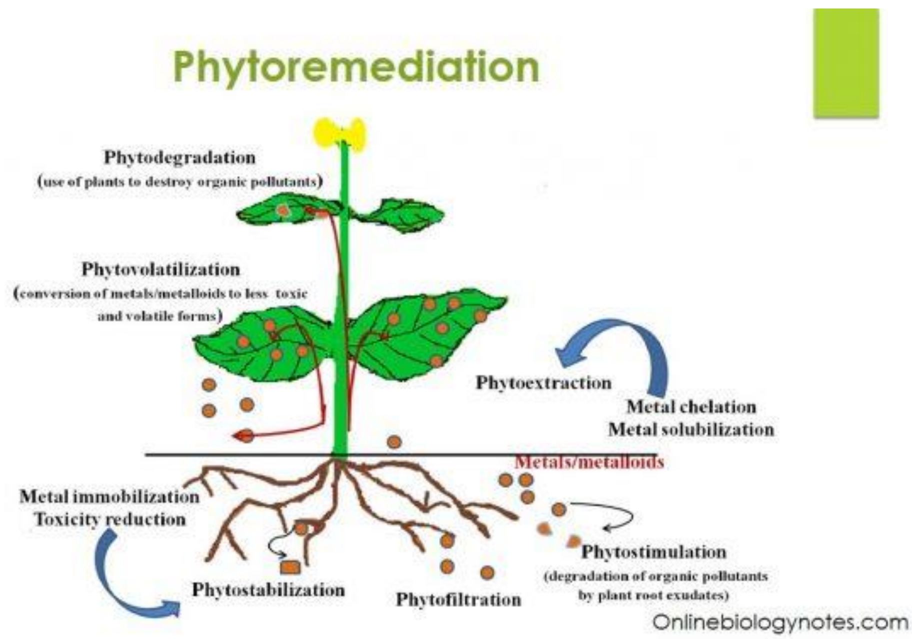

Figure 3.
Mechanisms of phytoremediation of organic pollutants.

Phytostabilization is another mechanism that involves the use of certain plants to reduce the transport of soil pollutants. It is also called local inactivation [85]. This type of treatment is ideal because it reduces the flow of pollutants [96]. Phytostabilization is very effective for a large site that is highly affected by contaminants [97]. Plant stabilization is a successful treatment, especially for large, heavily polluted sites [82]. Phytostabilization is simply a management strategy to inactivate/immobilize potentially hazardous contaminants; But it is not considered a permanent solution because only the movement of minerals is reduced, but they remain in the soil [98].

Root filtration involves using the ability of plants to draw and absorb pollutants, thereby restricting their movement in water [99]. Plant roots play an important role in root filtration. Factors such as fluctuations in pH values and root exudates help in the deposition of heavy metals in the outer layer of roots [85]. Thus, the toxins were collected through absorption by the plant and were easily removed [100].

Plant volatilization is a way in which plants convert pollutants into new volatile substances and release them into the environment using stomata. [101]. Among the most significant advantages of phytovolatilization is that it requires no additional management once the plantation is completed [85]. Additional benefits include no disturbance to the soil ,also avoiding soil erosion [103]. Bacteria that are present in the rhizosphere cabn help in pollutants biotransformation which then eventually improve the rate of phytovolatilization.

On the other hand, Phytodegradation is called Phyto transformation which include degrading the complex organic partials to simple once or the addition of these partials to the plant tissue, As with phytoextraction and phytovolatilization, the phytodegradation mechanism breaks down contaminants after they have been absorbed by the plant. Phytodegradation has been shown to remove certain organic contaminants, including munitions, herbicides, and chlorinated solvents. It can also remove contaminants from ground water, sediment, or soil [105].

Rhizodegradation, which occurs when pollutants break down in the rhizosphere, or plant root zone, is thought to be caused by bacteria or other kinds of microbes that proliferate in the rhizosphere. Researches have shown that rhizosphere soil contains up to 100 times more microorganisms than non-rhizosphere soil. [102]. The reason why microorganisms are so common in the rhizosphere could be that the plant secretes substances like sugars, amino acids, enzymes, and other substances that can promote the growth of bacteria. The roots also give the microbes more surface area to grow on and a channel for the transfer of oxygen from the surrounding air[85].

Rhizodegradation is mainly useful in polluted soil and has been found to be effective in treating many organic chemicals such as pesticides and hydrocarbons. It is also known as plant-assisted bioremediation which is stimulation of fungal and microbial degradation through the release of exudates and enzymes into the root zone [104].

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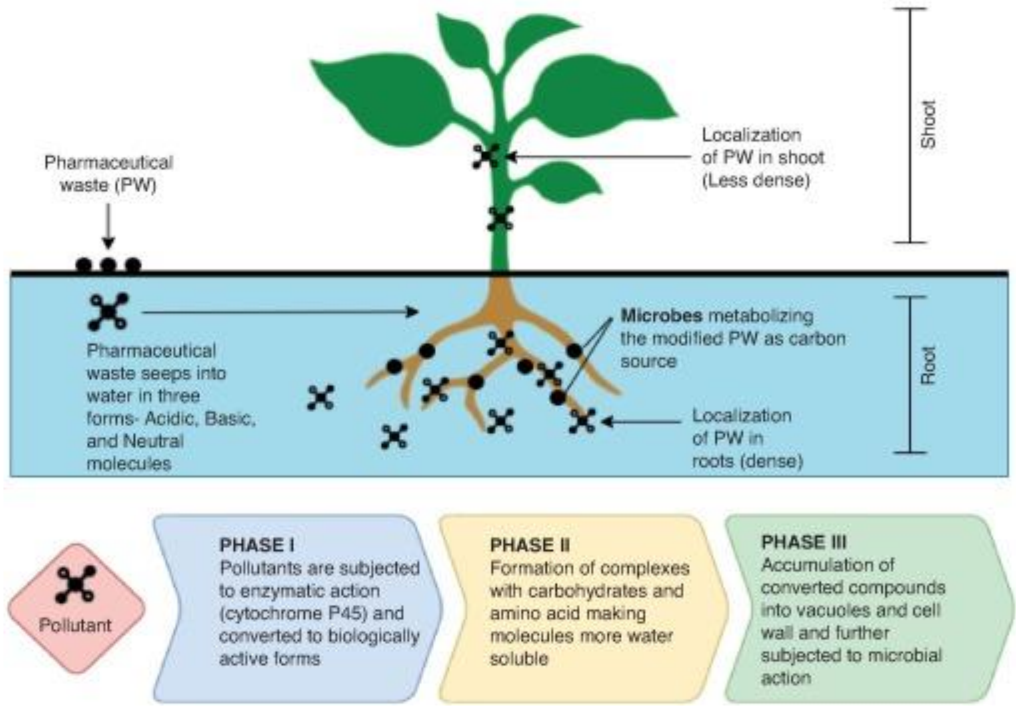

