Detection and Management of the Pharmaceutical Pollutants from Aquatic Systems - A Mini Review

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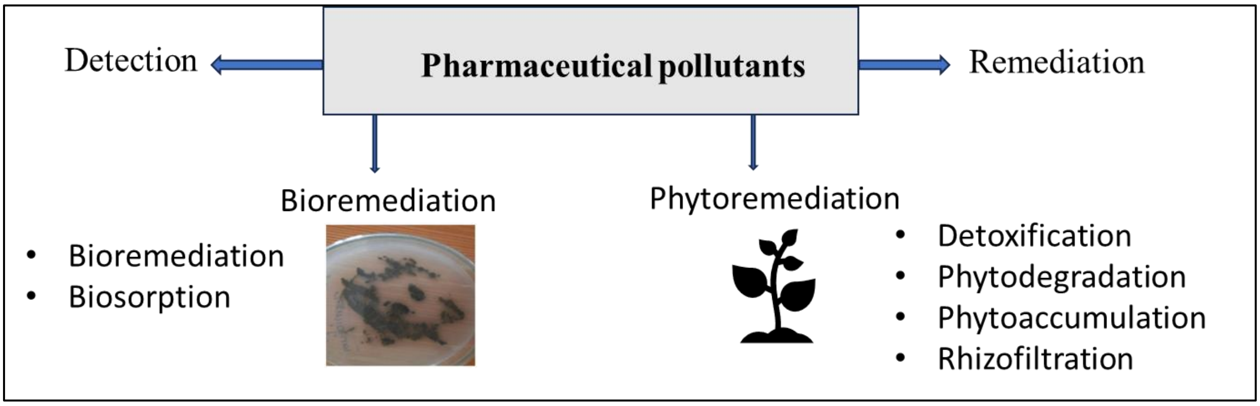

Abstract

Pharmaceutical residues in aquatic environments are common, and studies detailing their environmental fate has been given prominence in recent years. Since some pharmaceutical residues (environmentally persistent and stable drugs) are not eliminated using conventional wastewater treatments, research on the integrated methods is needed. Photocatalysis, ozonation, electrocoagulation, oxidation, adsorption, and biological treatments (phytoremediation, bioremediation) are generally used at waste water treatment plants. The most important environmental problem facing humanity is the increasing contamination of freshwater resources globally with hundreds of recalcitrant pharma micropollutants. In recent years, it has been acknowledged that research on the prevalence and destiny of pharmaceutical residues in aquatic habitats is vital. Detection of the drugs and finding solution for their removal from contaminated sites can be achieved with the optimization of biotic (microorganisms, algae, plant) and abiotic factors (light, pH, temperature, and carbon source). This mini review gives insight on the use of enzymes for the sensing of the drugs, enzyme assisted detoxification mechanism in plants as well as microorganisms. The biotic-abiotic coupled system and in site remediation processes are also discussed.

Keywords: *Drugs, Enzymes, Remediation, Toxicity, Phytoremediation, Wetland*

Highlights

- Pharmaceutical pollutants are considered as emerging environmental contaminant.
- Sensing of this pharma contaminant is difficult.
- Involvement of enzymes in sensing, and remediation of drugs is crucial.
- This review discusses about the biotic and abiotic coupled system for their removal.
- Drug detoxifying enzymes in conjunction with phytoremediation is a significant area of study.

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1. Introduction

1.1 Occurrence and toxicity of pharmaceutical pollutants

Release of the pharmaceutical pollutants, namely drugs (acetaminophen, metformin, hydroxychloroquine, acetylsalicylic acid, ibuprofen, dicoflenac, etc), antibiotics (macrolides, tetracyclines, penicillins, and quinolones), hormones (progesterone, testosterone, and 17α-ethinylestradiol) into the natural reservoirs is a global concern (Waghmode et al., 2022; Singh et al., 2024; Pérez-Lucas et al.,2024). The discharge points of pollutants are hospitals and manufacturing companies (Waghmode et al., 2023a).

