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A SHORT REVIEW ON OCCURRENCE OF PHARMACEUTICAL PRODUCTS IN DRINKING WATER

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Abstract:

The presence of various types of pharmaceutical substances and organic pollutants in significant amounts and in traces were reported by many researchers globally. India in the past few decades has grown as one of the top five large scale producers of low-cost pharmaceutical products. More than 50% of revenue generated by Indian large scale and small-scale industries is through exports to developed countries like the United States of America. These pharmaceutical companies dispose of complex and non-biodegradable wastes into the environment, especially water resources which are either untreated or partially treated, therefore contaminating the aquatic ecosystem. These pharmaceutical products reach the ground and surface water easily through various routes such as waste water treatment plants (WTPs), pharmaceutical industries, hospital services, and through human and animal excreta and due to improper disposal of unused and expired medications. Regulatory bodies should frequently monitor the impact of these pharmaceutical products and micro pollutants on human health and aquatic ecosystems. Laws should be enforced for disposal of pharmaceutical and personal care products to prevent contamination of water bodies by employing advanced analytical detection methods like gas and liquid chromatography with mass spectrometry (GC-MS and LC-MS) to determine very low concentrations of pharmaceuticals in ng/L level. Drugs like Atenolol (β-blocker) and Amoxicillin (penicillin antibiotic) are excreted as such unmetabolized were detected in wastewater influent in study conducted in the UK. There is no or limited data in assessing the potential harm and health risks from exposure to these pharmaceutical products in water. No standardised protocol was laid to determine these pharmaceutical pollutants analytically. This present review is aimed in focusing on the pharmaceutical pollution of different water bodies by pharmaceutical products and their metabolites and highlights the importance of strict enforcement of laws governing prevention and removal of these pharmaceutical wastes based on previously published works.

Keywords: *Pharmaceutical products, organic pollutants, wastewater treatment plants (WTPs), water resources and drinking water.*

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INTRODUCTION:

Pharmaceutical products and their metabolites including those for human and animal use have been reported and demonstrated to be present in the environment especially in the water bodies by many researchers and scientists from the past 30 years [1]. In spite of many recent advances made by different countries in treating wastewater, the presence of pharmaceutical compounds and trace amounts of organic pollutants were reported [2].

The occurrence of pharmaceuticals and their metabolites was first reported in the United States of America in 1970 and the awareness on impact of these pharmaceutical products on environment and aquatic bodies in particular has increased dramatically since the early 1990s in Europe and other developed countries including France, Japan, China and Germany. These countries implemented effective waste and industrial water treatment procedures and comply with the legal procedures [3]. However, many countries worldwide have not adopted or taken appropriate measures to reduce the emission and elimination of these sources of pharmaceutical products resulting in the pollution [2]. India being one of the topmost large-scale producers of low-cost pharmaceutical products has a turnover of over 55 billion USD per year which has been exporting pharmaceutical supplies to over 65 countries with about 300 large scale and 8000 small scale manufacturing industries, where the primary source of pharmaceutical contamination is through wastewater treatment plants (WTPs) outlets. The contaminant removal ability of these ranges from 12.5 to 100% and several factors like process of treatment, the age of sludge, area, affecting its efficiency [4].

The amount of pharmaceutical waste causing water pollution in the state of Andhra Pradesh, India was found to be 150 times greater than the amount of pharmaceutical pollution at its peak level in the USA. Researcher studies carried out at the PETL (Patancheru Enviro Tech Limited) WTP near Hyderabad, which received 1.5 MLD effluents from about 90 bulk drug firms in the Patancheru area is observed to be in higher amounts than anywhere else in the world. In India, the amount of sewage generated by a population of 1.3 billion is significantly higher than the amount that can be treated, therefore, comprehensive and effective management of pharmaceutical industrial waste and expired drugs should be prioritised and implemented using the latest tools and techniques [4,5]

Route of entry of pharmaceutical compounds into water system:

Pharmaceuticals have the capability to find their way into the environment through numerous routes, such as sewage treatment plants (STPs), industrial processes, healthcare centres, aquaculture operations, the runoff of agricultural fields into surface waters, and the runoff from animal farming and manure discharges into the soil [6]. Based on the location of the patients, whether they reside in private households, or in hospitals and other facilities, the distribution of pharmaceuticals is determined by qualitative, quantitative and temporal factors [3].

