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Photodegradation of six selected antipsychiatric drugs; carbamazepine, sertraline, amisulpride, amitriptyline, diazepam, and alprazolam in environment: efficiency, pathway, and mechanism—a review

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Abstract

Psychiatric drugs do not vanish after being carried to wastewater treatment plants by the urine or feces of patients and, a variable portion of their dose and also unused or expired drugs are lost to the environment. This is because the technology of plants is not intended to eradicate pharmaceuticals and their metabolites. Above all, psychotropics can change population dynamics and behavior at lower doses. We believe that antipsychotics have not gotten enough attention when it comes to drug pollution and that their importance as environmental pollutants has been underestimated. An innovative approach to eliminating pharmaceutical pollutants from water is the application of advanced oxidation methods. Among these oxidation methods are photocatalysis, ozonation, UV/hydrogen peroxide oxidation, and photo-Fenton oxidation. Photocatalytic degradation of pharmaceuticals is now the most widely used method since it is affordable and ecologically beneficial due to the reusable nature of the photocatalyst. When light is absorbed during photocatalytic degradation, electrons in the valence band (VB) get excited and migrate into the conduction band (CB). Consequently, hydroxyl radicals (•OH) are produced by VB's holes carrying out oxidation processes on photocatalyst surfaces. The charge difference between the two bands encourages reduction reactions by CB electrons at the surface. To perform successfully, a photocatalyst has to have enough surface-active sites, a favorable band edge location, modest bandgap energy, increased charge separation, and charge transfer. Due to the above-mentioned concerns, the investigation and analysis of the photocatalytic degradation of six psychiatric drugs—carbamazepine, sertraline, amisulpride, amitriptyline, diazepam, and alprazolam—are the main objectives of this review.

Keywords Photocatalitic degradiation, Antipsychiatric drugs, Environmental pollution of antipsychiatric drugs, Carbamazepine, Sertraline, Amisulpride, Amitriptyline, Diazepam, Alprazolam

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1 Introduction

The presence of contaminants in environmental samples is widespread. Persistent organic pollutants (POPs) are one type of pollutant found in wastewater and have long-term negative consequences on ecosystems, human health, and water quality [1, 2]. Many POPs have currently been found in surface water, groundwater, and urban wastewater treatment plants (WWTPs) [3–5]. Antibiotics, analgesics, steroids, antidepressants, antipyretics, perfumes, and cosmetics make up the majority of POPs [1, 6]. The World Health Organization (WHO) has reported that they are the primary causes of the current global health crisis [7]. Additionally, the growth in POPs could cost society and the government [7, 8].

The manufacturing of synthetic chemicals has increased, particularly in emerging nations, as a result of the population's rapid development and the expansion of agricultural and industrial activities. This has seriously contaminated the world's natural streams. Personal care items and medications are some of the synthetic organic compounds. Even at low concentrations of ng L^{-1}, the numerous organic contaminants in surface waters remain in aquatic ecosystems and endanger aquatic animals when exposed for an extended period [9–11].

Pharmaceuticals are necessary for better public health, but their effects on the environment are extremely harmful and require rapid action. Additionally, some medications' metabolites are more hazardous than the original drugs. Unfortunately, these medications are now commonplace in the aquatic environment as a result of their extensive usage and constant discharge. This is due to the ineffective removal of pharmaceuticals from various sources, including home sources, hospital effluents, agricultural, and pharmaceutical sectors, by traditional WWTPs [12]. The majority of industrial facilities discharge their effluents directly into the sewage system without sufficient processing or treatment [13]. This puts a strain on water ecosystems all across the world [14]. Different chemical stability and solubility in water are essential characteristics to measure the extent of contamination in pharmaceutical substances. Even though they are present in very small amounts, they are likely to bioaccumulate and reach the food chain. Some of them are tenacious and gradually build up in water bodies.

Different environmental conditions, such as heat intensity, temperature, humidity, etc., can have a significant impact on a drug's stability [15]. Additionally, there is not much research on how different drugs interact with one another. These organic and inorganic compounds contaminate the water and render it unsafe for drinking and other uses, which could have long-term negative impacts on one's health [16]. Toxic compounds disrupt aquatic life, creating structural changes in fish internal organs (such as kidneys and intestines) that influence fish reproductive and growth patterns [17]. Diverse conventional techniques, including adsorption, filtration, screening, sedimentation, coagulation, and flocculation, are used to reduce the water pollution; however, these techniques are unsuitable for the removal of pharmaceutical chemicals due to the nature of these POPs in water [18, 19]. The biological wastewater treatment methods that are being presented are as follows: (1) biological processes in WWTPs, which comprises anaerobic treatment (anaerobic bioreactors, anaerobic lagoons), aerobic treatment (oxidation ponds, aeration lagoons, aerobic bioreactors, activated sludge, percolating or trickling filters, biological filters, rotating biological contactors, biological removal of nutrients); (2) phytoremediation of wastewater, which comprises constructed wetlands, rhizofiltration, rhizodegradation, phytoaccumulation, phytotransformation, and hyperaccumulators; and (3) mycoremediation of wastewater [20].

Additionally, due to the formation of novel degradation products, straightforward biological treatments such as activated sludge treatment and microbe-mediated biodegradation are not considerably successful at breaking down these prescription medications [21]. If plants and animals consume contaminated water and it enters their metabolic processes, the water will become dangerous to them [22]. A few main causes of water contamination include the agricultural sector, illegal waste disposal, leaks from landfills, and the discharge of sewage and industrial effluents [23]. Long-term increases in the concentration of pollutants are inevitable if sewage is released daily, even though the majority of industrial enterprises have their WWTPs. River water is the primary supply for drinking water treatment plants (DWTPs), hence this phenomenon will provide a significant challenge in the future. The traditional treatment methods including screening, coagulation/flocculation, and chlorination/fluoridation are used by the majority of DWTPs worldwide; only some processes such as ultrafiltration, nanofiltration, and adsorbents (e.g., such as charcoal) to remove impurities [24–26]. Pollutants including large concentrations of organic carbon, nitrogen compounds, and heavy metals cannot be adequately treated by these treatment methods [22]. Typically, combined overflow causes problems in WWTPs.

The concentration and effects of pharmaceutical chemicals, including psychiatric medications, in the aquatic environment have been evaluated throughout the past few decades [27]. Advanced oxidation processes (AOPs) used in pilot-size WWTPs, including ozone or UV radiation, are not thought to be feasible at the industrial scale because of their high running costs and tendency to produce hazardous byproducts. In contrast, the most persistent active pharmaceutical ingredients (APIs) can be eliminated using photocatalytic AOPs by simply

activating a reusable photocatalyst with light. Photocatalysis, is characterized by a straightforward instrumental process, an easy-to-control process, non-selective oxidation, being economical, and causing a complete breakdown of pharmaceutical pollutants [28]. According to the photocatalysts' band energy gap, the breakdown of pollutants by photocatalysts happens by the electron-hole pairs produced by either visible or UV irradiation [29–31].

Regarding the treatment of POPs, various methods are cumbersome to use. Therefore, removing POPs in low quantities is extremely challenging and urgent [32]. It has to do with the production of reactive oxygen species (ROS), which are used as photocatalysts in semiconductors. If energy is larger than or equal to the energy gap of semiconductors, photo-excited holes (h^+) and electrons (e^-) are created under irradiation in the VB and the CB, respectively [33]. When they move to the semiconductor surface, they may produce radicals ($^{\bullet}OH$, $O^{\bullet 2-}$, etc.), which could trigger the redox process [8, 34].

So far, many review articles have studied the environmental pollution of antipsychiatric drugs, but these articles have usually either studied a specific category of these drugs or studied psychiatric drugs in general without referring to a specific class of them. Also, the effect of photocatalytic degradation on this category of drugs has not been specifically investigated. There was a need to investigate the environmental pollution of antipsychiatric drugs in a categorized way and to review the studies that have been conducted on them using photodegradation, as well as to study the effect of photodegradation on the pollution of these drugs. In 2021, Escudero et al. investigated antipsychotic drugs as environmental pollutants [35]. In this study, they have evaluated the environmental risks of antipsychotic drugs. Argaluza et al. have also studied the effects of psychiatric drugs on the environment in another review article [36]. They reviewed the data of previous articles about the occurrence, environmental effects, and toxicity of these drugs on non-target organisms. In a review article, Cunha et al. discussed the environmental risk assessment of 7 psychoactive drugs in the aquatic environment [37]. In another review article, studies related to the occurrence and fate of neuropsychiatric drugs and illegal drugs in sewage treatment plants (STPs) have been reviewed by Asimakopoulos and Kannan [38]. We will concentrate on the possible impact of antipsychotic medications as environmental pollutants in this review. We think that this type of therapy is unjustly undervalued. The goal of this paper is to give a thorough understanding of photocatalytic degradation and photocatalytic applications for the breakdown of contaminants from psychiatric medicines. The utilization of photocatalytic methods in the photodegradation of antipsychiatric drugs will be reported with some examples from literature. In the current study, photodegradation of six different psychiatric medications—carbamazepine (CBZ), sertraline (SER), amisulpride, amitriptyline (AMI), diazepam (DZP), and alprazolam—is the main emphasis.

2 Environmental pollution of drugs

Chemicals that create toxic issues, such as pesticides, heavy metals, polychlorinated biphenyls, aromatic compounds, etc., are well-known. But worries about the so-called "pollutants of emerging interest" are growing, with pharmaceuticals being the biggest source of worry. Two crucial qualities of pharmaceutical items are what motivates this preoccupation: First of all, at low quantities, like those present in the environment, they have pharmacological effects. Second, they are more likely to interact with their target molecules since they are created with stability in mind. Since the end of the 1990s, there has been an exponential increase in scientific journal articles discussing the presence of pharmaceutical products in the environment. This is because advances in analytical techniques have made it possible to identify pharmaceuticals at lower quantities in various matrices [39]. The amount of knowledge currently accessible on drugs' effects on the environment is just overwhelming. According to a recent study [36], over 4000 distinct pharmacologically active compounds, including prescription medicines for people and animals as well as over-the-counter medications, are currently being provided on a global scale. According to estimates, 4.5 trillion doses of drugs will be consumed worldwide in 2020 [36]. The following factors [36] indicate that the trend will probably continue: Populations are getting older and living longer, economies are expanding, especially in emerging economies, which raises the capacity and expectations for treating aging and chronic diseases, livestock and aquaculture practices are getting more intensive to meet demand, new pharmaceutical products are being developed, and climate change will worsen already-existing diseases (both communicable and non-communicable) [36].

Studies of pharmaceutical residues in the environment have been possible thanks to the rapid development of mass spectrometric analytical technologies during the past 25 years. Early reports [40–43] of APIs in the environment coming from factory discharges were sporadic and garnered little attention at the time.

When estrogens were identified in sewage effluents as the cause of fish feminization in the late 1990s, interest in pharmaceuticals in the environment, particularly the role of excreted medications, skyrocketed. Following that, ecotoxicologists focused mostly on sewage effluents and receiving rivers, which may have diverted attention from

potential alternate sources of pharmaceutical residues [44].

The pharmaceutical industry also stated that it is unlikely that considerable amounts of APIs will leak out during manufacture using a variety of justifications, including the fact that pharmaceuticals have such a high value that their release would be prevented for simply financial considerations [45]. This presumption was eventually shown to be false. We learned that exposure routes are not always predictable from the identification of diclofenac residues in cow corpses as the reason for the vulture population collapse in India and Pakistan [46].

The first of several articles demonstrating extremely high pharmaceutical emissions from medication manufacturers in Patancheru, close to Hyderabad, India, was published in 2007 [47–49]. This region, which has a huge concentration of industries in a small space, is a key hub for the global manufacture of bulk pharmaceuticals. For certain medications, the quantities in the effluent from a treatment facility that received wastewater from around 90 production units were higher than those discovered in the blood of patients taking medication. The development of resistance is worrisome due to the elevated concentrations of multiple broad-spectrum antibiotics. The most common medication, ciprofloxacin, has concentrations up to 31,000 μg L^{-1}, which are more than 1000 times more than what some bacteria can withstand [47]. The anticipated total discharge of ciprofloxacin was 44 kg d^{-1}, which is equal to Sweden's intake over five days or, put another way, enough to treat every person in a city of 44, 000 people. These discharges have caused previously unheard-of levels of contamination in river sediment [48], surface, ground, and drinking water [49], and a recent report also showed contamination of irrigated soils [50]. The research received a lot of media attention, which boosted interest in this exposure route among scientists and the public [44, 51].

