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# Pharmaceutical Pollution Crisis in the World: A Menace to Ecosystem

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**ABSTRACT**

Pharmaceutical pollution is an emerging concern in the world. Major manufacturing units of pharmaceutical companies are successfully running in the developed countries like the USA, UK, Canada, Germany, Australia, Ireland, and Japan and the developing countries like China, India, Brazil, Argentina, and Thailand. Pharmaceutical compounds are entering into the ecosystem finally end up in the drinking water as well as in the food web. Excessive usage of antibiotics for animals, as well as human beings, generates superbugs, this is the root cause of superbug crisis and untreated superbug infection. This review proposed the current scenario of pharmaceutical waste and its effects globally. Furthermore, it compile the pharmaceutical pollution in soil, water resources, and also discussed the suitable treatment process.

**Keywords:** Active pharmaceutical ingredients, Environmental pollutants, Hospital waste, Metabolic compounds, Microbial consortium.

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## INTRODUCTION

In the modern world human and animal life are not being without pharmaceutical products, most of the developed countries routines the usage of active pharmaceutical compounds (API) like hormones and personal care products which are present everywhere [1]. Across the world, numerous studies reported that the environment is highly contaminated by pharmaceutical compounds [2, 3]. Pharmaceuticals are chemical substances that have definite biological activity [4] and could not be completely removed by WWTP some amounts enter into the water system. Ministry of Health Labour and Welfare, Japan, 2013, reported that Japan is the second-largest country by the usage of pharmaceuticals than the United States. Worldwide 80% of people use Tamiflu (Oseltamivir), which is anactivecompound and has been responsible for the development of the drug-resistant virus. Several studies have noticed the presence of pharmaceutical compounds, in the river [5], soil [6], WWTP [7], stream [2], drinking water [8], surface and groundwater, aquatic organism, crop plant. The root cause of pharmaceutical waste in the environment thru human and animal excretion, hospital waste and effluents discharged from the pharmaceutical manufacturing industry, discarding of expired or unwanted medicine into landfills and leachate [9] which are harmful to the environment. According to commonly household waste contains unused and expired medicines that are disposed of in a landfill or often people flushing down the medications into the toilet. Pharmaceutical and personal care products (PPCPs) like therapeutic, veterinary, fragrance, and cosmetics are substances and have diverse physicochemical properties [10, 11]. Pharmaceutical compounds cannot be completely metabolized by human and animal it enters into municipal wastewater treatment plant [12]. According to [7], the traditional sewage treatment method removes only the organic matter, cannot remove the metabolized pharmaceutical compounds. The presence of toxic pharmaceutical ingredients in the aquatic system can alter the homeostasis of aquatic organisms, and induce tragic changes in the endocrine system like enzyme inhibition, cellular damage, atrophy of organs and tissues, decreased growth, cytotoxicity, reproductive abnormalities, and immune system damage [13]. Advanced technology is available for the treatment of effluent like oxidation and filtration, wastewater treatment plant (WWTP), Sewage treatment plant (STP), and among these methods ozone and activated carbon treatments efficiently remove these chemicals. Hence the cost of these effluent treatments is high; consequently, a lot of research is focused to develop green and sustainable pharmacies. This paper reviews and deliberates the pharmaceutical industry waste and its impacts on the environment, and suitable methods of remediation and suggestion for pharmaceutical waste contamination.