Following irrigation with wastewater effluent, surface soil samples showed a range of drug concentrations from 2 to 15 ng/g. The most common drugs found were analgesics and anti-inflammatories (10 ng/ g), followed by psychiatric drugs (up to 3.8 ng/g) and antibiotics (up to 5.4 ng/g) (Biel-Maeso et al., 2018; Pérez-Lucas et al., 2024). In the vertical soil profile, total amounts of pharmaceutically active compounds were found down to 150 cm and up to 15 ng/g (Biel-Maeso et al., 2018). Soils treated with cattle dung, poultry manure, or municipal biosolids contain hormones and the breakdown products of those hormones; 4-androstene-3,17-dione, oestrone, 5-androstan-3,17-dione, and 1,4-androstadiene-3,17-dione were all released into the environment (Jacobsen et al., 2005). Improper disposal of the drugs leads to a negative impact on the environment. As per the published literature, drugs in nanogram per Liter to microgram per Liter concentrations, it could affect the life of photosynthetic microorganisms, plants, and aquatic animals (Singh et al., 2024).

During the Covid 19 pandemic, the use of analgesic, painkillers and antiviral drugs increased. During COVID-19 treatment, paracetamol was the first-line analgesic and antipyretic medication (Tan et al., 2020). One of the most popular analgesics and antipyretics, paracetamol (also known as paracetamol; N-acetyl-para-aminophenol) has now become a global pharmaceutical contaminant (Waghmode et al., 2022).

Hydroxychloroquine was used during the pandemic to control the viral infection (Boulware et al., 2020). Due to its ability to bioaccumulate in vegetation through contaminated soil and groundwater, hydroxychloroquine continues to exist in the environment (Tuo et al., 2012, Howard and Muir, 2011, Chen et al., 2013). Due to its bio resistance, even hydroxychloroquine's natural degradative metabolites are hazardous (Neuwoehner et al., 2009).

According to the RECOVERY (Randomised Evaluation of COVID-19 Therapy) experiment, steroidal medication was used to manage mucormycosis cases during the COVID-19 pandemic (Tandon and Pandey, 2021).

The pharmaceutical industry can implement a sustainable strategy through appropriate process, production and disposal section design, monitoring, and action. Global adherence to eco-friendly protocols for detection and disposal of the drugs are needed (Waghmode et al., 2023b).

1.2 Enzymes for the sensing of the drug

To find out the concentration of drugs using biological as well as environmental samples, sensors with high efficacy are required. Fast, reliable, and sensitive detection of drug in biological sample is needed to avoid toxic effects on human health which is imposed by abuse, acute and chronic misuse of the drugs (Prabakar, and Narayanan 2007). The release of the antibiotics, cytostatic, antineoplastic and antidepressants, pose a serious threat due to their reported short term as well as unknown long-term effects. However, to find the actual concentration of the drug, some analytical and technical problems occur due to sampling errors, and non-detectable concentration (Martins et al., 2004).

For the above specified reasons, the general enzyme-substrate based biosensor system has been revolutionised as illustrated in Table 1.

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Table 1. Enzyme based biosensor for the drug sensing

Components of the sensor	Pharma pollutant	Sensitivity range	Reference
Amidases/Cerium dioxide/Graphene nanoparticles	Paracetamol (Acetaminophen)	1-100 µM	Stanković et al., 2019
Morphine dehydrogenase (MDH)/salicylate hydroxylase (SHL) /Clark oxygen electrode	Codeine	2-1000 µM	Bauer et al., 1999
Morphine dehydrogenase (MDH)/salicylate hydroxylase (SHL)/ Clark oxygen electrode	Morphine	5-1000 µM	Bauer et al., 1999
Laccase (LACC)/ PQQ dependent glucose dehydrogenase (GDH) / Clark oxygen electrode	Morphine	32 nm-100 µM	Bauer et al., 1999
Laccase (from *Bacillus* sp.) on a surface plasmon resonance (SPR)carboxymethyl dextran surface	Bromocriptine	0.001 ng/ml to 1000 ng/ml	Jabbari et al., 2017
Cytochrome P450 2D6 on screen-printed Ag/AgCl electrode	Codeine	-	Asturias-Arribas et al., 2014
Glutathione-S-transferase on carbon paste electrode	Cisplatin	8.8 µM	Materon et al., 2014
Laccase on pomegranate peel biochar	Diclofenac, Amoxicillin, Carbamazepine, Ciprofloxacin	50 mg/L	Al-Sareji et al., 2023
Screen-printed electrode/ Prussian blue/xanthine oxidase	Allopurinol	0.125–2.5 µM	El Harrad, & Amine, 2016
Carbon nano fibers/ cytochrome p450 (CYP3A4)	Ketoconazole	58.5 mM	Xue et al.,2013
Pyrolitic graphite/DNA/Cytochrome p450 (CYP101)	Sulconazole	204.2 µM	Hull et al.,2009
Screen-printed electrode /Carbon nanotubes/Tyrosinase	Methimazole	0.074–63.5 µM	Martinez et al.,2008