Figure 4.
Phytoremediation of pharmaceutical substances present wastewater.

5.2.2. Factors Affecting Phytoremediation

There are some of the factors that can effect on phytoremediation of pharmaceuticals at aquatic habitats involve the kind of medicament to be cleaned up, the types of plants employed in phytoremediation, the surrounding circumstances, the targeted compound's bioavailability, the water flow rates, the existence of additional pollutants, and the duration of the treatment. Higher pollution concentrations can reduce phytoremediation's effectiveness, and the toxicity and durability of certain medications can vary [106]. For example, when constructed wetland is used as the primary mode of treatment in phytoremediation, more than 98% of the constituents such as ibuprofen, caffeine, naproxen, acetaminophen so the triclosan were eliminated from [107].

The choice of plant species is crucial since certain plants are more adept than others at absorbing and breaking down medications, the study using Lythrum salicaria, Iris pseu dacorus, and Phragmites australis against twenty seven tiny pollutants suggests that the provided findings are equivalent, were Medications found in this micropollutant included n-acetyl sulfamethoxazole, prolol, propranolol, erythromycin, bezafibrate, ciprofloxacin, Atenolol, cyclophosphamide, diclofenac, ketoprofen, carbamazepine, and clarithromycin [108]. It was proposed that L. salicaria possessed higher phytoremediation potential than *P. australis* and *I. pseudocorus* because of its removal efficiency of over 20% for the majority of tiny pollutants, including drugs in aquatic environment. Furthermore, the design of the wet land plays a significant role in eliminating certain pharmaceuticals [109,110]. Employed Heliconia rostrata to examine the removal of ibuprofen and caffeine in two different settings (free-floating and vertical flow), their removal rates were very high [111]. Nutrients, Temperature, pH and light, are just a few examples of environmental factors that can have a significant impact on plant survival and growth, which can then have an impact on the plant's grow and eliminate pharmaceuticals from the water [112]. One such factor is the way that medicinal molecules can change and produce extremely harmful byproducts [113, 114]. For example [115] found that the interaction of diazepam with chlorine yields more hazardous and mutagenic compounds than the original medication. The efficacy of phytoremediation can be affected by variables like pH, salinity, and the existence of other organic materials, all of which might alter the bioavailability of medicines in aquatic environments [116,117].

Cattails (Typha sp.), for example, have vascular plant roots that are very good at absorbing substances with log Kow values (Octanol-water partition coefficient) between 1 and 3.5 [118]. This is because these compounds are both soluble in water, which allows them to enter cells, and lipophilic enough to penetrate the lipid bilayer of plant cell membranes, making them extremely accessible. The duration of water-plant interaction can be influenced by the flow rate of the water; on the other hand, the presence of other pollutants, like pesticides or heavy metals, might interact with medications to change their toxicity and bioavailability [119].

Artificial wetlands were created using Scirpus grossus, a built wetland (CW) with an aeration system and at pilot scale for vertical subsurface flow, and their effectiveness was assessed by [116]. The goal was to assess the system's ability to remove nutrients, chemical oxygen demand, and ibuprofen from residential wastewater all at once. Ibuprofen and paracetamol are less successfully removed by hydraulic retention time (HRT), also proposed that a longer HRT period might boost the efficacy of pharmaceutical elimination utilizing Scirpus grossus. It follows that how long drugs are phytoremediated can have an impact on how successfully plants remove pollutants from water [120].

6. Conclusion

It has long been thought that excretion in the form of Feces and urine are the main ways that active ingredients in pharmaceuticals intended for human use arrive in the environment as tiny pollutants but, in recent time, hospitals have become the main reason for releasing pharmaceutical compounds in to wastewater due to the increasing demand for them as treatment materials. for this reason, Interest in the environmental effects of pharmaceuticals and the proper removal of these compounds from wastewaters in the hospitals has increased recently due to the inherent features of medications, their widespread use, and their negative effects on both individuals and the environment. Pharmaceuticals were developed to maintain life, but when used carelessly, they can permanently damage the environment, one of the technically that use to treatment these pharmaceuticals is the phytoremediation used environmental friendly,in the US,(for example) large-scale phytoremediation of contaminated sites has been accomplished by the quick development of promising phytoremediation techniques in recent years. Over 300 contaminated sites have been profitably treated. Numerous businesses offering phytoremediation services have also emerged in Europe, cleaning up the environment for various large-scale industrial companies. These developments imply that phytoremediation will continue to grow quickly and, as technology advances, will be able to more fully repurpose the pollutants it removes, like metals.

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