*Active pharmaceutical compounds and their metabolite*

Globally the production and consumption of drugs are increased due to thegrowth of health care units and people hope that being longer life [8]. Environmental Production Agency's (EPA's) regulations classified solid waste as hazardous by the authority of the Resource Conservation and Recovery Act(RCRA). By their classification, hazardous waste is listed as F (non-specific source waste, K list are source-specific waste, P and U list are discarded commercial chemical products, this list is found in 40 CFR 261.33.Based on the Resource Conservation and Recovery Act (RCRA) regulation, P listed waste are pharmaceuticals and commercial chemical products, therapeutic agents and characterized as acutely hazardous. The U Listed wastes are chemicals, when drugs manufactured with these chemicals are called hazardous waste [14]. **Table 1** shows Pharmaceutical compounds listed waste by RCRA. Some of the medicine (aspirin, ibuprofen, paracetamol, caffeine, ranitidine, and diclofenac) are non-prescription drugs that are commonly sold over the counter (OTC), hence, the prescription drugs like carbamazepine, codeine, and diazepam are also sold by OTC in India without prescription.. Many countries like (European Union, Germany, Hungry, Italy, Portugal, and Spain) banned the drug dipyrone. Anticancer drugs are designed to stop cellular proliferation by disturbing DNA synthesis, and the mutagenic, fetotoxic and teratogenic properties of anticancer drugs are dangerous contaminants [15]. According to more than 150 anticancer drugs were consumed over the year 2007-2015 in Portugal, the study proposed that most of the drugs are Antineoplastic and Immuno modulating agents, in addition, megestrol (H02AB07), Cyproterone (G03HA01), a sex hormone and corticosteroid are used for the treatment of cancer. Anti-influenza drugs Inavir (laninami viroctanoate) was developed in 2014, Tarbet, Avigan (favipiavir), and Rapiacta (peramivir) were developed in 2012, from this Inavirare transformed into pharmacologically active metabolite laninamvir.



**Table 1.** Pharmaceutical compounds listed waste by Resource Conservation and Recovery Act (RCRA).

| P listed waste (Waste code) | U Listed waste(Waste code) |
|---|---|
| Arsenic trioxide(P012) | Hexachlorophene(U132) |
| Epinephrine base(P042) | Lindane(U129) |
| Nicotine( P075) | Melphalan (chemo)(U150) |

| | |
|---|---|
| Nitroglycerin(P081) | Mercury(U151) |
| Phentermine(CIV)(P204) | Mitomycin C (chemo)(U010) |
| Physostigmine salicylate(P188) | Paraldehyde (CIV)2(U182) |
| Warfarin(P001) | Phenacetin(U187) |
| **U Listed waste** | Phenol(U188) |
| Chloral Hydrate (U034) | Reserpine(U200) |
| Chlorambucil (U035) | Resorcinol(U201) |
| Chloroform (U044) | Saccharin(U202) |
| Cyclophosphamide (U058) | Selenium sulfide(U205) |
| Daunomycin (U059) | Streptozotocin (chemo)(U206) |
| Dichlorodifluromethane(U075) | Trichloromonofluromethane(U121) |
| Diethylstilbestrol (U089) | Uracil mustard (chemo)(U237) |
| Formaldehyde (U122) | Warfarin(U248) |

*Source of pharmaceutical waste*

Generally, pharmaceutical waste is separated into point source pollution and diffuse pollution. Point source pollution is detectible source from distinct location such as hospital and industrial effluents, sewage treatment plants, and septic tanks [16]. The unsafe release and rise of pharmaceutical compounds in the environment due to Lack of policy implementation, ineffective regulation, and lack of awareness on public health are the major issues [2]. Household, commercial and industrial waste is collected by the local municipality and dumped as landfill. The source is entered through dumping of expired, unused drugs, waste medicine from the house and health care centres, and human, animal excretion to landfill. According to [17] the lack of monitoring system, regulatory body, and guidelines for the discarding of expired drugs increased the pollution level in the environment. Generally, some pharmaceutical compounds (PCs) and antibiotics are not be completely removed by the wastewater treatment plant, when using for irrigation pharmaceutically active compounds are leached into groundwater. According to [4], human excretion enters the aquatic system by the release of the septic tank. Similarly, pharmaceutical compounds enter the aquatic by the main route of sewage treatment plants [18]. Diffuse pollution is very hard to be found in sustenance environmental scales [16]. For example, runoff from agricultural land, domestic waste, animal waste, and sludge from WWTP [19]. The release of scantily treated effluents is the major cause of PPCPs contamination in the environment, high concentration acetaminophen (21-119 μg/L) and ibuprofen (0.3- 63 μg/L) were found in two hospitals WWTPs in South Africa [7]. According to [6] Continual input and presence of antibiotics in the environment are considered pseudo persistent contaminants. Irrational antibiotic usage as growth promoters for poultry and cattle is a source of antibiotic contamination in theenvironment. Sewage sludge is the semisolid, solid, or liquid waste produced during the treatment process of domestic sewage. Based on EPA standards additional treatments are required for sludge to land application, after treatment process these are referred to as bio solid and it can be used as a soil amendment, it contains organic as well as inorganic matter by the way it can improve the quality of soil or contaminate soil [14]. European Commission reported (2016) that, use of reclaimed wastewater for irrigation is an emerging contaminant. A study was conducted in Sweden and Germany, in this research high nutrient sand fewer pharmaceuticals were found in black water (un separated toilet waste) [20]. In America, 50% of these bio solids are applied to agricultural land to improve crop production. Indicated that the land application of bio solid is one of the major causes of groundwater contamination due to the high soluble nature of halogenated hydrocarbon and the high concentration of pharmaceutically active compounds in bio solid.