Amperometric biosensors has been utilized for the detection of drugs like codeine, morphine, acetaminophen, bromocriptine etc. For the immobilization of biological element (enzyme), electrochemical transducers like screen-printed electrodes, carbon or oxygen electrodes can be used. Screen printed electrodes has been reported in the sensors for the electrochemical detection of fentanyl (synthetic piperidine opioid analgesic drug) (Ott et al., 2020). An enzyme-based sensor for drug detection typically operates by leveraging the specific catalytic activity of an enzyme to detect a target drug molecule. Enzymes which are involved in the detoxification of the drugs, heavy metals, dyes are primarily used as the component of biosensor. In humans, cytochrome P 450 and glutathione -S-transferase (GSTs) are reported in the liver for detoxification (Smith et al. 2006).

The biosensor preparation involves the key steps like enzyme selection and immobilization on transducer surface (electrode, optical fiber), drug-enzyme interaction and signal transduction

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(electrical or optical methods) (Ott et al., 2020). For detecting a drug like penicillin G, a penicillinase enzyme was immobilised onto tiny bio-chips using thioglycolic acid self-assembled monolayer (TGA-SAM) (Rahman and Asiri 2015). Penicillinase hydrolyzes penicillin into penicilloic acid, and hydrogen ions by releasing electrons. This current is directly proportional to penicillin concentration (Rahman and Asiri 2015).

A disposable biosensor based on inkjet-printed CNT electrodes (IJPCNT) improved with amidase/cerium dioxide graphene nanoribbons composite was developed (ACeO2@GNR/IJPCNT) for the detection of acetaminophen in biological fluid (Stanković et al., 2019). A report is available on the application of morphine dehydrogenase (MDH) for the sensing of morphine and codeine where enzyme catalyses the oxidation of morphine or codeine into morphinone or codeinone with concomitant formation of NADPH which can be quantified by using electrochemical based or luminescence-based method (Holt et al., 1995; Holt et al., 1996; Abraham et al., 2020). The drug bromocriptine is used for the treatment of patients suffering from Parkinson's disease. Very low concentration of this drug in plasma, suggests the direct label-free detection of drug using surface plasmon resonance (SPR) method and laccase enzyme based sensors (Jabbari et al., 2017).

1.3 Enzyme assisted remediation of pharma micropollutants

Physico-chemical and biological techniques have been used to remove pharmaceutical contaminants from the wastewater treatment facility. Properties of macro and micropollutants enables primary physico-chemical treatments, followed by biological methods. Biological methods are less costly and eco- friendly as compared to physico-chemical methods. In biological methods, aerobic and anaerobic microorganisms are used in free or immobilized form.

Bioremediation is a method which is based on the natural biological activity for the reduction in the toxicity of harmful compounds (Vidali, 2001). Biological contribution for the remediation of toxicants is an extensively studied research area due to changes in the microbial behaviour or alteration of the microbial community in presence of toxicant (Iwamoto and Nasu, 2001). With progressive developments in the field of molecular biology, researchers are trying to explore the activity of culturable as well as unculturable bacteria or their metabolites through synthetic biology strategies viz., gene editing, data mining, CRISP, metabolic engineering, synthetic microbial community (Waghmode et al.,2023). For the effective bioremediation process, some factors like viability of microorganisms, optimal concentration of pollutant, solubility of pollutants, environmental conditions like pH, temperature, gases etc. are important (Waghmode et al., 2022). Potential of the microorganisms to degrade drugs is attributed to the role of enzyme as given in Table 2.

Table 2. Enzymes in drug degradation

Enzyme	Source	Drug	References
Deaminase	*Pseudomonas moorei* KB4	Acetaminophen	Żur et al., 2020
Hydroquinone-1,2-dioxygenase	-	Acetaminophen	Zur et al., 2018b
Acyl amidase E.C. 3.5.1.13	Bacteria	Acetaminophen	Ko et al., 2010
Amidase [EC:3.5.1.4]	*Pseudomonas* sp.	Acetaminophen	Rios-Miguel et al., 2022
Amidase, cytochrome P450, laccases, and extradiol-dioxygenases	*Penicillium chrysogenum* var. *halophenolicum*	Acetaminophen	Enguita et al., 2023