Animal or human drug usage can release chemicals into the environment either directly or indirectly. Some pharmaceutical chemicals that have not been metabolised or dissolved by the body are eventually eliminated through the faeces and urine and dumped into the sewer systems. Humans can introduce personal care products such as shampoos, body washes, toothpastes, sunscreens, cosmetics and hand lotions into sewage and surface water during their regular washing habits [6]. The inappropriate disposal of unused or expired medications, such as flushing them down toilets or throwing them in landfills, and the presence of pharmaceutical residues from manufacturing spills are additional important sources of potential contamination at the local levels [3]. The pharmaceutical companies release both treated, partially treated and untreated effluents into open spaces and into streams that allow them to reach the environment [5].

The management and utilisation practices of pharmaceuticals exhibit variations across different regions of the world. Thus, the importance of different ways in which people can be exposed to pharmaceuticals also varies depending on the geographical location [6].

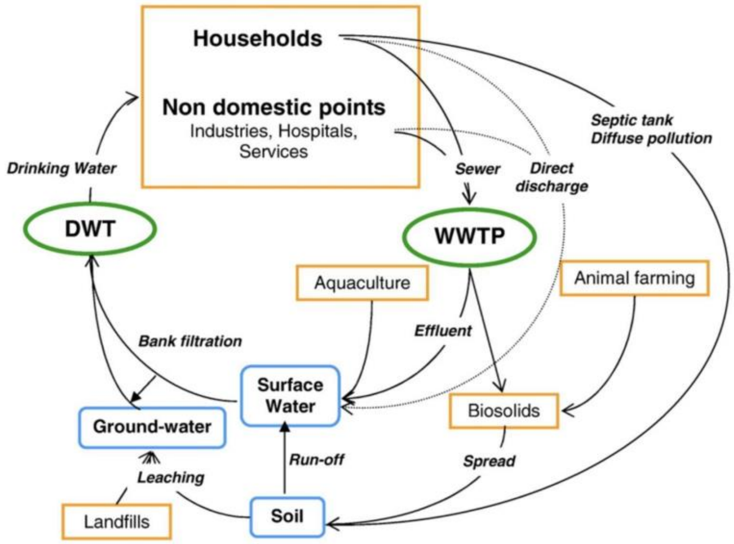

Fig. 1. Origin and routes of entry of pharmaceutical products into drinking water (Adapted from Petrovic etc al.,2003) [14].

Fate and occurrence of pharmaceuticals in environment:

Over 20,000 approved prescription drugs are available in the market and due to their low volatility, these pharmaceutical compounds are primarily disseminated in the environment through aquatic media to drinking water treatment plants (DWTPs) and wastewater treatment plants (WTPs), seawater, sediments, surface waters, and groundwater at concentrations ranging from parts per trillion (ng/L) to parts per billion (µg/L) [5-7]. Groundwater and surface water are interconnected physically, as a result, contamination can easily transfer between these two compartments [3].

Although the concentration of pharmaceuticals in influent sewage is relatively low, the presence of individual pharmaceutical molecules or complexes can seriously impact the efficacy of activated sludge bacteria, leading to deteriorated removal efficiency [6]. Previous research studies have shown that approximately 10-90% of administered pharmaceuticals are excreted from the human body in their original form, while the remaining part is excreted as metabolites and/or conjugated forms [4]. Despite the efforts to mitigate the issue, both humans and animals treated with pharmaceuticals remain a significant source of contamination for drinking water resources [3].

The numerous mechanisms that can effectively eliminate the pharmaceutical contaminants from aqueous phase of wastewater are biodegradation, sorption, air stripping and abiotic transformation. Complete biodegradation, also known as mineralisation, leads to the production of carbon dioxide and water, whereas partial or incomplete biodegradation involves the conjugation and breakdown of pharmaceutical compounds into a polar metabolite that can be easily excreted from the body [1,5].

Most of the time, conventional treatment serves to meet compliance requirements, and expensive advanced treatment techniques are rarely utilised to treat wastewater [8]. Activated sludge methods are frequently employed in conventional wastewater treatment. Pharmaceuticals that are biodegradable or quickly bind to particles have been removed significantly by biological treatment methods including activated sludge and biofiltration [9-11]. Higher pharmaceutical removal efficiency has been demonstrated by enhanced wastewater treatment procedures using membranes, complex oxidation technologies, etc. (for instance, diclofenac can be eliminated completely using advanced oxidation processes) [12]. About half of the pharmaceuticals studied were found to be oxidised by free chlorine, while chloramine was more ineffective. Among the chemicals that indicated a high elimination by free chlorine were antibiotics such sulfamethoxazole, trimethoprim, and erythromycin [13].