3 Environmental pollution of antipsychiatric drugs

About 700 different drug residues have been found in several environmental compartments, including wastewater, surface and groundwater, soil, air, biota, and even the tap water [45]. There are comprehensive books that examine the use of psychiatric medications in the environment [52]. Due to its ubiquitous nature, CBZ has even been proposed as a marker for wastewater-influenced aquatic bodies [53].

Additionally, parent drugs (or metabolites) continue to change and go through intricate metabolic processes once they are in the environment due to various organisms and physicochemical mechanisms (e.g., photodegradation, adsorption to solids, etc.). This results in "transformation compounds." Trawinski and Skibinski [54], for instance, studied the photodegradation of psychiatric medications. Some compounds are particularly persistent because they can linger unaltered in the environment for decades. In this instance, oxazepam, which has been present unaltered in the bottom of Swedish lakes for more than 30 years [55], is a typical case.

3.1 Antipsychiatric drugs pollution's effects on human health and ecotoxicology

The impact of drug contamination on human health has not been extensively researched. Drug concentrations in tap water should not be harmful, according to a WHO assessment in 2012 [36]. A subsequent study conducted in China [56] verified these results. However, the most susceptible patient populations, such as allergic [36] patients, may experience issues due to the presence of medications in the environment. Even while there is no proof that short-term consequences on human health exist, there are still some unknowns, especially regarding long-term exposure (chronic exposure) to a combination of pollutants [36]. The main exposure pathways are drinking water, and eating fruits, vegetables, meat, fish, shellfish, and dairy products [36]. The rise in bacteria resistant to antibiotics, which is currently acknowledged as the major public health issue in the world, is likely the best-known illustration of the harmful impact of drug pollution on human health. In this regard, we believe that the "One Health" approach or concept, which holds that human health and environmental health are inextricably linked, is crucial [57]. However, we think it is important to apply this strategy to other treatment classes, not just antibiotics, such as psychiatric medications [58, 59]. Since psychoactive drugs can bypass maternal barriers that affect the development of the embryonic brain, some authors have hypothesized that they may be linked to human neuropsychiatric disorders like autism, Alzheimer's disease, and schizophrenia [60].

Drugs can have toxic effects on the environment that go much beyond those on growth, death, or reproduction. For instance, psychoactive substances can change population dynamics by influencing the behavior and fitness of organisms [61–64]. The physiological systems that medications affect as well as their therapeutic goals are not unique to humans. Numerous living creatures share many of these phylogenetically highly conserved features and signaling pathways [65]. For instance, numerous behavioral test for investigational medications intended for human use are carried out on fish, including tests for anxiety, fear, and stress [66]. Fish and humans have many the same neurotransmitter and signaling pathways. In reality, both vertebrates and invertebrates, such as amphibians, fish, insects, and echinoderms, contain biogenic monoamines (such as serotonin, dopamine, norepinephrine, etc.) [67, 68]. From an evolutionary perspective, some compounds are so old that they can be

found in animals that do not belong to the animal world. Acetylcholine, for instance, can be found in bacteria and fungi [69] and serotonin in plants [70]. Crickets' behavior has been demonstrated to vary in response to fluoxetine [71]. The antipsychotic clozapine also causes constipation in fish [72], plants collect benzodiazepines that may influence their GABAergic system [73], and SER alters the nitrification processes by changing the microbial trophic chain [36, 74].

3.2 Antipsychiatric drug toxicity for creatures that are not the intended targets

Like other pharmacological categories, psychiatric drugs can be found in the environment. It is important to keep in mind that these substances do not occur isolated but rather as complex combinations, even though these concentrations are below the range projected to harm humans and cause acute or even chronic toxicity to non-target animals [75]. Psychiatric medications are one of the most relevant groups when it comes to the evaluation of ecotoxicological effects in terrestrial and aquatic non-target organisms because of their intrinsic biological activity, which could disrupt nervous and endocrine systems [76]. Additionally, the increasing number of research on chronic toxicity in aquatic creatures that are not the intended targets highlighted the need for a unique strategy to be developed to more clearly address this issue [77]. Considering how frequently medications are exposed to aquatic creatures, it would be more crucial to comprehend life cycle toxicity than to carry out acute toxicity experiments [78–80].

4 Photodegradation of drugs

Pharmaceuticals are compounds or combinations of substances used to cure or prevent diseases in humans. They do, however, represent a significant group of point or diffuse pollution-related micropollutants. Conventional wastewater treatment methods have only been shown to partially remove pharmaceutical contaminants, and as a result, municipal and/or hospital WWTPs have become important sources of their release into the environment. Pharmaceutical substances are present in aquatic media in quantities between ng L^{-1} and μg L^{-1}. Pharmaceuticals have been demonstrated to have harmful impacts on both human health and ecology (loss of biodiversity, extinction of aquatic creatures, etc.) even at low concentrations [81–85]. Innovative technologies, such as AOPs, have been developed for the effective removal and degradation of pharmaceutical compounds from wastewater and the prevention of their release to ground and surface waters. AOPs have been proposed as a tertiary treatment in WWTP effluent. AOPs are thought to be promising techniques for the treatment of contaminated wastewater including non-biodegradable organic contaminants since they comprise various mechanisms of producing ROS, primarily •OH. Complete elimination of numerous pharmaceutical contaminants is possible using heterogeneous photocatalysis, which is based on the effective generation of ROS in aqueous media [86–89].

Novel approaches to treating pharmaceutically rich sewage influent have been developed to increase removal efficiency. AOPs [90], UV irradiation alone [91, 92], UV irradiation and hydrogen peroxide combined to produce •OH as an efficient oxidizing agent [93–96], and combining hydrogen peroxide with Fe^{2+} ions (photo-Fenton) to increase the efficiency of •OH radical generation [97–101] are some examples of these treatment methods. More recently, •OH radicals have been produced using heterogeneous photocatalysts like suspended titanium dioxide (TiO_2) [102]. TiO_2's physicochemical characteristics as a semiconductor determine how effective it is as a photocatalyst [103, 104].

4.1 Drug photodegradation by photocatalysts

Another new method that can be used to remove pharmaceutical contaminants from water is the use of sophisticated oxidation techniques for drug breakdown. Photocatalysis, ozonation, UV/hydrogen peroxide oxidation, and photo-Fenton oxidation are some of these oxidation mechanisms. Non-thermal plasma and sonolysis are two further cutting-edge methods for drug breakdown. The first method takes advantage of oxidizing agents produced by non-thermal plasma, including H_2O_2, •OH, and ozone [105–108]. The oxidizing agents in sonolysis are created by ultrasonic radiation. Due to the reuse of the photocatalyst, which makes it economical and environmentally friendly, photocatalytic degradation of medicines is currently the most common approach [109]. Nano-based photocatalysts are easy to make and can effectively break down pollutants. ZnO, TiO_2, and CeO_2 nanoparticles (NPs) are among the most popular and efficient nanophotocatalysts used in this context [110]. In photocatalytic degradation, light is absorbed, which causes electrons in the VB to be excited and move into the CB. As a result, VB develops holes that carry out oxidation processes on photocatalyst surfaces, generating •OH. CB electrons are responsible for carrying out reduction processes at the surface by the charge separation between the two bands. A photocatalyst must have adequate surface-active sites, a good band edge position, a small bandgap energy, a low rate of charge recombination, enhanced charge separation, and charge transfer to function well. Additionally, at the nanoscale level, NPs' optical and electrical properties are impacted by a high surface-to-volume ratio and high atom concentration at the surface. As a result, when a particle gets smaller and smaller, the surface atoms become less strongly bonded to the bulk atoms and more chemically active. This

enables them to participate in chemical reactions and act as catalysts because of the high surface energy that results from this. A quantum size effect results from these modifications, which are related to the material's electrical structure. Their optical characteristics are likewise impacted by this [111]. Bandgap is a crucial characteristic that represents the conductance and photoactivity of the nanomaterial. With a bandgap energy of 3.4 eV, TiO_2 NPs are the most studied photocatalysts, whereas ZnO NPs, which have a smaller bandgap of 3.2 eV, exhibit photocorrosion and a high rate of photoexcitation recombination. The bandgap energy of CeO_2 NPs is 3.1 eV. Therefore, the bandgap must be reduced to absorb visible light. By mixing NPs with noble metals and doping, this problem can be resolved. To increase photoactivity, TiO_2/ZnO and CuO/ZnO nanocomposites both possess synergistic qualities [26, 112].

A wide range of photocatalysts have been created over the past ten years. Among them, graphitic carbon nitride (g-C_3N_4) combines several benefits that make it suitable for a variety of photocatalytic applications [113, 114]. These include a mild band gap (2.7 eV), a good response to visible light (up to 460 nm), a simple preparation method, high chemical stability and non-toxicity, and low cost. However, there are not many published research studies that deal with hospital wastewater. In genuine wastewater effluent spiked with g-C_3N_4 and taken from a full-scale WWTP in Brisbane, Queensland, Australia, Zhong et al. [115] examined the photocatalytic degradation of CBZ under simulated solar irradiation. They found that 100% destruction of CBZ had occurred after 15 min. Furthermore, Kane et al. [116] investigated the photodegradation of CBZ using g-C_3N_4 when it was exposed to UV light. Using a composite g-C_3N_4-based photocatalytic material called Ag/TiO_2/M-g-C_3N_4, Gao et al. [117] investigated the removal efficiency of amoxicillin in real hospital wastewater and in a WWTP. In the two sample types, a clearance of amoxicillin of 71 and 49%, respectively, was seen after 60 min of the photocatalytic process [89].

4.2 Psychiatric drugs' photodegradation

After being transported to WWTPs by patients' urine or feces, psychoactive drugs do not disappear. However, a variable portion of the dose is lost to the environment, where pharmaceuticals and their metabolites have been found in virtually every matrix, including hospital effluent, municipal wastewater, rivers, lakes, and even drinking water. This is because the technology of these plants is not intended to eradicate pharmaceuticals and their metabolites. We believe that the environmental quantities that have been recorded may be high enough to noticeably affect aquatic species. Antipsychotics and other medications may also be bioaccumulating through web food. Most importantly, psychotropics have the potential to alter behavior and, at lower concentrations, population dynamics. In terms of drug pollution, antipsychotics, in our opinion, have not yet received adequate attention, and their relevance as environmental pollutants has been undervalued [35].

Due to this, the investigation and analysis of the photocatalytic degradation of six different psychiatric drugs—CBZ, SER, amisulpride, AMI, DZP, and alprazolam—are the main objectives of this review.

5 CBZ

Psychiatric medication CBZ (Table S1 in the Supplementary materials file), which was first sold in 1963, has amassed a sizable market share to date. According to estimates, there were around 1.01 kt consumed annually worldwide and 34.9 t in the US in 2008 [118]. Due to its high consumption and stable chemical composition, CBZ is continuously released into the environment and persists there. CBZ cannot, however, be efficiently removed (10%) by conventional WWTPs [119], since it is a persistent pharmaceutically active compounds (PhACs). However, some investigations even found a higher concentration of CBZ in effluent than in influent [120, 121]. As a result, research has shown that CBZ is one of the most commonly found PhACs in WWTPs and surface water around the world [122–127].

5.1 Photocatalytic degradation of CBZ

Due to their high persistence during wastewater treatment operations, the presence of pharmaceutical and personal care products (PPCPs) in the environment is a growing source of concern [128–130].

One of the most often found pharmaceuticals among the numerous PPCPs is CBZ, which is used in human medicine to treat seizures. A daily dosage of 100–2000 mg of CBZ is given chronically to patients, leading to significant global production [131]. The removal efficiency of CBZ in typical WWTPs is extremely low because of its biorefractory nature. Approximately 50% of the CBZ and its metabolites discharged in urine and feces are directly released to the municipal WWTPs [132]. Numerous investigations have reported the presence of CBZ in ambient samples at quite high amounts [128, 133, 134].