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Monooxygenase and Glucuronidase	Microbial consortium (*Alcaligenes faecalis, Staphylococcus aureus, Staphylococcus haemolyticus* and *Proteus mirabilis*)	Sodium Diclofenac and Mefenamic Acid	Murshid, and Dhakshinamoorthy, 2019
Laccase	*Streptomyces mutabilis* A17	Sulfa drugs	Reda et al., 2019
Monooxygenase and Catechol 1,2-dioxygenase	*Bacillus thuringiensis B1*	Ibuprofen	Marchlewicz et al., 2017
4-Hydroxyphenylpyruvate dioxygenase, homogentisate 1,2-dioxygenase, long-chain acyl-CoA synthetase, acetyl-CoA acyltransferase and enoyl-CoA hydratase	*Pseudoalteromonas* sp.	Ibuprofen	Li et al., 2022
Catechol 1,2-dioxygenase, Laccase	*Achromobacter spanius* S11 and *Achromobacter piechaudii* S18	Ibuprofen	Fetyan et al.,2024

1.4 Approaches for pharmaceutical pollutant removal from WWTP

1.4a Biotic-abiotic coupling-based method

In the biotic- abiotic coupling method, the coupling action of biogenic reactive oxygen species (ROS) and enzymes is used for the degradation of the emerging pollutants (Li et al.,2022). The source of the ROS can be chemical-based or bio-based. To check the possibility of biological treatment for the removal of drugs, modified Sturm-test (OECD 301 B) results are used. Toxicity imposed by the parent drug or its degradative metabolite (with hydroxyl or carbonyl group) limits the biodegradation process. Hence, primary treatment with physicochemical process is recommended to reduce the toxicity of target compound and to increase the microbial interaction with the xenobiotic.

For the efficient and complete mineralization of pharma pollutants with the aid of photocatalytic and biodegradation mechanism, there is need to optimise the biotic-abiotic factors. Environmental elements that control the microbial/plant interaction with specific contaminants/pollutants include abiotic parameters, which include temperature, pH, moisture, solubility in water, soil structure, nutrients, oxygen content, site features, and redox potential (Somasundaram et al., 2022). Biological based methods are not sufficient for the removal of drugs like carbamazepine (Keen et al., 2012), tetracycline (Guo et al., 2015; Yahiat et al 2011), tylosin antibiotic(Yahiat et al 2011). Complete mineralisation of recalcitrant drugs can be achieved with help of integrated technologies of ozonation and biodegradation. Integrated methods of ozone–hydrogen peroxide, ozone-activated carbon, and ozone-biological treatment was used for the tetracycline and its byproduct removal from water (Gómez-Pacheco et al., 2011). Less toxic products are generated when longer ozonation process is followed by biological method during tetracycline removal from water (Gómez-Pacheco et al., 2011). The combined system ozone-biological activated sludge is highly effective to degrade 100 % tetracycline (50 ppm) and mineralize the drug. But during the process, ozonated sample reduces the bacterial population which can be avoided with longer preozonation time (Gómez-Pacheco et al., 2011). The removal of amoxicillin (1000 ppm) has been achieved up to 80% in 70 min by using Fenton-activated sludge combined system, suggesting that the Fenton process reduces the time for biodegradation (Guo et al., 2015). Integrated approach of UV/hydrogen peroxide advanced oxidation and subsequent biological method, has been reported for the complete mineralization of carbamazepine drug (Keen et al., 2012). During the process, to maintain the bacterial count, addition of bovine catalase

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is needed to scavenge residual hydrogen peroxide (Keen et al., 2012). Laccase immobilised on pomegranate peel biochar was found to be efficient for the treatment of wastewater contaminated with diclofenac, amoxicillin, carbamazepine, ciprofloxacin drugs (Al-Sareji et al., 2023).

Drugs and their hazardous byproducts can be immediately removed from WWTPs by using integrated physicochemical and biological treatments. Bioremediation techniques can be used after previous treatments because many medications are resistant to traditional biological approaches. Optimisation of both biotic and abiotic operational parameters is necessary for the implementation of cost-effective integrated methods.

1.4b Insite remediation

Most of the pharmaceutically active compounds and heavy metals get leached out from the contaminated water streams into the drinking water reservoirs. African water bodies have been found to contain antiretroviral medications (167 ng/ml lamivudine and 1.640 ng/ml nevirapine), indicating the necessity of developing remediation techniques (Zitha et al., 2022). Elbe river basin water showed residue of anticonvulsant medications such as carbamazepine, lamotrigine, and gabapentin, as well as the analogue gabapentin (gabapentin-lactam) (Ferencik et al., 2022).