*Occurrence in the environment*

Pharmaceutical compounds and their metabolic products are increasing and quickly contaminate the environment. Worldwide the pharmaceutical compounds witnessed in various countries, groundwater from the USA; soil from Victoria, Australia [21] Sydney estuary in Australia River Avon, from Salford, England Yodo River, Japan [5] wastewater from the hospital, residential, dairy and WATP, Albuquerque, New Mexico; Sewage effluents, Nova Scotia, Canada, Sewage treatment plant, Spain; Eschede, Germany [22] Sewage treatment plant, Beijing, China [23] Rivers Lakes, Groundwater, Hyderabad, India [3]. According to [4] occurrence of active pharmaceutical ingredients in groundwater, drinking water, seawater, landfill, leachate, effluents from Sewage Treatment Plant (STP), Wastewater Treatment Plant (WWTP) is a major concern. **Table 2** shows the occurrence of pharmaceutically active substances in soil and water resources.

**Table 2.** Concentration of pharmaceutical compounds found in soil, WWWTP/STP, freshwater, ground water and Tap water from different countries.

| Compound | Source | Concentration ng/l | Country | Reference |
|---|---|---|---|---|
| Acetaminophen | Ground water | 1890 | California, Canada | [24] |
| | WWTP | | India | [25] |
| Amantadine | Effluent | 75000,150000 | Japan | [5] |
| Atenolol | WWTP | 232 | India | [25] |
| Azithromycin | WWTP | 300000 | India | [25] |
| Caffeine | Ground water | 150000-300000 | California, Canada | [24 |
| | Surface water | 290 | China | [26] |
| | WWTP | | India | [25] |
| | Fresh Water | 3500 | California | [24] |
| | Ground water | | China | [26] |
| | Surface water | 150000 | India | [8] |
| | Lakes | 735 | India | [8] |
| Capecitabine | River | | India | [8] |
| Ciprofloxacin | Well | 420 | India | [8] |
| | Lakes | | USA | Gómez-Canela *et al*., 2013 |
| | River | 15.70,5.21 | Lisbon, Algarve | Gómez-Canela *et al*., 2013 |
| Cyclophosphamide | River | | China, | López-Serna *et al*., 2012 |
| Diazepam | Soil (μg/kg) | 6.5 mg/l | China | [26] |
| Ibuprofen | WWTP/STP | 2.5 mg/l | Canada | [27] |
| | Fresh Water | 14000 ng/l | Italy Taiwan, Korea | [24] |
| | River | 1.2 mg/l | China | [26] |
| | Tap water | 131 | Algarve,Portugal | [28] |
| | Surface water | 44,88,102 | India | [25] |
| | Surface water | 0.35-1.16 | China | [26] |
| Meprobamate | Lakes | 1.3 | India | [8] |
| Metformin | River | 11900,8000,1600 | Japan | [5] |
| Mycophenolic acid | Wells | | Japan | [5] |
| Mycophenolate | River | 203,468,30 | Japan | [5] |
| mofetil | Effluent | | Japan | [5] |
| Naproxen | River | 5.67,0.94 | Canada | [29] |
| Norfloxacin | Effluent | | USA | [30] |
| | Drinking water | 5.37 | Japan | [5] |
| | Ground water | | Germany | [5] |
| Oseltamivir | River | 5.9 | Germany | [31] |
| | Tap water | 149.06,10.75 | India | [31] |
| Oseltamivir carboxylate | Tap water | 555 | India | [25] |