AOPs were designed to further dispose of wastewater containing CBZ to cover the insufficient treatment from WWTPs to remove CBZ residues and reduce its harmful effects on ecological systems and human bodies. AOPs have been shown to have stronger degrading effects and efficiency when compared to traditional biological processes, according to methods like Fenton oxidation [135], UV irradiation combined with chemical oxidizers or catalysts [136], or ultrasonic irradiation [137]. AOPs

have shown to be effective treatments and disposal methods for PhACs like CBZ. Although AOPs offer a variety of benefits, some current shortages should not be overlooked either. For instance, technologies that express a well-disposal impact always call for the employment of harsh chemical additives or high energy input, which can result in high operational costs as well as secondary pollution production [138]. Therefore, it is imperative to find methods for dealing with refractory PhACs that are both ecologically benign and energy-sustainable [139]. The treatment approach, CBZ efficiency, occurrence in the environmental samples, and concentration are presented in Table 1 [140–142].

5.1.1 Photocatalytic degradation of CBZ using heterostructures GQD/$BiVO_4$

Solar-driven Graphene quantum dots (GQDs) loaded with $BiVO_4$ heterostructure catalysts were created and used by Wu and colleagues to degrade CBZ under artificial sunlight. GQDs, which are sensitive to visible light, were made and loaded onto $BiVO_4$ heterostructures in this study. The catalytic degradation of the drug CBZ was then carried out using the novel ternary heterojunction catalysts (GQD/m-$BiVO_4$/t-$BiVO_4$) (Fig. 1). Under simulated sun irradiation, the catalyst had outstanding performance and catalytic processes for CBZ [139].

5.1.2 Photocatalytic degradation of CBZ using BiOCl-10

In a different study, Gao et al. [143] directly manufactured visible-light-driven BiOCl microspheres using a simple one-pot ethylene glycol-mediated solvothermal process. The degradation of CBZ under visible light irradiation (>420 nm) allows for the examination of the photocatalytic activity of the obtained photocatalysts. Additionally, an active species trapping experiment was used to systematically explore the photocatalytic process. Finally, the use of BiOCl-10 in real wastewater was investigated. The objective of this study was to improve BiOCl's responsiveness to visible light so that CBZ could be degraded effectively (Fig. 2). Analysis was also done on the relationship between catalyst activity and characterization. Most notably, BiOCl-10 proved effective without any additives in natural water. This research expands the potential uses of visible-light-driven photocatalysts in the eradication of resistant pharmaceutical contaminants [143].

5.1.3 Photocatalytic degradation of CBZ using magnetic BiOCl/Fe_3O_4

Chen et al. [144] successfully created a magnetic BiOCl/Fe_3O_4 catalyst through precipitation with a simulated solar light response. The effectiveness of photodegrading CBZ was used to further study the photocatalytic activity of BiOCl/Fe_3O_4 nanocomposites. In this investigation, after 60 min of irradiation with the BiOCl/Fe_3O_4 catalyst, 90.3% of the CBZ was eliminated. Furthermore, by using an external magnetic field, the BiOCl/Fe_3O_4 photocatalyst could be easily removed from the solution. This kind of magnetic photocatalyst, which is distinguished by ease of separation, might find use in the treatment of wastewater. Liquid chromatography-mass spectroscopy was used to establish how quickly CBZ vanished and how its intermediates formed, and it also suggested potential photocatalytic breakdown pathways. In comparison to prior CBZ degradation investigations, it was noteworthy that some of the intermediates were reported for the first time (Fig. 3). By using an external magnetic field, the BiOCl/Fe_3O_4 catalyst may be easily recycled from the reaction system. It showed that BiOCl/Fe_3O_4 might be a promising catalyst for use in actual applications to degrade organic pollutants [144].

5.1.4 Photocatalytic degradation of CBZ using TiO_2

CBZ was photodegraded in 2015 by Carabin et al. [119] using suspended photocatalysts made of TiO_2. This study looked at how the photocatalytic activity at 365 nm could reduce the CBZ in a water solution. Using P90 photocatalyst concentration of 1.5 g L^{-1} for 90 min of treatment with HOF-5 and light intensity of 18.9 W m^{-2}, 4% less than the standard condition to be obtained, the best operating parameters for CBZ degradation in solution (99% CBZ elimination) were reached. Low concentrations of CBZ (37 g L^{-1}) or relatively high concentrations of CBZ (5 to 20 mg L^{-1}) in water can both be treated using this improved photocatalytic method with the reaction rate of 3.2 µg L^{-1} min^{-1} at 20 °C [119].

5.1.5 Photocatalytic degradation of CBZ using $BiPO_4$

Xu et al. [134] investigated how specifically formulated $BiPO_4$ catalyzed the breakdown of CBZ. Hydrothermal synthesis was used to create $BiPO_4$. The obtained samples' physicochemical characteristics were examined, and the findings showed that the hydrothermal

Table 1 The treatment, CBZ's uses, occurrence in the environmental samples, and concentration

Treatment	Drug for	Occurrence	Concentration	Reference
Anti-inflammatory, anti-manic, anti-depressive	Treatment of epilepsy, trigeminal neuralgia, and acute manic and mixed episodes in bipolar I disorder	Sewage water treatment effluents; Germany	2.1 µg L^{-1}	[140]
		River water; Germany	0.25 µg L^{-1}	[140]
		Groundwater Arizona and California	~610 ng L^{-1}	[141]
		Drinking water; United States	~18 ng L^{-1}	[142]

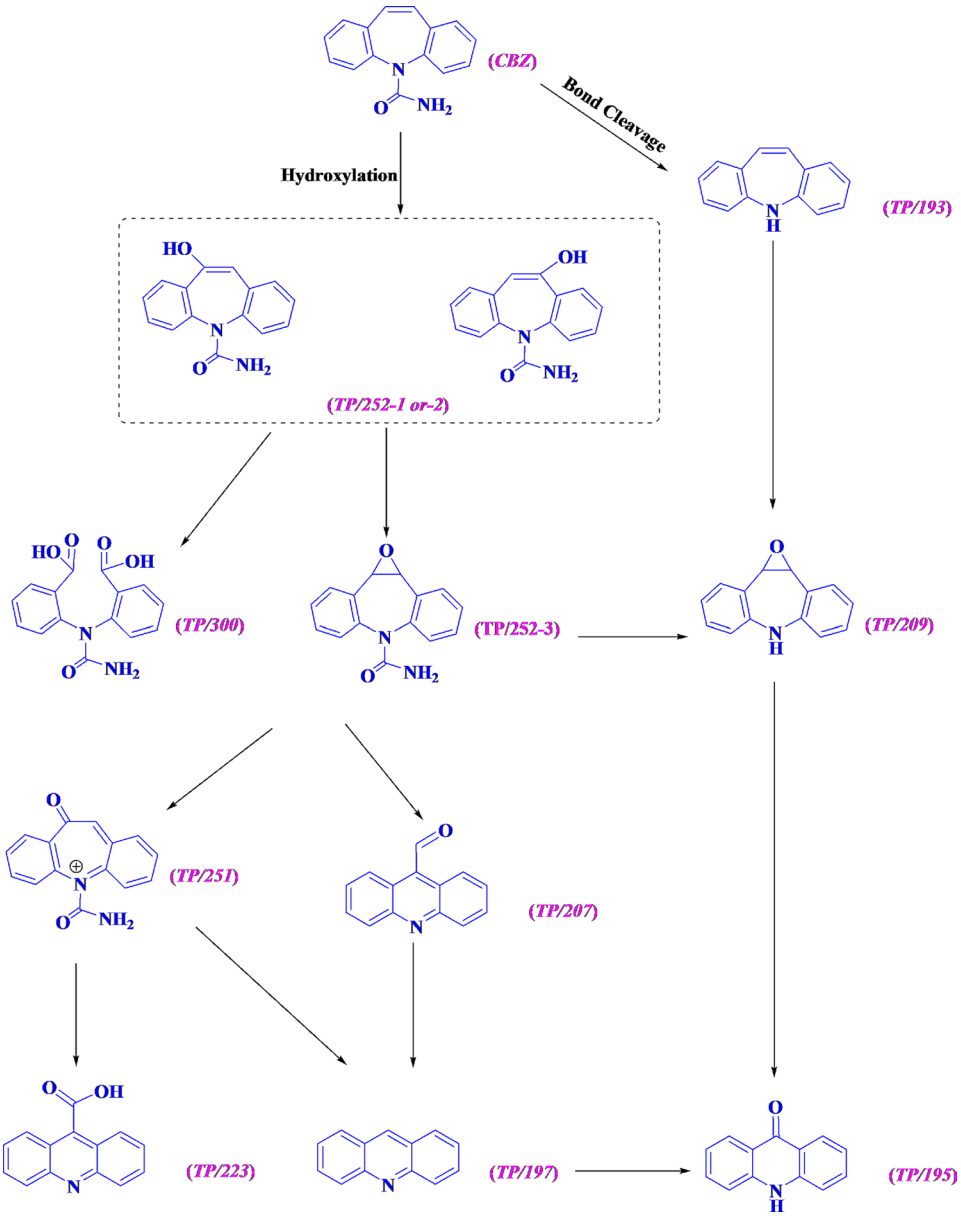

Fig. 1 Diagrammatic representation of suggested CBZ degradation routes using GQD/$BiVO_4$ hybrids to replicate solar-induced photocatalysis [139]; TP: transformation products

temperature and reaction time had an impact on the phase, morphology, and optical characteristics of the $BiPO_4$ catalysts, which may further dictate their unique photocatalytic performances. The catalysts' crystal properties were somewhat reflected in the intrinsic microstructure and optical characteristics. The $BiPO_4$ made at 180 °C for 72 h (BPO-180-72) demonstrated the best photocatalytic activity when exposed to UV light; CBZ was almost entirely removed from ultrapure water after 60 min of exposure. The monoclinic phase and reasonably organized shape of the resultant $BiPO_4$ were said to have a synergistic effect that led to positive photocatalytic activity. For $BiPO_4$, it was initially demonstrated that the monoclinic phase was more active than the hexagonal phase. After 60 min of exposure, BPO-180-72 eliminated roughly 72.4% of CBZ from laboratory-prepared simulated wastewater, indicating a possible use for this substance in wastewater treatment (Fig. 4). The system's photodegradation of CBZ was shown to be mostly mediated by photogenerated holes and •OH [134].

6 SER

In the past ten years, numerous reports of SER (Table S2 in the Supplementary materials file), an antidepressant of the selective serotonin reuptake inhibitors (SSRIs) family, in environmental matrices have been made [145].