When surface water utilised for groundwater recharge under the effect of sewage effluents, polar drug residues may seep into the groundwater. Flocculation and sand filtration are not efficient to remove the drug residues. To circumvent the problem of the occurrence of such anthropogenic agents and pathogenic microorganisms, bank filtration as well as artificial recharge of ground water has been opted (Heberer et al., 2007).

Some aquatic plants have the potential to use as a remediation tool for the insite remediation. *Lemna minor* L. could significantly lower the flumequine concentration (0.05-1 ppm) in culture media on a five weeks period. Initially phytotoxic effects like retarded growth, decreased chlorophyll be content, damaged leaves and roots were observed, but with prolonged incubation pronounced growth was observed in duckweed (Cascone et al.,2004). Drug resistant macrophytes can be used in the future to treat the fluoroquinolone antibiotic polluted water.

In one study, *Lemna minor* and *Salvinia molesta* were tried as monoculture and mixed culture to retrieve ciprofloxacin (1.5 µg/L) and sulfamethoxazole (0.3 µg/L) from artificially contaminated water (Kochi et al., 2023). Based on the data of Abbot modelling, both drugs demonstrated antagonistic effects on plants with increase in the antioxidant activities, followed by increase in the growth rate with prolonged exposure. *Salvinia molesta* showed good uptake of the drugs as compared to the *Lemna minor* (Rocha et al.,2022). *Salvinia molesta* has been reported as effective for phytoremediation programs due to their rapid and fruitful growth and easy management (Rocha et al.,2022). Natural degradation along with the floating and submerged macrophyte community, could be helpful for the removal of antibiotics from the water.

Factors such as plant species selection, climate, contaminant concentration, and the presence of multiple plant species in the system all affect the aquatic macrophytes' ability to bioaccumulate drugs. It appears that systems that use aquatic macrophyte polycultures are generally more effective at eliminating contaminants than those that use monocultures (Kochi et al., 2020).

Macrophytes based phytoremediation uses the concept of green liver system (GLS) for the drug removal. Diclofenac removal mechanism via uptake (internalization) was observed in various species of *Myriophyllum* sp. like *Myriophyllum roraima* (2.1 ng/g/Hr) ,*M. spicatum* (1.9 ng/g/Hr), *M. aquaticum* (1.7 ng/g/Hr), *M. mattogrossense* (1.7 ng/g/Hr), and *M. tuberculatum* (1.1 ng/g/Hr) (Esterhuizen, & Pflugmacher, 2023). Green liver systems may be fully customised to remove specific environmental pollutants with no detrimental effects on efficiency when scaled up, according to research on laboratory optimisation.

The combination of the pond and the constructed wetland demonstrated significant (up to 87%) removal of stimulants (nicotine and caffeine) and non-steroidal anti-inflammatory drugs (ibuprofen and naproxen) with a decrease in ecological risk. However, effluent recirculation was necessary to

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fully remove the pollutants to improve dissolved oxygen concentration and hydraulic residence time (Guedes-Alonso et al., 2022).

1.4c Phytoremediation

Phytoremediation is the process of using plants and their colonising microorganisms for the detoxification of recalcitrant compounds (Pilon-Smits, 2005). Phytoremediation is gradually becoming recognised as a promising environmentally friendly solution for eliminating many kinds of drug pollutants from the environment. Phytoremediation can be studied by using artificial wetlands (Kochi et al.,2023), hydroponics system (Moogouei et al., 2018) or invitro studies (Kitamura et al., 2023). Flowchart of the construction of the wetland for the pharmaceutical pollutant removal is illustrated in Figure 1.