| | | | | |
|---|---|---|---|---|
| | Tap water | 0.5 mg/l | China | [25] |
| Paracetamol | WWWTP | 4700 ng/l | Taiwan, Korea | [27] |
| | Fresh Water | 31 ng/l | Spain, Taiwan, | [31] |
| Peramivi | Soil (µg/kg) | 20 | Vietnam | [24] |
| | Ground water | 140 | China | [26] |
| PDP | Surface water | 70 | Mexico | [27] |
| Propyphenazone | Soil (µg/kg) | 0.298 | China | [31] |
| | WWTP/STP | 6.5 | | [24] |
| Ranitidine | Ground water | 157,1708,274 | New Mexico, Spain | [26] |
| | Surface water | 10 | New Jersey, Canada, | [5] |
| Sulfadiazine | | 0.24 | California, Canada, | |
| Sulfamethoxazole | River | 250-400 | China | [5] |
| Tridosan | Surface water | 80-240 | | [5] |
| Trimethoprim | Surface water | 75000 | | [5] |
| Zanamivir | Effluent | | Japan | [26] |
| | | 184 | Canada | [5] |
| | | | USA | |
| | | 170,33,4330 | Japan | [5] |
| | | | Germany | [5] |
| | | 458,38,3 | Germany | |
| | | | India | [5] |
| | | 380 | India | |
| | | | China | [26] |
| | | 16.7 | | [5] |
| | | | Canada | |
| | | 2550,39,2000 | USA | |
| | | | Japan | |
| | | 145,59.9,1808 | Germany | |
| | | 18 | Germany | |
| | | 4500 | India | |
| | | 89 | | |
| | | 200 | | |



*Pharmaceutical compounds in soil*

Water demands and scarcity are a major threat, to overcome this most of the countries turned to use wastewater for irrigation. Organic pollutants enter into the soil by the way irrigation of septic tank water, application of biosolids and manure directly to the environment. Commonly the existence of pharmaceutical compounds in the soil is lower than water resources. Li *et al*., [32] reported that the concentration of anticonvulsant carbamazepine is the recurrent compound in soil; it enters the soil through irrigation of wastewater in Mexico and China. Generally, the antibiotics levels in soil were higher due to the addition of sewage sludge, biosolids, and manure to the agricultural land. The highest amount of tetracycline-chlortetracycline (12900 µg/kg) [33], doxycycline (728 µg/kg), and oxytetracycline (50000 µg/kg) [32] were observed from manure similarly considerable amount of sulfonamides of sulfamethazine (200-25000 µg/kg), sulfoxide (9.1 µg/kg), sulfadiazine (85 µg/kg) and fluoroquinolones of ciprofloxacin (5600 µg/kg), enorfloxacin (1347 µg/kg), norfloxacin (2160 µg/kg) [34]. In [35] **Table 2** shows the concentration of some pharmaceutically active compounds in soil and water resources. According to [36] when sludge applied to soil bioactive compounds are enter into soil and transfer into the plant, he measured high concentration of Metformin (12 mg/kg) than naras in and ciprofloxacin (11.3 and 6.5 mg/kg) in soil. Soil samples were collected from the garden of Jerez de la Frontera, Spain, this garden was fully irrigated with treated WWTPs water and effluent, the samples contain high concentrations (ng/g) of acetaminophen (5.95), diclofenac (5.06), caffeine (3.21), flumequine (5.31) [37].