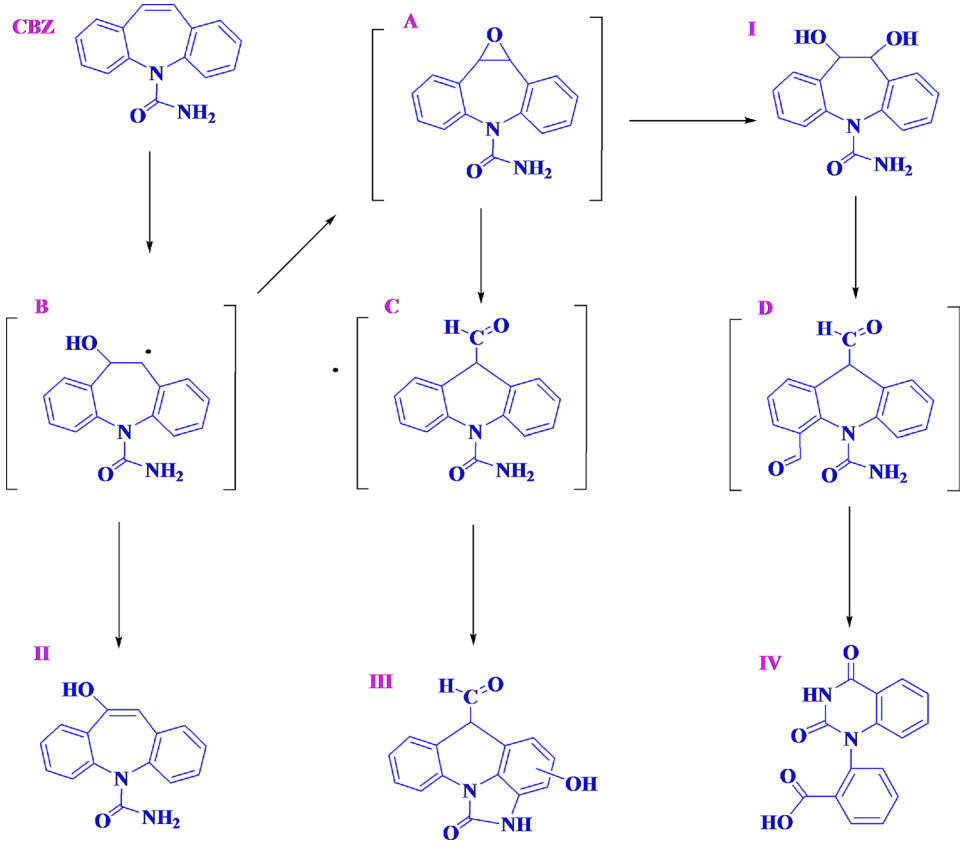

Fig. 2 Potential CBZ degradation products and the BiOCl-10 pathway [143]

One of the pharmaceuticals, SER hydrochloride, is primarily used to treat adult outpatient clinical depression as well as adult and pediatric obsessive-compulsive, panic, and social anxiety disorders [31, 146].

6.1 Photocatalytic degradation of SER

One of the primary contaminants in the aquatic environment is antidepressants. Due to their widespread usage, potential health impacts, and partial removal from WWTPs using traditional techniques, they are the subject of extensive research. As a result, SER is now among the medications that are most frequently found in surface water and WWTP effluents [147]. Traditional treatment processes are ineffective for removing contaminants from wastewater, thus it is important to look for more efficient treatment options [31].

While this SER molecule's occurrence and toxicology have received the majority of research attention, little is known about how this chemical changes in response to environmental conditions like solar irradiation [31]. The treatment approach, SER efficiency, occurrence in the environmental samples, and concentration are presented in Table 2 [148–150].

6.1.1 Photocatalytic degradation of SER using photolysis in an aqueous environment

Gornik et al. [145] looked into the photodegradation of SER in an aqueous environment. By analyzing SER photodegradation in laboratory-size trials supported by additional tests on actual surface water, the current work attempted to close these gaps. It has been determined that direct photolysis dominates the first-order kinetics of SER degradation, however, the presence of some reactive species, such as $^{\bullet}OH$, $CO_3^{\bullet}$, and $^3CDOM^*$, may speed up the process. The anticipated SER half-life of 1.4 d was used to validate the projected results in surface water that had been injected with the drug and exposed to real sunshine. Overall, their research sheds light on how SER is transformed in surface waters and shows that photodegradation is a crucial—and likely the primary—transformation pathway for this pollutant [145].

6.1.2 Photocatalytic degradation of SER using xenon lamp irradiation

In the other study [151], the photodegradation of two of the most commonly used psychiatric medications, DZP and SER, were caused by exposure to xenon lamp radiation, which overlaps the spectrum of sunlight, and to natural. In this study, the photodegradation of

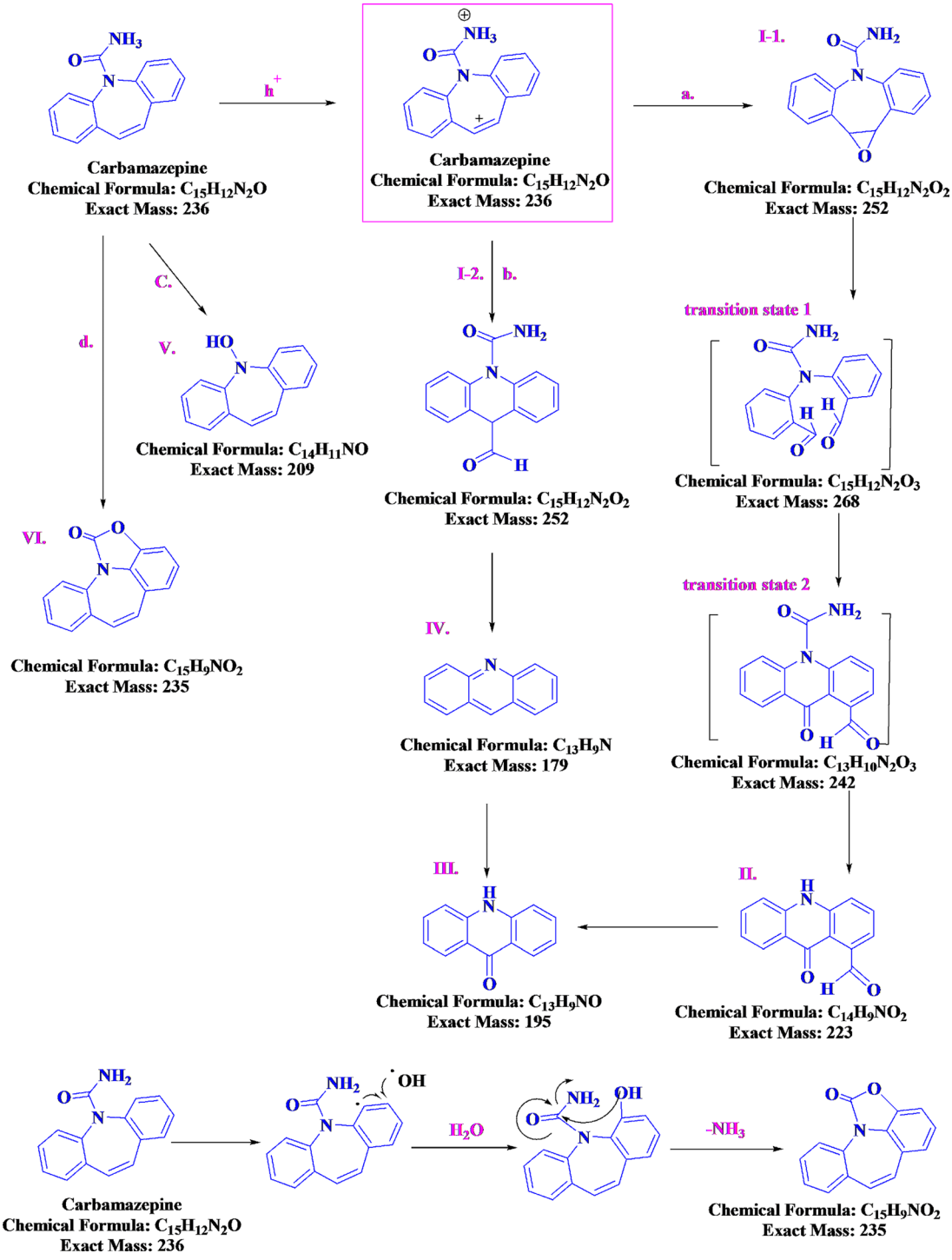

Fig. 3 Fe_3O_4/BiOCl-mediated degradation mechanisms of CBZ under simulated solar light radiation [144]

the psychiatric medications DZP, and SER was examined using the hyphenated UHPLC-QTOF-MS method, which produced extremely precise and reliable results. To model a process that might occur in the environment, the kinetics of deterioration were examined under two different forms of lighting: (1) xenon lamp light, and (2) natural sunlight (Fig. 5). In all cases, the degradation kinetics were pseudo-first order; however, in the second experiment, autocatalytic processes were seen for a variety of natural water samples. In total, nine photoproducts of DZP and seven altered SER compounds were identified, and their presence in various water samples was examined. However, none of the compounds were found, most likely as a result of the medicines' adsorption on

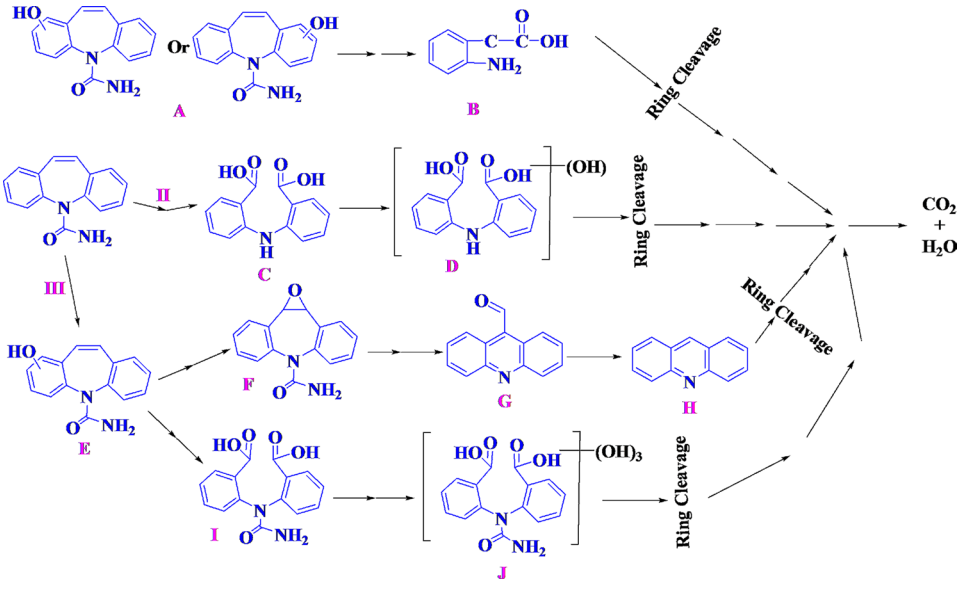

Fig. 4 Suggested mechanism for BPO-180-72 to break down CBZ when exposed to UV rays. The starting dose of the catalyst was 1 g L^{-1}, and the concentration of CBZ was 5 mg L^{-1} [134]

Table 2 The treatment, SER's uses, occurrence in the environmental samples, and concentration

Treatment	Drug for	Occurrence	Concentration	Reference
Anti-depressant	Treatment of depression, panic disorders, social phobia, obesity and obsessive-compulsive disorders, post-traumatic stress disorder	Tehran South Municipal Wastewater; Iran	~11 ng L^{-1}	[148]
		Sjølund pump station; Norway	16.3 ng L^{-1}	[149]
		Langnes STP influent; Norway	1.8 ng L^{-1}	[149]
		Langnes STP effluent; Norway	1.6 ng L^{-1}	[149]
		Breivika STP influent; Norway	2.5 ng L^{-1}	[149]
		Breivika STP effluent; Norway	2 ng L^{-1}	[149]
		Hamna STP influent; Norway	2 ng L^{-1}	[149]
		Hamna STP effluent; Norway	0.9 ng L^{-1}	[149]
		Nursing facility wastewater; Texas	129 ng L^{-1}	[150]

sediment, sewage sludge, or other environmental elements [151].

6.1.3 Photocatalytic degradation of SER using P25/Chitosan composites

In addition, Degussa P25/Chitosan composites for the photocatalytic removal of SER and Acid Red 18 from water were investigated in 2021. In this study, P25/chitosan composites were created utilizing three different preparation techniques and two different chitosan sources. On the chitosan matrix, titanium dioxide was equally distributed without creating any unnecessary agglomerates. The photocatalytic activity was shown to be unaffected by the preparation method, although the rate of SER breakdown increased after 240 min when medium molecular weight chitosan was used instead of high molecular weight chitosan. Due to the shielding effect occurring above a specific level of photocatalysts, the amount of applied photocatalysts has a significant impact on how successful the photocatalytic reaction is. SER and Acid Red 18 both required optimal concentrations of 0.3 and 0.6 g L^{-1}, respectively. Additionally, it has been demonstrated that under identical reaction circumstances, the photocatalytic degradation of SER operates more effectively than the decomposition of Acid Red 18. These chemicals decompose significantly more quickly through photocatalytic breakdown than through photolysis. In comparison to pure Degussa P25, the presence of chitosan in the photocatalytic materials greatly improves the separation of the catalyst from the reaction mixture. These nanocomposites can be used to successfully remove organic contaminants from water by photocatalytic degradation [152].