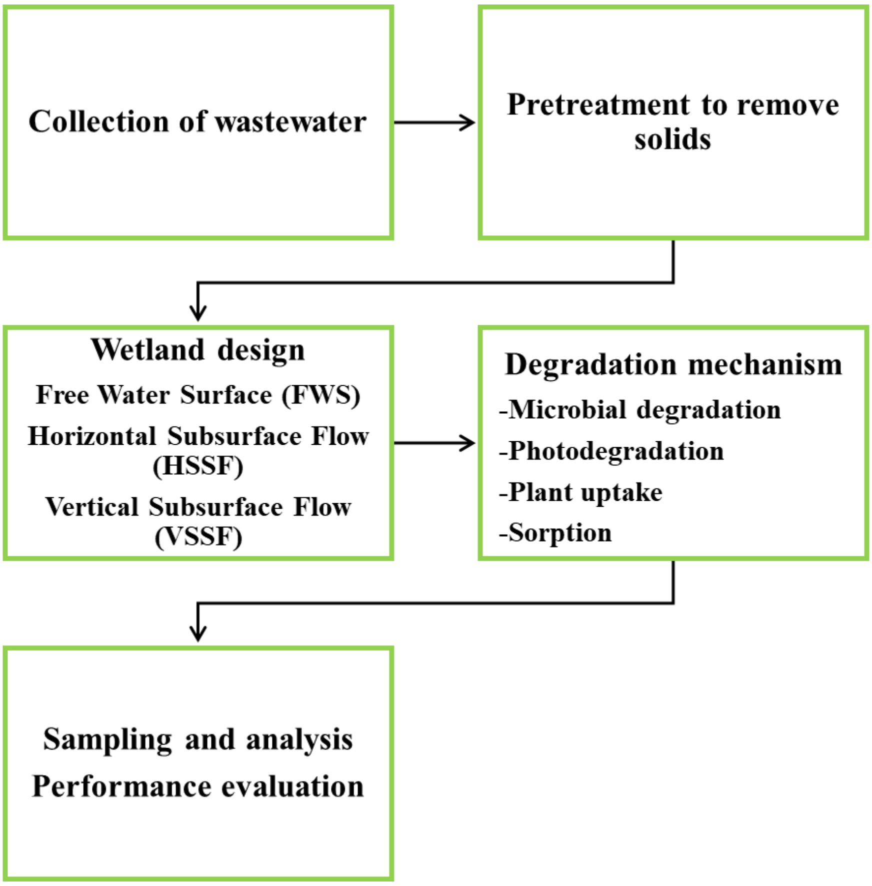

Figure 1: Illustration of wetland design and working for the removal of pharma pollutant.

In wetlands, submerged (*Myriophyllum aquaticum* and *Rotalaro tundifolia*) and floating plants (*Salvinia molesta* and *Lemna minor*) are used for the elimination of the pharmaceuticals (Kochi et al.,2023). *Ceratophyllum* spp., *Myriophyllum* spp., and *Egeria densa* have been reported to have good diclofenac uptake capacity where drug removal efficiency was found to be affected by the flow rate (Esterhuizen and Pflugmacher, 2023).

Aquatic plants (*Lemna minor* and *Azolla*) have advantages such as ease of handling (during planting, growth, harvest), more biomass, and potential to tolerate and eliminate toxic compounds. Phytoremediation activity of these plants is mainly due to the associated microorganisms (association of *Azolla* with *Anabaena* and *Arthrobacter* bacteria like nitrogen fixers), and detoxification machinery (Bianchi et al., 2020; Maldonado et al.,2022).

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Different mechanisms like volatilization, phytoextraction, degradation, stabilization has been adopted by plants for the removal process. As reported earlier, unlike mammal's plants also adapt enzymes (cytochrome P450 monooxygenases, glutathione S-transferases, glycosyltransferases, and transporters) dependent defence mechanisms for the detoxification of the drugs (Schäffner et al., 2002; Bartha et al., 2010). There are mainly 3 phases of the pollutant detoxification by plant as schematically represented in Figure 2.

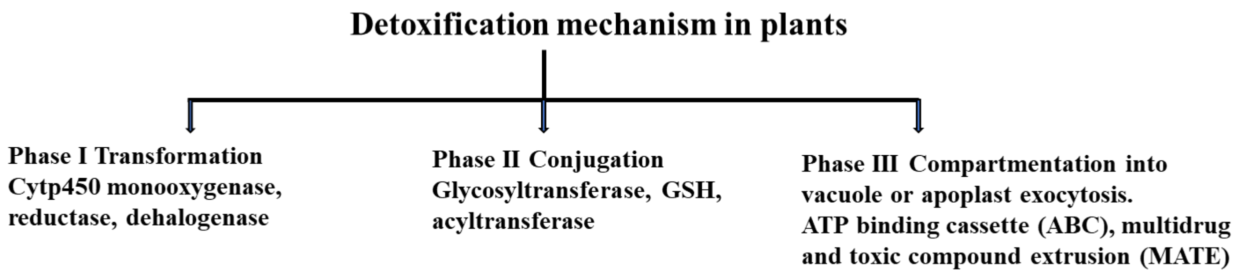

Figure 2: Illustration of detoxification mechanism in plants (Schäffner et al., 2002).