*Pharmaceutical compounds in water*

A study published by [38] by their investigated pharmaceutical residues found in the Yamuna River due to STP effluents released to the river. Based on the results in location (YMN-1) drugs like ibuprofen, paracetamol and caffeine were found in the winter season, except for ibuprofen two drugs observed in the summer season, no drugs were found in monsoon. Therefore, in location YMN-2 high concentrations of aspirin, ibuprofen, paracetamol, caffeine, carbamazepine, codeine, and diazepam were witnessed in summer, but throughout the year maximum concentration of caffeine was found. Similarly, found anticancer drugs from Portuguese surface water such as mycophenolic acid (117-213 ng/l), hydroxycarbamide (55-81 ng/l), bicalutamide (4-10 ng/l), capecitabine (8-17 ng/l), imatinib (3-8 ng/l) and cyproterone (2ng/l). [26] detected some pharmaceutically active compounds in the surface water of China and compared with other countries, for example, carbamazepine was lower (69 ng/l) than South Korea (95 ng/l), United States (190 ng/l) and South Africa (3240 ng/l) [39], the levels were higher than Japan (15ng/l) and in Spain 53.8 ng/l. Paracetamol is generally used as a pain reliever and reduces fever and selling as OTC because most people in India taking the drug without physician consultation. For this reason, the concentration of paracetamol 157, 1708, 274ng/l was noticed in river water in India [38]. Codeine concentration in Sydney estuary water (9.5ng/l), wastewater (1000ng/l), river water (100ng/l), estuarine from Taff and Ely River (258-333 ng/l). Similarly, fluconazole concentration (236,950µg/l) is 20 times higher than therapeutically desired levels in blood detected from sewage samples around industrial Zone in India. In a study conducted by [19] in China, they detected 42 PPCPs in WWTP effluent, sludge, and suspended solids, the study proposed that Ketoprofen, Metoprolol, Ibuprofen, Triclocarban, Ofloxacin, and propylparabens were most abounded in effluent and also caffeine, oxytetracycline, ibuprofen. Similarly, 103 pharmaceuticals and 21 hormones were detected in groundwater used as drinking water in the United States, particularly hydrocortisone concentrations higher than human health. In a study micropollutants (in ng/L) were analyzed in groundwater downgradientin Minnesota, the USA they found sulfamethoxazole (965), carbamazepine (1000), methocarbamol (550), metformin (206), and fluconazole (184). Likewise, Ketoprofen (1820), gemfibrozil (1910), atenolol (1140), ranitidine (2770), and hydrochlorothiazide (2270) were detected in WWTPs effluent from Jerez del Frontera city in Spain [37].

*Pharmaceutical compounds in the plant*

Treated wastewater reused for agriculture irrigation and which introduce pharmaceuticals and personal care products (PPCPs) and endocrine-disrupting chemicals (EDCs) into the soil environment, which are taken up by plants enter into food web [22, 40]. Biotransformation and bio concentration of PPCPs and EDCs were studied by [40] in the plant (Carrot, tomato, and lettuce). In his study, the least accumulated compounds were atorvastatin, clofibric acid, and diclofenac (Bioconcentration factor (BCF) 0.0-69.3 µg/Kg), but diazepam, diuron, and perfluorooctanoic acid were most accumulated (BCF 4.5-718.6 µg/kg), and BCF value of root tissues was higher than leaves. Soybean [41], and ryegrass [20] uptake more carbamacepine than root. But the opposite statements reported by [42] showing more concentrations of salbutamol, carbamazepine, trimethoprim, and sulfamethoxazole were taken by roots of cabbage and fluoxetine and diphenhydramine uptake by the root of soybean [41]. Antimicrobial Triclosan and triclocarban were reduced from the soil by pumpkin and zucchini plants. Cui *et al*. studied the uptake process of Metformin (MET) in the plant, he reported that MET compounds enter root through the apo plastic pathway by diffusion and are transported by active transport through a symplastic pathway. Similarly, [36] said Plant uptake a higher concentration of motor man than nursing and ciprofloxacin.