6.1.4 Photocatalytic degradation of SER using ZnO-NPs

The photocatalytic degradation of SER in aqueous solutions by zinc oxide (ZnO-NPs). The photocatalytic degradation of SER hydrochloride in water was examined in the work employing nanoscale ZnO-NPs [31]. Using the sol-gel process, the ZnO-NPs were created using zinc gluconate as a precursor. H_2O_2/UV, ZnO-NPs/H_2O_2/UV, and ZnO-NPs/UV were three different procedures

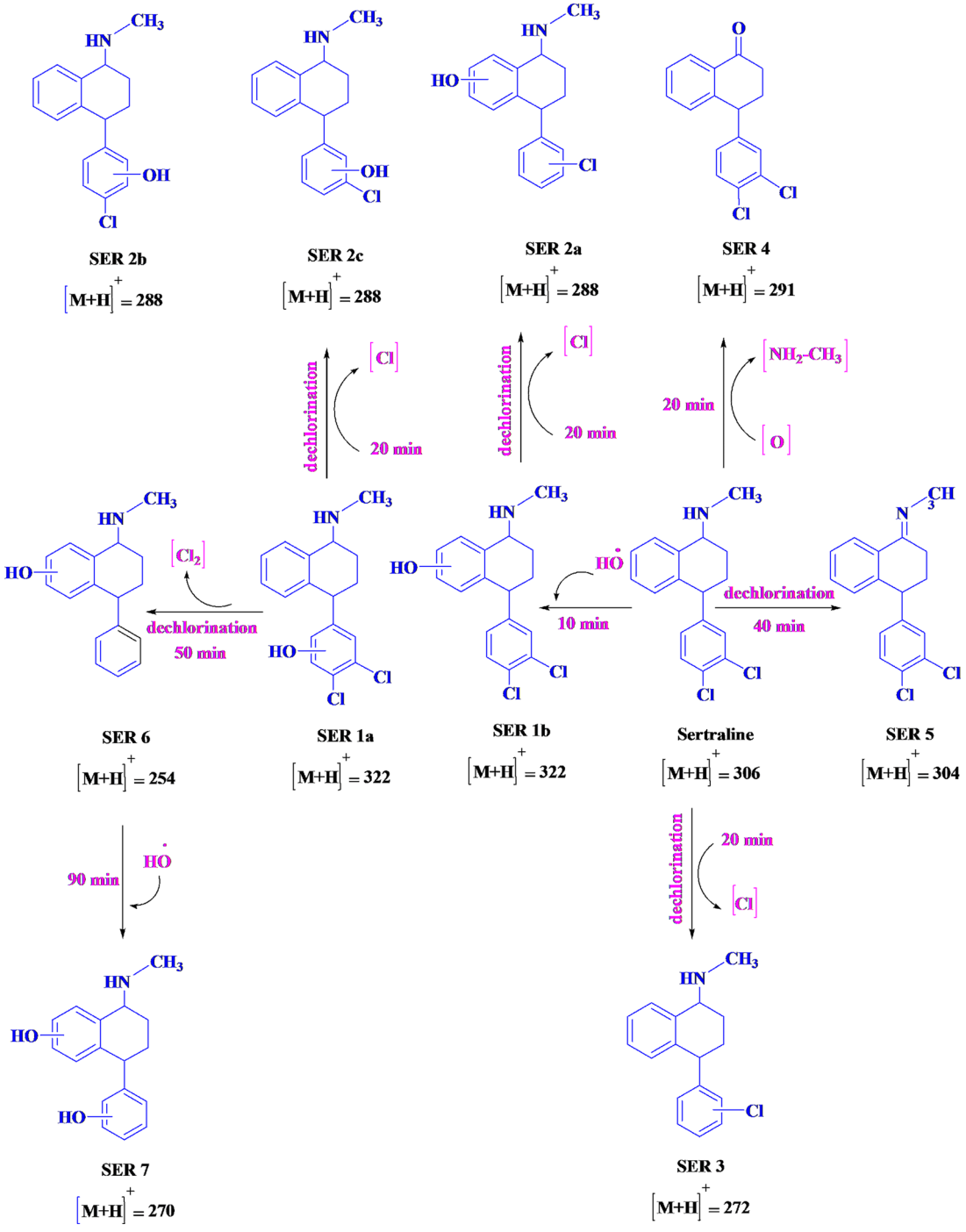

Fig. 5 SER's suggested photodegradation pathway [151]

that were investigated for the elimination of SER hydrochloride in water. The outcomes show that for the effective degradation of the medication, ZnO-NP as a catalyst and UV irradiation were both required. With the ZnO-NPs/UV method, nearly 100% of SER hydrochloride was removed (98.7%) in 30 min at room temperature. SER hydrochloride photodegrades according to first-order kinetics at a rate of 0.068 min^{-1}. The highest drug clearance was attained at pH 11, indicating that SER hydrochloride degradation with ZnO-NPs/UV is pH-dependent. Important factors in the elimination of SER hydrochloride included the initial drug concentration, catalyst dosage, and hydrogen peroxide concentration. The results show that ZnO-NP has an enhanced photocatalytic activity toward the photodegradation of SER

hydrochloride due to its high specific surface area and porous structure.

7 Amisulpride

Amisulpride is an atypical antipsychotic medication whose pharmacological effect is based on the selective binding to D2 and D3 dopaminergic receptors (Table S3 in the Supplementary materials file). Compared to traditional antipsychotic medications, this medication has a lower risk of extrapyramidal side effects and generally greater tolerability.

Nowadays, amisulpride is mostly used to treat various forms of schizophrenia [153], while it can also be used to treat depression in low doses [154, 155]. According to the most recent studies, amisulpride can also be used to treat chronic fatigue syndrome [156, 157].

7.1 Photocatalytic degradation of amisulpride

The use of psychiatric medications, a class of pharmaceuticals that are often prescribed and used to treat a variety of mental health issues, is rising globally. Numerous investigations have so far been conducted to look into the existence of psychiatric substances in the environment. Amisulpride is a standard antipsychotic medication [158], and new monitoring investigations have drawn attention to its presence in the environment. For instance, amisulpride has been found in hospital WWTP effluent in Ioannina (northwestern Greece) at concentrations ranging from 102 to 929 ng L^{-1} [159]. amisulpride was found in concentrations between 0.2 and 5.5 ng L^{-1} in the seawater of the Eastern Mediterranean Sea [160]. Additionally, amisulpride was found in the effluent of the Athens WWTP at a concentration of 0.07 ng L^{-1} [161]. Amesulpride was measured at 16.8 ng L^{-1} during the first wave of COVID-19 in wastewater samples from the WWTPs in Milan and Monza (Italy) [162]. A persistent pollutant known as amisulpride has also been found to be able to enter the aquatic environment and get into groundwater. Furthermore, the requirement for enhanced treatment has been demonstrated by the verification of the production of its distinctive non-biodegradable N-oxide product during its standard treatment [163, 164]. New methods must be used for removing various contaminants, including pharmaceuticals, from conventional WWTPs [85, 165]. As a tertiary wastewater treatment method, AOPs have been suggested [166, 167]. Heterogeneous photocatalysis is one of the AOPs that holds promise for the elimination of organic chemicals [164, 168].

Today, the development and registration of pharmaceutical products must take into account photostability testing because it is a crucial component of the stability study of medications [169]. Drug photodegradation is a significant area of research since it can cause the drug to lose its effectiveness and have negative side effects because it produces hazardous degradation products. The manufacturing, storage, and administration of pharmaceuticals can benefit greatly by knowing exactly what is created from the drug during this process, which may also greatly increase the safety of therapy [157, 170, 171]. The treatment approach, amisulpride's efficiency, occurrence in the environmental samples, and concentration are presented in Table 3 [159–161, 163].

7.1.1 Photocatalytic degradation of amisulpride using g-C_3N_4

In 2023, Antonopoulou et al. [168] did research on the photocatalytic degradation of amisulpride using g-C_3N_4 as a catalyst while exposed to UV-A rays. The ability of the photocatalytic method to extract amisulpride from both ultrapure and actual municipal wastewater was assessed. Both aqueous matrices have high removal efficiencies. However, a slower rate of degradation was seen when wastewater was used as the matrix, which could be explained by its intricate chemical makeup. Liquid chromatography-mass spectrometry (LC-MS) was used to pinpoint the transformation products (TPs) in both ultrapure and actual municipal wastewater. The photocatalytic degradation routes of amisulpride, which mostly involve oxidation, dealkylation, and cleavage of the methoxy group, are hypothesized based on the detected TPs. Additionally, the importance of h^+ and $O_2^{\bullet-}$ in the reaction mechanism was demonstrated while studying the contribution of reactive species to the degradation mechanism utilizing well-researched scavengers (Fig. 6). Additionally, *Dunaliella tertiolecta* and *Chlorococcum* sp. microalgae were used to determine the progression of ecotoxicity. When ultrapure water was employed as the matrix, little toxicity was seen throughout the entire process without the development of hazardous TPs. In the

Table 3 The treatment, amisulpride's uses, occurrence in the environmental samples, and concentration

Treatment	Drug for	Occurrence	Concentration	Reference
Antiemetic, antipsychotic	Treatment for acute and chronic schizophrenic disorders, as well as secondary negative symptoms in mental health disorders such as affective disorders, depressive mood, and mental retardation	Effluent of WWTP; Athens	0.07 ng L^{-1}	[161]
		Wide area of Saronikos gulf; Greece	< 0.2–5.5 ng L^{-1}	[160]
		Hospital WWTP effluent of Ioannina; northwestern Greece	102 to 929 ng L^{-1}	[159]
		Groundwate; Germany	0.07 µg L^{-1}	[163]
		Seawater; Eastern Mediterranean Sea	< 0.2–5.5 ng L^{-1}	[160]

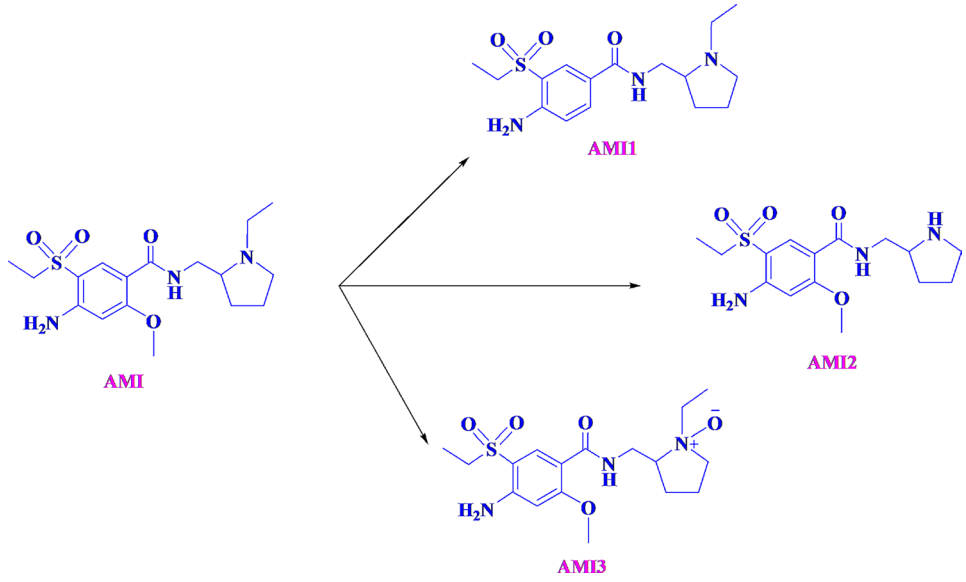

Fig. 6 Amisulpride's photocatalytic degradation route [168]

case of actual municipal wastewater, an early increase in toxicity was noted and is attributable to the matrix's composition. Heterogeneous photocatalysis was used to minimize the toxicity, and at the end of the procedure, practically full detoxification had been accomplished [168].