There are ten different classes of glutathione S transferase viz. GST-U (tau), GST-F (phi), GST-L (lambda), GST-T (theta), GST-Z (zeta), DHAR (dehydroascorbate reductase), TCHQD (tetrachloro hydroquinone dehalogenase), EF-1Bγ (elongation factor 1B, hemerythrin and iota) (Liu et al., 2013; Estévez and Hernández,2020).

Glutathione S transferase (GSH) is a pseudopeptide (Glu-Cys + Gly) which is created by the action of two consecutive enzymes: γ-glutamyl cysteine synthetase (γ-ECS; GSH1) and glutathione synthetase (GSH-S; GSH2) (Martins, & Teixeira 2021). After exposure to the 5-ppm acetaminophen concentration for 6 days, GSH-acetaminophen conjugates were recorded in cucumber roots (15.2 nmol /g) and leaves (1.2 nmol/ g) (Sun et al., 2019).

In *Brassica juncea* L. Czern, acetaminophen glutathione conjugate were observed suggesting the role of glutathione -S-transferase for detoxification (Bartha et al., 2010). Acetaminophen exert growth-promotion in *Solanun nigrum* upto 0.5 ppm concentration.

Glutathione S transferase (GSH) and γ-glutamyl cysteine synthetase (γ-ECS) mediates the conjugate formation in roots and shoots as plant defence mechanism (Martins, & Teixeira 2021). In *Solanum lycopersicum* L. cv. Micro-Tom (tomato) was also found to use the activity of GSH (encoded by SlGSTF4 and SlGSTF5 genes) to form diclofenac glutathione conjugate to avoid the bioaccumulation of the diclofenac (5 ppm) in the fruit (Sousa et al.,2021). In maize crop, GSH make conjugate with the antibiotic chlortetracycline as stress response (Farkas et al.,2007).

Ibuprofen (1.03 ppm) exposure increased the activity of cytochrome P450s, glutathione S-transferases, UDP-glycosyltransferases, and ABC transporters in *Arabidopsis thaliana* (L.) Heynh (Landa et al., 2017). Cytochrome P450 monooxygenase and glycosyltransferase were implicated in the uptake and modification of ibuprofen (IBP) in the wetland plant species *Phragmites australis* (He et al., 2017).

The toxicological effects on the photosynthetic microorganisms (*Chlorococcum infusionum* and *Synechococcus elongatus*) imposed by anti-HIV drugs polluted water, could be reduced with the help of phytoremediation by *Lemna minor* plants (Kitamura et al., 2023). Phytoremediation of water polluted with ciproflaxin (1-10 μg L^{-1}) was done with *Salvinia molesta* or *Egeria densa* for 96 h followed by the ecotoxicity testing on *Desmodesmus subspicatus* (microalgae). Based on the results, it was concluded that water after phytoremediation did not contain any toxic compounds either from drug or from plants. (Kitamura et al., 2023).

Plant -bacteria synergism could be beneficial for the pharmaceutical pollutant removal program. In this synergistic activity, root associated or endophytic microorganisms engages in the

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phytoremediation of the toxicants by enhancing the stress response. Removal of carbamazepine (antiepileptic drug) has been reported due to the synergistic activity of bacteria (*Chryseobacter iumtaeanense, Rhizobium daejeonense, Diaphorobacter nitroreducens and Achromobacter mucicolens)* associated with *Phragmites australis* (Sauvêtre and Schröder 2015). Upto 90% drug degradation was observed after 9 days of exposure due to the plant -bacteria synergistic mechanism (Sauvêtreand Schröder 2015). One study evaluated the interactions between roots and endophytic bacteria during carbamazepine exposure by inoculating *Rhizobium radiobacter* and *Diaphorobacter nitroreducens* (*Phragmites australis* isolates) with horseradish (*Armoracia rusticana*). Endophyte-inoculated tests showed increased clearance efficiencies of carbamazepine (10–21%) compared to control samples (5%) (Sauvêtre et al. 2018). During the degradation of the carbamazepine, cytochrome P450 and/or peroxidases, epoxide hydrolases, catechol oxidase, γ-glutamyl-transpeptidase like enzymes were involved (Sauvêtre et al. 2018).

Phytoremediation of painkillers, antidiabetic, antiretroviral and antiepileptic drugs, has been reported by different plant species as given in Table 3. The main limitations in phytoremediation are the phytotoxic effects exerted by the contaminants towards plants, depth of the rooting system of the plants, time requirement. Remediation potential of plants gets impacted due to the PGPR activity of associated bacteria (endophytes and rhizophytes) where growth rate is more compared to the remediation rate (Nguyen et al.,2019). Pharmaceuticals that are extremely polar or soluble (like caffeine) or somewhat resistant to biodegradation (like clofibric acid) are thought to benefit most from phytoremediation (Zhang et al.,2014).