*Impact of pharmaceutical contamination in the environment*

Pharmaceutical compounds are metabolized and release a complex mixture of bioactive compounds, which are highly active than the parent compound [43]. The conventional wastewater treatment process is not completely removed the PPCP compounds therefore pharmaceutical pollution is rising globally, while using treated wastewater for irrigation. Such practice highly contaminates the soil and water resources, as well as increasing drug-resistant bacteria. Pharmaceutically active compounds contamination directly affects the human by the way of respiratory disorder, loss of reproductive ability, cancer, skin allergies, and congenital problems. For example, anticancer drugs of tamoxifen & 40HTam induced adverse effects on the aquatic organism for example in *Daphnia pulex*the drug highly influences the size and reproductive rate of the organism **Figure 1**. Shows pharmaceutical waste entry and its effects on environment. According to [22] the biguanidine class of antidiabetic II drug MET acts as a glucose suppressor by the way it can suppressing glucose production in the liver. This could not metabolize by the human body and directly enters into the environment through urine. Antibiotic in the environment generates superbug crisis, present-day this is the challenging issue worldwide. Excessive use of antibiotics creates resistance, it succumbs to untreatable superbug infection. The effluents from the pharmaceutical manufacturing industry contaminate the ecosystem and growing drug resistance at the global level. Another study reported that seasonal variation noticed in the occurrence of the drug in river water, this study said anti-influenza drugs of oseltamivir, oseltamivir carboxylate, peramivir, and zanamivir were not observed at the end of December 2015 in river water but from January 2016 to February 2016 they appear in the concentration 20, 70, 10, 89ng/respectively. Then concentration was rapidly diminished and become not detectable in March 2016. Consequently, the anti-influenza drugs laninamivir, laninamiviroctanoate, and favipiravir were witnessed only in the influenza season [5]. The toxicity and risk arevarying with the concentration of individual compound contamination. An investigation said, trimetho prime in the surface water is extremely risky to the aquatic organism, hence ibuprofen, roxithromycin, and gemfibrozil show medium risks. Generally, in hospitals no separate sewage system for cancer patient wards, due to this the radioactive waste and cancer drugs are directly going to the sewage system. Discussed [17] in their review estradiol concentration in water resources can induce vitellogenin production and structural changes in sex organs observed. [37] Assessed environmental risk factors in soil irrigated with WWTPs treated water, the study shows the concentration of trimethoprim, caffeine, flumequine, and acetaminophen were in low risk and maximum risk observed for diclofenac and phenazone.