7.1.2 Photocatalytic degradation of amisulpride using UVA irradiation in methanol solution

In 2011, Skibinski [157] examined the photostability of amisulpride under UVA irradiation in methanol solution and carried out structural elucidation of its photodegradation products. The reversed phase UHPLC-DAD technology coupled with an accurate mass hybrid ESI-Q-TOF mass spectrometer was utilized for the quantitative and qualitative analysis of amisulpride and the elucidation of the stress degradation products. The information for determining the photodegradation kinetics and elucidating the structural formulae of the products was gathered during a single run (10 min) using the auto MS/MS mode. Four degradation products were discovered and their masses with good accuracy (0.53–3.05 ppm) and formulas were determined – 258.0666 ($C_{10}H_{14}N_2O_4S$), 367.1564 ($C_{17}H_{25}N_3O_4S$), 341.1412 ($C_{15}H_{23}N_3O_4S$) and 385.1665 ($C_{17}H_{27}N_3O_5S$). For all the investigated substances MS/MS fragmentation spectra were obtained (collision energy 19.8–26.1 V) allowing structural elucidation of unknown degradation products and suggesting photodegradation pathways of amisulpride (Fig. 7). It was discovered that the UHPLC-DAD/ESI-Q-TOF system is an effective analytical instrument for the quick and precise stability study of pharmaceutical compounds [157].

7.1.3 Photocatalytic degradation of amisulpride using UVA exposure

The other study [172] examined the UVA photostability of amisulpride, doxepin, haloperidol, risperidone, venlafaxine, and zopiclone. An ultrahigh-performance liquid chromatography approach combined with tandem mass spectrometry (UHPLC-MS/MS) was used to assess the photodegradation process. It was discovered that the type of medicine and any co-existing excipients had an impact on these examined compounds. From MS/MS data, fragmentation routes for the photodegradation products were discovered (Fig. 8). To verify the quality, efficacy, and safety of the formulated products during the production process, storage, as well as usual usage, photostability testing is a crucial component of the medication stability assessment [172].

8 AMI

Antidepressants and psychoactive medications can be used to treat depression and lessen its effects. AMI (Table S4 in the Supplementary materials file), a tricyclic antidepressant, prevents the neurotransmitters noradrenaline and serotonin from being reabsorbed from the synapses in the central nervous system [11].

A common tricyclic antidepressant used to treat psychiatric illnesses is AMI hydrochloride [173]. Due to its inexpensive cost, AMI is nevertheless used often even though it is relatively more hazardous than other SSRIs [174, 175].

8.1 Photocatalytic degradation of AMI

Since standard wastewater treatments are ineffective for removing these toxins, the drug is primarily excreted through urine after ingestion, making its way to the

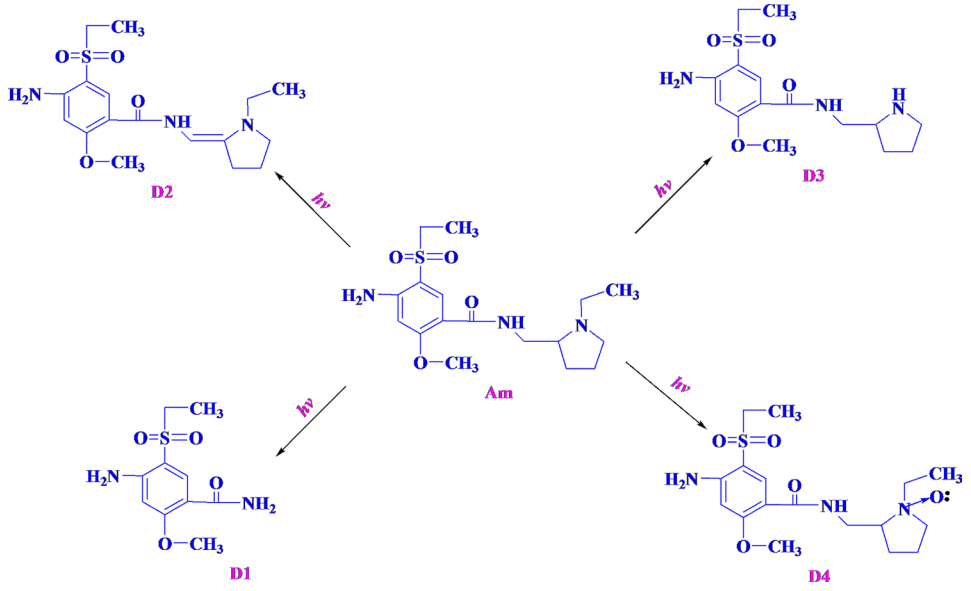

Fig. 7 Amisulpride's photodegradation process in solution [157]

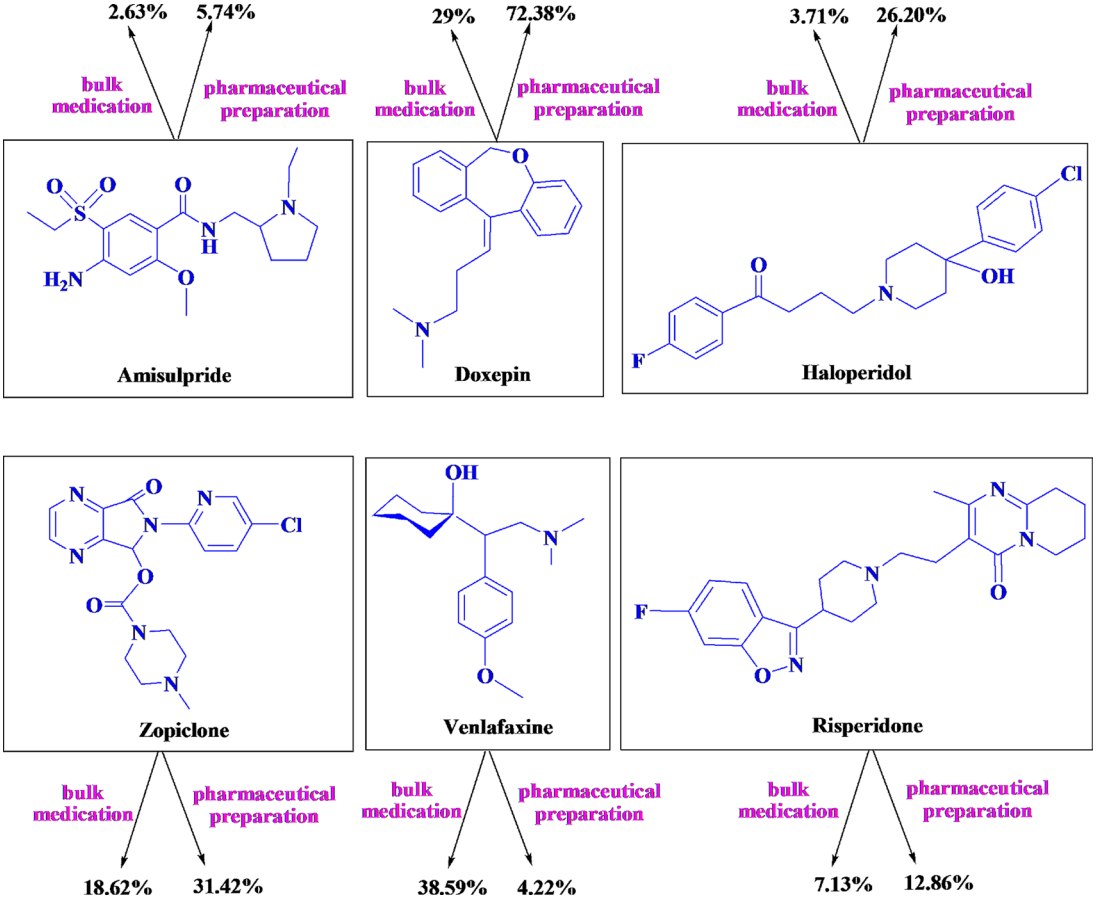

Fig. 8 Using UVA exposure, the photodegradation of amisulpride, doxepin, haloperidol, zopiclone, venlafaxine, and risperidone in bulk drug and pharmaceutical preparation was assessed

WWTP and ultimately the surface waterways. AMI was shown to be removed between 65 and 85% in WWTPs, according to several studies [176, 177], and at quantities of 71.6 ng L^{-1} [178] and 1.4 ng L^{-1} [179], respectively, in surface water and tap water [180].

Previous research claimed that in the presence of naturally occurring HS, amine medicines experience photosensitized degradation via electron transfer interaction. However, even though a significant portion of these medications are metabolized by humans and animals and ultimately released into the environment with their metabolites [181] these investigations mostly focused on the photodegradation of the parent medicines in aqueous solutions [182–185]. Limited research has been done on the photochemical breakdown of their metabolites in the environment [180–185]. The treatment approach, AMI's efficiency, occurrence in the environmental samples, and concentration are presented in Table 4 [176, 177, 179, 186].

8.1.1 Photocatalytic degradation of AMI using ZnO/SnO_2

In 2023, researchers looked into sunlight-driven degradation of alprazolam and AMI by application of binary ZnO and tin oxide powders [11]. This study suggests using solid-state synthesized ZnO and tin oxide (SnO_2) photocatalysts for the photocatalytic degradation of two specific psychoactive drugs, AMI and alprazolam, in an aqueous system while simulating solar and UV radiation. The gathered information validated the novel materials' effective synthesis and potential for photocatalytic use. Regarding the photocatalytic evaluation, the main findings show that the presence of ZnO/SnO_2 synthesized in a molar ratio of 2:1 and calcined at 700 °C, under 1 mg mL^{-1} catalyst loading, led to the highest removal efficiency of AMI and ALP. Based on the reutilization data, it can be inferred that the specified photocatalyst had not lost its efficiency after three sequential runs for the photodegradation of alprazolam. Additionally, pure ZnO powders demonstrated the maximum activity following calcination at 500 °C, in the case of both investigated contaminants. The tert-butanol, sodium fluoride, and ethylenediaminetetraacetic acid tests provided evidence that the proportional contributions of different reactive species altered in the following order: positively charged holes > $^{\bullet}OH_{free}$ > $^{\bullet}OH_{ads}$. This is essential because solar radiation is a free source of energy that is renewable and should be used instead of more expensive radiation sources [11].

8.1.2 Photocatalytic degradation of AMI using fulvic acid (FA)

In 2017, Chen et al. [187] carried out a study. The objective of this work was to look at how the common tricyclic antidepressant AMI and its active metabolite nortriptyline are indirectly photodegraded in the presence of FA. AMI and its active metabolite nortriptyline hardly underwent photodegradation in deionized water, but under the simulated sunlight in the FA solutions, they underwent efficient photodegradation. Nortriptyline photodegraded more slowly than AMI did. The substrates' shapes were related to the photodegradation. The photosensitized reaction in the FA solutions was made easier by the deprotonated form. AMI and nortriptyline both degraded more quickly after the dissolved oxygen was removed, by 10- and 16-fold, respectively. The electron transfer from the nitrogen atom to the excited triplet state FA and subsequent a-hydrogen transfer caused the photodegradation to take place. The amine compounds underwent photosensitized degradation, which reduced the amines to lower ranks, such as tertiary to secondary amine (AMI) and secondary to primary amine (nortriptyline), with the former being the simpler process (Fig. 9). The findings imply that a major method of AMI and its active metabolite removal from natural waters is indirect photodegradation [187].