Particularly in wastewater treatment systems like built wetlands, phytoremediation presents a viable, environmentally friendly substitute for eliminating pharmaceutical pollutants. Slow kinetics, incomplete elimination efficiencies, and possible ecological hazards from transformation products and plant buildup, however, restrict its practical use (Carvalho et al.,2014). Combining phytoremediation with additional methods (such advanced oxidation or bioaugmentation) could improve results and assist to overcome its drawbacks.

Challenges and future perspectives

Even though most of these pharma micropollutants are typically only found in trace amounts, one of the most significant environmental issues confronting humanity is the growing contamination of freshwater resources worldwide with hundreds of micropollutants. Research on the incidence and fate of pharmaceutical residues in aquatic environments has been recognised as necessary in recent years. Since many pharmaceutical residues are not eliminated after traditional wastewater treatment, they may find their way into receiving surface water systems. Some drugs e.g. sulfamethoxazole is the most persistent drugs of all antimicrobial residues. There is need of extensive research for the exploration of the drug sensing methods, followed by their removal with biotic-abiotic coupled methods. Improved understanding of the mechanisms influencing rhizosphere processes, pollutant accessibility, pollutant uptake, translocation, degradation, chelation, and volatilization is required to further increase the efficacy of phytoremediation.

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Table 3: Phytoremediation of drugs

Name of the drug	Concentration	Name of the plant	Conditions	Degradation rate (%)	Reference
Aspirin	8 to 60 ppm	*Brassica juncea*	*Invitro*	90	Gahlawat, and Gauba, 2016
Tetracycline	5 to 10 ppm	*Brassica juncea*	*Invitro*	71	Gahlawat, and Gauba, 2016
Tenofovir	412 ng/ L	*Lemna minor*	*Invitro*	>70	Kitamura et al., 2023
Lamivudine	5428 ng/ L				
Efavirenz	4000 ng/ L				
Metformin	20 ppm	*Helianthus annuus*	Hydroponics	69.53	Moogouei et al., 2018
Clofibric acid	20 µg/L	*Typha*	Hydroponics	80	Dordio et al., 2009
Acetaminophen	-	Indian mustard (Brassica juncea L. Czern.)	Hydroponics	-	Bartha et al., 2010
Acetaminophen	-	Spinach (*Spinacia oleracea*)	Hydroponics	-	Badar et al., 2022
Acetaminophen	0.1 or 0.2 mM	*Lupinus albus*	Hydroponics	100	Kotyza et al., 2010
Amoxicillin	2 ppm	*Lemna minor*	Hydroponics	92	Cerbaro, K. A.,and da Rocha,2022
Ofloxacin	-	*Spirodelapolyrhiza*	-	93.73–98.36	Singh et al., 2019
Oxytetracycline	0.05–1.00 ppm	*Lemna aequinoctialis*	Livestock wastewater.	-	Hu et al.,2021
Erythromycin	1.7 µg/L	*Salvinia molesta* and *Lemna minor*	Wetland	9 to 12	Rocha et al., 2022
		Myriophyllum aquaticum and *Rotala rotundifolia*		31 to 44	
Levofloxacin	1 µg/ L	*Azolla filiculoides and*	Wetland	60	Bianchi et al., 2020
		Lemna minuta		51	

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Conclusions

The pharmaceutical sector contributes significantly to environmental contamination by releasing sewage water into municipal wastewater, which then finds its way into the surrounding ecosystem. The prevention of environmental pollution places a high premium on the management of pharmaceutical micropollutants. The municipal wastewater treatment facilities face challenges of sensing of the drugs, followed by their subsequent removal with physical, chemical, and biological methods. Therefore, a thorough understanding of drug ecotoxicity and its detrimental effects on ecosystems is necessary. Pharmaceutical micropollutants can be effectively detoxified by biotic-abiotic coupled methods. As a result, extensive research in this area is needed to create green sustainable technologies. Abiotic-biotic coupling degradation process in pollutants biotransformation can offer fresh perspectives on the environmental behaviour and fate of pharmaceuticals and personal care products. This can update the traditional notion that pollutants transformation can be carried out by integrated methods of physicochemical and biological based method.

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