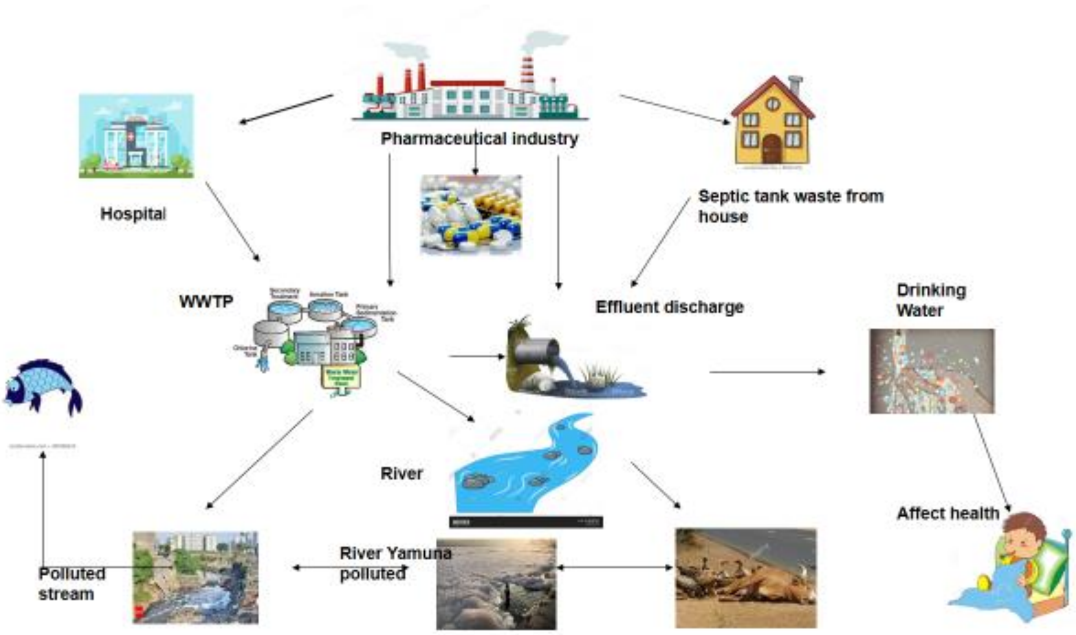


**Figure 1.** Pharmaceutical waste entry and its effects on environment

*Methods of pharmaceutical waste degradation*

Pharmaceuticals are one of the essential products in our daily life; however, poor removal is a great concern. Several studies focused to remove active compounds by various methods, but some limitations are present. This review discussed the overview of the wastewater treatment process, the following methods of physical adsorption, biological degradation, and chemical oxidation are involved [19]. Several studies analyzed the removal efficiency of these methods, wastewater treatment method is considered as the central unit to remove pollutants from the wastewater. The removal efficiency is vastly different, it depends on the environmental condition and physicochemical properties of the substances, adsorption materials, and combination of the treatment process [44]. Numerous studies witnessed the pharmaceutical compounds from WWTP effluents, also the release of improperly treated effluents to lake and river water APC will contaminate the environment. Even trace (ng-mg/l) level of pharmaceutical compounds in the water cycle is a high risk to humans. Various studies focused to improve the removal efficiency with physical adsorption materials in the wastewater treatment process such as powdered activated carbon (PAC), granular activated carbon (GAC), graphene, graphene oxide, carbon nanotubes. Activated carbon is highly used for the removal of PCs from wastewater and groundwater, therefore adsorption capacity depends on the hydrophobicity and charge of PCs. In the pilot-scale, the treatment process of remaining organic matter in the water can compete with PCs to the binding sites of powdered activated carbon, which can reduce the adsorption capacity [45]. Therefore, to avoid the problem higher dose of PAC was needed to improve the removal efficiency. Various factors influenced the removal efficiency such as molecular weight of compounds, presence of organic matter, theconcentrationof PAC, contact time, and structure of activated carbon materials. **Table 3** shows the removal efficiency of PCs by activated carbon. Graphene is composed of carbonatoms and graphene oxide is a precursor of graphene, due to the remarkable properties of graphene and graphene oxide has high attention for the removal of PCs [19]. Their removal efficiency varied with physicochemical properties of PCs, pH, and contact time influence the rate of adsorption. Comparatively graphene and graphene oxide have aspecific surface area than activated carbon hence it can potentially remove the PC. Carbon nanotubes have excellent properties in the removal of PCs than PAC, GAC, graphene, and graphene oxide. Adsorption efficiency varied with the structure and properties of carbon nanotubes. Multi-walled nanotubes can effectively remove PCs of ibuprofen, carbamazepine, caffeine, triclosan, prometryn, carbendazim [19].

Pharmaceutical waste compounds are frequently identified by the above-mentioned methods, therefore advanced chemical oxidation methods are required to remove pollutants. Recently chemical oxidation processes of ozonation, Fenton oxidation, and ultraviolet (UV) treatment are used for the treatment of waste. Ozone is anoxidation method, and which are effective removes the PCs, ozonationis mainly based on the oxidizing activity of hydroxyl radicals to remove PCs. The concentration of hydroxyl radicals influences ozonation, threat of ozonation decrease when there is an increase in hydroxyl radicals. Fenton oxidation ismostly used in industrial wastewater treatment, in which iron salts and hydrogen peroxide are used to remove pollutants. Fenton oxidation and Fenton like oxidation mainly depend on the hydroxyl radicals, in this oxidation process $H_2$ $O_2$decomposed and generate hydroxyl radicals [19]. Another method is UV treatment, it is mainly applied for drinking water and wastewater treatment, for the removal of PCs V light destroys chemical bonds of pollutants by the process called photolysis. Hence photolysis is not effective in all the compounds for example concentration of carbamazepine is not reduced by this process. According to [46] revealed that the new methodology is to increase the efficiency of removal of PCs. In which combination of UV with hydrogen peroxide effectively reduce the pollutants. The above-mentioned methods are an effective treatment for the removal of PCs but are economically not suitable for undeveloped and developing countries.