8.1.3 Photocatalytic degradation of AMI using TiO_2/WO_3

The photocatalytic degradations of the tricyclic antidepressant AMI in aqueous solutions under UV irradiation were examined in the other study [175], which used TiO_2 and TiO_2/WO_3 coatings as photocatalysts. Plasma electrolytic oxidation (PEO) was used to create coatings on a pure titanium substrate. Utilizing non-contact atomic force microscopy and micro-Raman spectroscopy, researchers have examined the influence of certain synthesis parameters on the structural characteristics of produced coatings. Different quantities of crystalline anatase TiO_2 and monoclinic WO_{3-x} phases, as well as amorphous and/or disordered phases of both oxides, were found in coatings, according to Raman scattering tests. Additionally, the data showed that as the PEO's time increased, the coatings' surface became more

Table 4 The treatment, AMI's uses, occurrence in the environmental samples, and concentration

Treatment	Drug for	Occurrence	Concentration	Reference
Antidepressant, anti- inflammatory	Treatment of low mood and depression, types of pain and to prevent migraines	Wastewater treatment plants; United Kingdom	357 ng L^{-1}	[177]
		River basin; Brazil	196 ng L^{-1}	[186]
		Drinking water; France	1.4 ng L^{-1}	[179]
		Large river; United Kingdom	71 ng L^{-1}	[176]

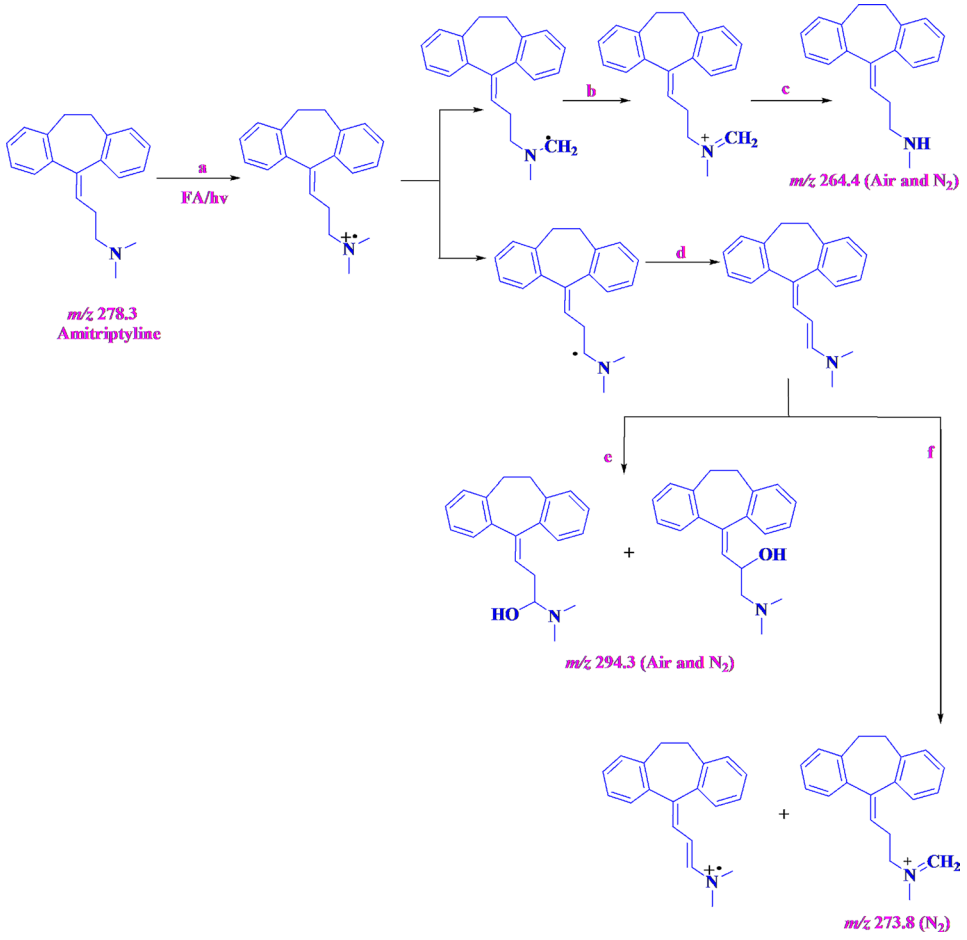

Fig. 9 The suggested photosensitized AMI breakdown process in FA solution [187]

disorganized and uneven. The coating TiO_2/WO_3 (T/W) (45 s) created during PEO has demonstrated the greatest effectiveness in the elimination of AMI induced by UV light. After four consecutive trials, T/W (45 s) showed a small decline in photodegradation efficiency. The findings demonstrated that the ionic by-products of AMI's breakdown included nitrite, nitrate, ammonium ion, acetate, and formate, while the highest degree of mineralization (38.8%) was achieved employing coating T/W (45 s) after 120 min of irradiation. Additionally, no discernible harm was seen after four mammalian cell lines—rat hepatoma, mouse neuroblastoma, human colon adenocarcinoma, and human fetal lung—were exposed to radiation from AMI solutions using various coatings. The results of this work show that the catalyst-recovering (removing) phase following the degradation process might be eliminated if coatings employed in the current investigation are applied as photocatalysts. This could facilitate the use of photocatalytic technologies for bigger volumes of wastewater [175].

8.1.4 Photocatalytic degradation of AMI using fe(III)-citrate-oxalate

Wan et al. [188] investigated photodegradation of AMI in a binary Fe(III)-citrate-oxalate system. This study aims to examine the Fe(III)-citrate-oxalate binary system's synergistic effect in a sun-simulation environment. With a Fe(III)/citrate/oxalate molar ratio of 10:150:500, the Fe(III)-carboxylate binary system displayed good photoreactivity and up to 90% AMT was removed after 30 min at pH 6. In the pH range of 5–8, a synergistic effect was seen in the binary system of Fe(III)-citrate-oxalate. The presence of oxalate citrate depletion. The synergistic impact in the Fe(III)-citrate-oxalate system was made possible by the increased concentration ratios of oxalate to citrate. A putative AMT breakdown pathway based on •OH mechanism was suggested by LC-MS studies. The synergistic mechanism of Fe(III)-citrate-oxalate binary complexes may be better understood as a result of this discovery, which has significant potential for use in environmental photocatalysis at pH values close to neutral (Fig. 10) [188].

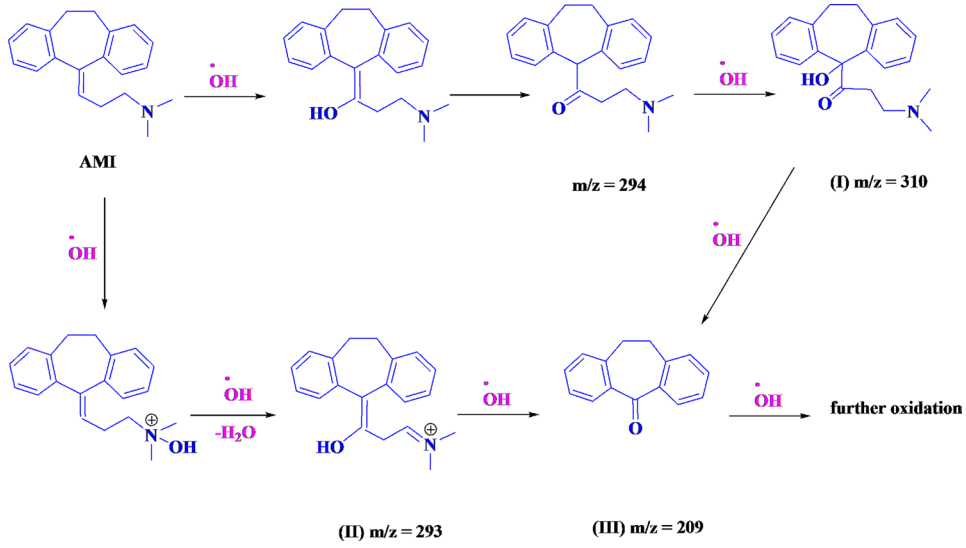

Fig. 10 Potential AMI photodegradation route [188]

Table 5 The treatment, DZP's uses, occurrence in the environmental samples, and concentration

Treatment	Drug for	Occurrence	Concentration	Reference
Anti-depressant, anti-anxiety, anti-stress	Treatment of insomnia, seizures and alcohol withdrawal	Llobregat River; Northeastern Spain	~3 ng L^{-1}	[199]
		River water; Madrid	~21 ng L^{-1}	[200]
		River water; Germany	~33 ng L^{-1}	[201]
		Nansha River; suburban Beijing	~5 ng L^{-1}	[202]
		Municipal sewage treatment plant (STP) effluents; Xiamen	~10 ng L^{-1}	[203]
		Slaughterhouse wastewater; suburban Beijing	~16 ng L^{-1}	[202]

9 DZP

The most widely used benzodiazepine drug is DZP (Table S5 in the Supplementary materials file), which is used as a sedative, tranquilizer, anticonvulsant, and muscle relaxant. Residues of this drug were discovered in effluent at 1 g L^{-1} and in river and drinkable water at 10 ng L^{-1} [78]. DZP, also referred to as Valium, is the most commonly prescribed benzodiazepine used to treat anxiety and alcohol withdrawal [151, 189].

9.1 Photocatalytic degradation of DZP

The medicinal treatment of people and animals is the main source of medicines found in the environment. These medications are broken down by the body and then eliminated as metabolites or the original medication after partial or complete absorption. These pharmaceutical byproducts are either released into the environment or sent to the STP [140]. The presence of pharmaceutical residues in STP effluents demonstrates that these compounds cannot be effectively removed by treatment plants [190]. Because they can generate highly oxidizing species like •OH, AOPs are creative and effective ways to eliminate organic contaminants. H_2O_2 and iron are combined in the Fenton reaction, which promotes the degradation of several pollutant classes in a straightforward procedure under benign operating circumstances [191].

The breakdown of PhACs may be influenced by a variety of mechanisms, including sorption, biodegradation, volatilization, and photolysis [192]. Biochemical responses only remove a small portion of these contaminants because of the pseudo-persistence of many medications [193, 194]. The key process thought to be involved in the alteration of PhACs in the surface layer of water bodies is photolysis [195, 196]. The pollutant can absorb a photon in direct photolysis, which causes it to degrade because it contains aromatic rings, heteroatoms, and other functional groups in its structure. In indirect photolysis, degradation happens as a result of a reaction with active molecules, such as •OH, $^1O_2$, ROO•, $^3DOM^*$, and e^-_{aq} (produced by photosensitizers like dissolved organic matter) [151, 192, 197, 198]. The treatment approach, DZP's efficiency, occurrence in the environmental samples, and concentration are presented in Table 5 [199–203].

9.1.1 Photocatalytic degradation of DZP using $Fe(NO_3)_3$

Lincomycin (LCM) and DZP were two drugs whose photo-Fenton degradation was examined by Bautitz and Nogueira [191]. It was determined whether ferrioxalate or iron nitrate had any impact on the photo-Fenton degradation efficiency of the drugs LCM and DZP. Under black light or sun irradiation, the degradation of both medicines was sped up in the presence of ferrioxalate in comparison to $Fe(NO_3)_3$. The drugs' deterioration was next assessed in an effluent from a STP while being exposed to black light. Comparing ferrioxalate to $Fe(NO_3)_3$, the photo-Fenton degradation of LCM and DZP was improved, leading to the total oxidation of both medicines in a matter of minutes. The initial oxidation of the medicines was not appreciably hampered by the STP effluent [191].

9.1.2 Photocatalytic degradation of DZP using xenon lamp irradiation

In the other study, Jakimska et al. [15] conducted experimental investigations to look into the photodegradation of DZP and SER, two of the most commonly used psychiatric medications, caused by exposure to xenon lamp radiation, which overlaps the spectrum of sunlight, and natural sunshine. The current study focuses on the photodegradation of two common psychiatric medications, SER, and DPZ, caused by exposure to xenon lamp radiation that overlaps the spectrum of sunshine and natural sunlight. In this study, photodegradation was examined using the hyphenated UHPLC-quadrupole time-of-ligh (QToF)-MS technology, which produced extremely precise and reliable results. The development of degradation kinetics revealed the presence of autocatalytic processes (Fig. 11). When liquid chromatography was used in conjunction with QToF-MS, reliable mass measurements and appropriate fragmentation of the target compounds were made possible, allowing for the structure elucidation of the numerous photoproducts of DZP and SER generated during the forced photolysis [151].

10 Alprazolam

The environment has been found to contain a sizable number of pharmaceutically active chemicals [80, 204, 205]. The usage of benzodiazepines is primarily for the treatment of anxiety, forgetfulness, and drowsiness. They are a class of psychiatric medications that act on the central nervous system. These medications are often eliminated in the urine after being heavily metabolized in the liver to create glucuronides conjugates, which are easily broken down by bacteria and transformed back into the original active component. Due to the presence of the fecal bacteria *Escherichia coli*, it appears possible that the glucuronides conjugates indicated above are deconjugated in home wastewater in the same manner. In sewage circumstances, these reactions lead to a rise in the parent compound's quantity [80, 206]. Alprazolam (Table S6 in the Supplementary materials file), a member of the new generation of 1,4-benzodiazepines, is an anxiolytic that is primarily used to treat anxiety disorders [207, 208]. In addition to this, alprazolam is commonly used for its antidepressant impact in the treatment of pathologies that implicate chronically severe anxiety disorders, such as social phobia, and it is also used to treat panic disorders with or without agoraphobia [209, 210].