The biological degradation process is considered a cost-effective and eco-friendly method in the excellence of pharmaceutical waste removal mechanisms. Microorganisms are utilizing pollutants as an energy source for metabolic functions. Pure culture isolated from activated sludge predominantly removes the PCs, some strains highly degrade a wide range of components. In the presence of glucose, *StreptomycesMIUG* and *Basidiomycete* can degrade carbamazepine and iopromide can degrade with the extra substrate noticed that microorganisms use ibuprofen and paracetamol as a carbon source, the metabolic product of hydroquinone and 4-aminophenol were formed during the microbial degradation of paracetamol. Diclofenac has high resistance in the activated sludge process. However, revealed that the white-rot fungus completely removes diclofenac and eliminates its lethal toxicity to an organism in the absence of extra substrate. Likewise, in another study white-rot fungi and their oxidoreductase enzymes are effective for the removal of PCs contaminants; hence the removal efficacy of fungal cells is highly dependent on the molecular structure of targeted PCs, fungal species, and secreted enzymes. Mixed culture easily degrades the pharmaceutical compounds than pure culture. [47] Reported that removal of compounds enhanced by adding mixed cultures in the activated sludge process. Comparatively, a mixed culture has a higher degradability of mixed pharmaceutical compounds than individual compounds.

**Table 3.** Removal efficiency of pharmaceutical compounds through various activated carbons.

| Compounds | Adsorbent | Initial concentration | Source | Removal efficiency (%) | Reference |
|---|---|---|---|---|---|
| **Antibiotic** | | | | | |
| Sulfamethoxazole | PAC (5mg/l) | 100 ng/l | Surface water | ~35 | [1] |
| | PAC (50 mg/l) | 600 ng/l | WWTP | ~60 | [48] |
| | PAC (20 mg/l) | 100 ng/l | Synthetic water | ~95 | [48] |
| | PAC (5 mg/l) | 100 ng/l | Surface water | ~65 | [1] |
| **Antidepressant** | PAC (5 mg/l) | 100 ng/l | Surface water | ~60 | [48] |
| Diazepam | | | | | |
| **Hormone** | | | | | |
| Estriol | PAC (50 mg/l) | 1.3 mg/l | WWTPs effluents | ~90 | [1] |
| **Lipid regulator** | | | | | |
| Bezafibrate | Graphene | 100 ng/l | Surface water | 95.5 | [49, 50] |
| **Non-steroidal anti-inflammatory drugs** | | | | | |
| Ibuprofen | PAC (50 mg/l) | 10 mg/l | Synthetic water | ~80 | [1] |
| Diclofenac | PAC (20 mg/l) | 5.8 µg/l | WWTPs effluents | ~100 | [48] |
| Paracetamol | Graphene | 100 ng/l | Synthetic water | 97 | [49, 50] |
| Naproxen | PAC (20 mg/l) | 10 mg/l | Synthetic water | ~85 | [48] |
| | PAC (20 mg/l) | 100 ng/l | Synthetic water | ~95 | [48] |
| | | 100 ng/l | Synthetic water | | |

## CONCLUSION

Pharmaceutical pollution is rising globally while using treated wastewater for irrigation. Such practice highly contaminates the soil and water resources, as well as increasing drug-resistant bacteria. The entry of such active pharma compounds in water resources will affect the aquatic population and pollutants enter into food webs. The conventional mode of discharge and treatment of pharmaceutical wastes is not completely removing the pharmaceutically active compounds. The review proposed that carbon nanotubes have excellent properties in the removal of PCs than PAC, GAC, graphene, and graphene oxide, however, few compounds are frequently identified by the above-mentioned methods. Consequently, advanced chemical oxidation methods of Ozonation, Fenton oxidation, and UV treatment are required to remove pollutants. Ozonation and Fenton oxidation highly depends on the concentration of hydroxyl radicals. UV treatment is based on the process of photolysis hence it is not effective for all compounds, while the combination of UV with hydrogen peroxide effectively reduces the pollutants. The above-mentioned methods are an effective treatment for the removal of PCs but are economically not suitable for undeveloped and developing countries. Even though, the Biological degradation process is considered acost-effective eco-friendly method and has an excellent removal mechanism for organic pollutants in the environment. Pure culture of bacteria, algae, and fungi can remove PCs effectively, whereas microbial consortium easily degrades the pharmaceutical compounds than individual culture. Globally, they are many surveys conducted and proposed that the need for awareness within people about the proper disposal of waste will control pollution. Adhering to the environmental monitoring system, regulatory body and stringent guidelines for the discarding of expired drugs in developing and under-developing countries increased the pollution level.

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