10.1 Photocatalytic degradation of alprazolam

Pollutants are removed using a variety of chemical and physical processes, such as coagulation, chemical precipitation, etc., but one drawback of these procedures is that they are not destructive; rather, they merely move the contamination from one phase to another. So-called advanced oxidation techniques, which include homogeneous and heterogeneous photocatalytic oxidation, are an alternative to the methods already stated. These procedures rely on the production of $^{\bullet}OH$, which oxidizes a variety of organic contaminants [211].

Because the aromatic triazole ring appears to prevent the hydrolytic ring opening, alprazolam is insensitive to acid or base hydrolysis [207]. Alprazolam showed resistance to photodegradation by sun radiation, and it is anticipated that the photodegradation process would require many months to completely remove alprazolam from surface waters [206]. Vystavna et al. [212] looked at the presence of 21 medicines in river waters in two distinct regions: Kharkiv, Ukraine, and Bordeaux, France. Less than 100 ng L^{-1} of alprazolam revealed almost the same degree of contamination in the rivers under study. The treatment approach, alprazolam's efficiency, occurrence in the environmental samples, and concentration are presented in Table 6 [148, 213, 214].

10.1.1 Photocatalytic degradation of alprazolam using Mg-doped ZnO

In a work by Ivetic et al. [215], Mg-doped zinc powders are described structurally and optically using a straightforward solid-state procedure to account for variations in their photocatalytic efficacy in the breakdown of alprazolam. The structural and optical alterations in the ZnO NPs brought on by the manufacturing process and Mg-doping and their effects on the photocatalytic effectiveness in the breakdown of alprazolam were documented. It appeared that the Mg-doped ZnO photocatalyst developed at 700 °C was the most effective. Grain growth, altered shape, and surface reduction in the samples are causes of the Mg-doped ZnO catalyst's lower photocatalytic activity at higher temperatures (900 °C) [215].

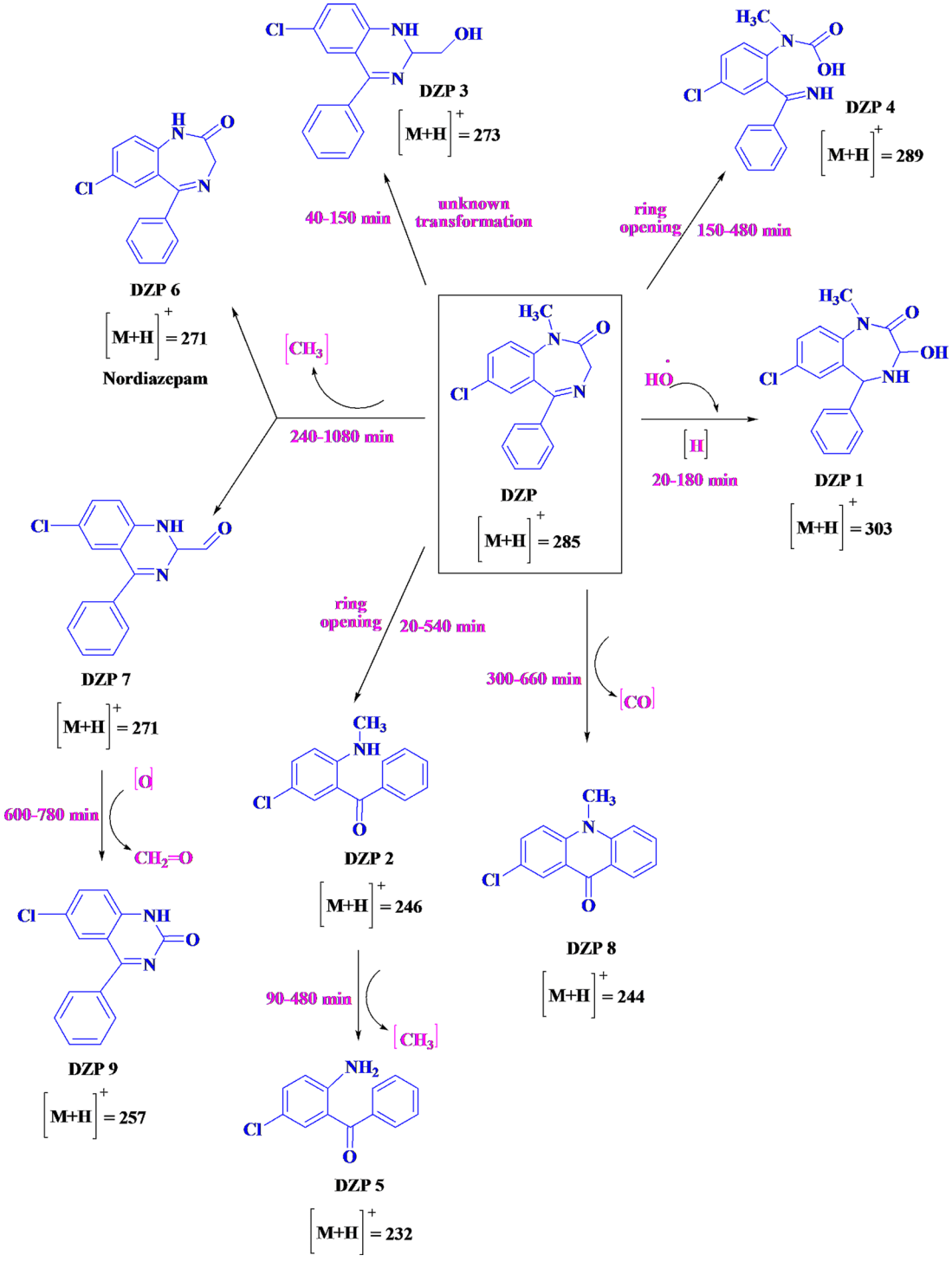

Fig. 11 The suggested DZP photodegradation route [151]

10.1.2 Photocatalytic degradation of alprazolam using UVA/ZnO system

Fincur et al. [210] looked into the effectiveness of heterogeneous photocatalytic degradation of alprazolam in water suspension in 2017. In this study, the effectiveness of alprazolam's photocatalytic degradation in water suspension was examined. The study tested the effects of many factors on the photodegradation of alprazolam, including the kind of radiation (UVA, Vis, solar) and photocatalyst (ZnO, P25), loading of the photocatalyst, pH, and the presence of •OH and positive hole scavengers. The findings of this investigation unequivocally show

Table 6 The treatment, alprazolam's uses, occurrence in the environmental samples, and concentration

Treatment	Drug for	Occurrence	Concentration	Reference
Anti-anxiety, antidepressant	Treatment of anxiety disorders and panic disorder (sudden, unexpected attacks of extreme fear and worry about these attacks)	Secondary clarification (SC) effluent (Tehran South Municipal Wastewater Treatment Plant); Iran	5.0 ± 2.3 ng L^{-1}	[148]
		Drinking water; Shanghai, China	2.3 ng L^{-1}	[213]
		Natural water sample, Spring water Riacho Carro Quebrado; Brazil	< 0.4 µg L^{-1}	[214]
		Natural water sample, Cascavel River – upstream of STP; Brazil	< 0.4 µg L^{-1}	[214]
		Natural water sample, Cascavel River – downstream of STP; Brazil	5.9 ± 0.5 µg L^{-1}	[214]
		Natural water sample, Lake of CEDETG; Brazil	< 0.4 µg L^{-1}	[214]

that the UVA/ZnO system was more effective at removing alprazolam. Here, reaction intermediates produced by both catalysts were carefully examined; hydroxyl derivatives constituted the majority of the intermediates. Following three successive cycles, ZnO demonstrated remarkable photodegradation stability [210].

10.1.3 Photocatalytic degradation of alprazolam using water suspension of brookite type TiO_2 nanopowders

Another study [216] from 2015 looked at how the composition and morphology of brookite-type powders affected how well they removed alprazolam through photocatalysis when exposed to UV light. By combining the solegele hydrothermal method with $TiCl_4$ as a precursor, the hydrothermal temperature and reaction time were varied to create two series of nanocrystalline brookite-type powders. To produce a pure brookite phase, the ideal hydrothermal conditions have been identified. The sodium-titanate-dominated powders produced at lower temperatures (120 and 160 °C) were almost inactive in the breakdown of alprazolam, but the brookite-rich powders synthesized at 200 °C demonstrated remarkable photocatalytic efficiency. The most effective sample was pure brookite, which removed more than 98% of alprazolam within the first 30 min of the photocatalytic reaction. Instead of brookite crystallite size and specific surface area of nanopowders, increased amounts of brookite phase in hydrothermally synthesized TiO_2 samples have been attributed to improved photocatalytic efficiency in the photodegradation of alprazolam. This improvement may be related to the higher energy of direct and indirect transitions in pure brookite samples, as well as a slight increase in the most frequent pore diameter with increased brookite content in brookite [216].

11 Conclusions

Pharmaceuticals are compounds or combinations of substances used to cure or prevent diseases in humans. They do, however, represent a significant group of point or diffuse pollution-related micropollutants. Conventional wastewater treatment methods have only been shown to partially remove pharmaceutical contaminants, and as a result, municipal and/or hospital WWTPs have become important sources of their release into the environment. Pharmaceutical substances are present in aquatic media in quantities between ng L^{-1} and µg L^{-1}. Like other pharmacological classes, psychiatric drugs can be found in the environment. It is important to remember that these substances do not occur alone but rather as complex combinations, even when these concentrations are below the range projected to damage humans and cause acute or even chronic toxicity to non-target animals. Psychiatric medications are one of the most important classes when it comes to evaluating ecotoxicological consequences in terrestrial and aquatic non-target organisms because of their inherent biological activity, which could disrupt nervous and endocrine systems. Additionally, the growing body of research on chronic toxicity in aquatic organisms that are not the intended targets has shown that extrapolating between acute and chronic toxicity is not advised, underscoring the necessity of coming up with a unique strategy to more clearly define this problem. Considering how frequently medications are exposed to aquatic creatures, it would be more crucial to comprehend life cycle toxicity than to carry out acute toxicity testing.

The environmental pollution brought on by organic pollutants is escalating into a global crisis as a result of industrialization and population increase. Adsorption, ultrafiltration, coagulation, and other traditional biological and physical treatment methods (such as those mentioned above) have traditionally been the go-to methods for removing organic contaminants from various fluids and wastewater. However, new methods must be developed to chemically change many emergent anthropogenic organic pollutants into non-hazardous molecules, especially those with significant toxicity but at extremely low concentrations. These methods ought to be effective enough to quickly eliminate the organic contaminants. In a perfect world, they would also be affordable and "green," meaning that no secondary pollution is created and the energy source, catalysts, and chemical reagents employed are all readily available, affordable, and ecologically benign. Innovative technologies, such as AOPs, have been developed for the effective removal and degradation of pharmaceutical compounds from wastewater and the prevention of their release to ground and surface waters. AOPs have been proposed as a tertiary treatment

in effluent wastewater. AOPs are thought to be promising techniques for the treatment of contaminated wastewater including non-biodegradable organic contaminants since they comprise various mechanisms of producing ROS, primarily •OH. The efficient generation of ROS in aqueous environments, the foundation of heterogeneous photocatalysis, enables the total elimination of a variety of pharmaceutical contaminants. Due to this, a wide range of photocatalysts for the photodegradation of psychiatric medications have been created over the past ten years. Results showed that the primary reactive species for the photodegradation of psychiatric medications in the system were photogenerated holes and •OH.

Supplementary Information

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Supplementary Material 1

Author contributions

F.M1 and F.M2 designed the study, F.M1 and F.M2 analyzed and visualized the data, F.M1 and F.M2 wrote the first draft of the manuscript, F.M1, and F.M2 proofread the manuscript, and F.M1 and F.M2 contributed substantially to revisions.

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Data availability

All data generated or analyzed during this study are included in this published article.

Declarations

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