Regulations for monitoring the presence of drugs in environment:

To prevent deterioration of the environment, guidelines and procedures for routine monitoring and enforcement of laws controlling the proper disposal of pharmaceutical wastes must be mandatory for all healthcare facilities and the pharmaceutical sector in general [1,5,15].

In an effort to address the environmental impacts of both human and animal medications, from design and production to use and disposal, the European Commission and OECD acknowledged the European Union Strategic Approach and a set of policy guidelines to pharmaceuticals in the Environment, respectively. The approach comprised a number of actions that aimed to: (1) enhance awareness to promote responsible use of pharmaceuticals; (2) encourage the development of pharmaceuticals that are beneficial to the environment by nature and greener manufacturing; (3) raise the evaluation of environmental risks and its review; (4) minimise waste and improve waste management; and (5) extend environmental monitoring [7]. The US Environmental Protection Agency (USEPA) supported the launch of handling Pharmaceutical Waste Management: A 10-Step Blueprint for Healthcare Organizations in the United States, which demonstrates a methodical approach to assist health-care facilities in establishing and carrying out an extensive pharmaceutical hazardous waste management programme. In order to satisfy laws and regulations for the disposal of pharmaceutical waste and protect human health and the environment in an economical way, this blueprint promotes best practices in waste minimization [1].

In India, the Central Pollution Control Board, commonly referred to as the CPCB, along with the state pollution control boards (SPCBs), which were set up by the Water Act of 1974 and the Water Cess Act of 1977, had the authority to charge a fee on water users whose disregarded these regulations. The CPCB has released Minimum National Acceptable Standards which mandate that SPCBs follow the legislation in the pharmaceutical industry. In cases where an industry violates the Water Act, SPCBs hold the power to disconnect electricity and water supplies, shut down companies, and even initiate lawsuits in the public interest before the Supreme Court [5].

Detection of pharmaceutical compounds in fresh water and wastewater samples:

The rise in reported findings of trace amounts of pharmaceuticals in various environmental systems such as water resources (e.g., surface water, groundwater, treated wastewater effluent, and drinking water), can be credited primarily to advancements in detection technologies and analytical techniques. Advanced methods like Gas chromatography with mass spectroscopy (GC-MS), tandem mass spectroscopy (GC-MS/MS) and liquid chromatography with mass spectroscopy (LC-MS) or tandem mass spectroscopy (LC-MS/MS), high-performance liquid chromatography (HPLC), or high-performance liquid chromatography with tandem mass spectroscopy (HPLC-MS/MS) have significantly strengthened our ability to detect target compounds at extremely low concentrations from ng/L to μg/L in water and wastewater.

The choice of method depends upon the specific physical and chemical characteristics of the target compound. The target compounds that are more polar and highly soluble in water are detected by LC-MS/MS, whereas target compounds that are more volatile are detected by GC-MS/MS. Furthermore, a standardised practice or protocol for the sampling and analytical determination of pharmaceuticals in water or any other environmental media that ensures the comparability and quality of the data generated has not been established at present [1,5].

Table 1
Different classes of pharmaceuticals and their metabolites reported in wastewater from wastewater treatment plants (WTPs) in India (adapted from keshava et al., 2016)

Classes of pharmaceuticals	Contaminants
Anti-Schizophrenics	Quetiapine Norquetiapine
Sedatives-hypnotics-anxiolytics	Lorazepam Alprazolam
Antidepressants	Venlafaxine Bupropion
Antihypertensives	Propranolol Atenolol
Antimicrobial	Triclocarban Triclosan
Antibiotics/fungicides	Trimethoprim Sulfamethoxazole
Analgesics	Ibuprofen Acetaminophen
Antihistamine	Diphenhydramine DMPA
Antiplatelet	Clopidogrel Clopidogrel carboxylic acid
Antihypercholesterolemic	Atorvastatin
UV-filter	Oxybenzone
Illicit drugs	Cocaine Benzoylecgonine
Stimulant	Caffeine Paraxanthine
Artificial sweeteners	Saccharin Sucralose

The comparison of certain frequently discovered pharmaceuticals in sewage treatment plants throughout the world was published by Keshava et al., 2016, upon reviewing 19 published articles on the presence of pharmaceutical products in the aquatic environment such as wastewater treatment plants that utilise conventional activated sludge, healthcare facilities, rivers, and farms. The different countries included were India [16,17], Portugal [18], USA [19,20], Canada [21,22]; Australia [23], Italy [24], and China [25] shown in fig. 2. India reported the highest concentrations of ciprofloxacin and metoprolol, while China reported the highest concentrations of ofloxacin [4].

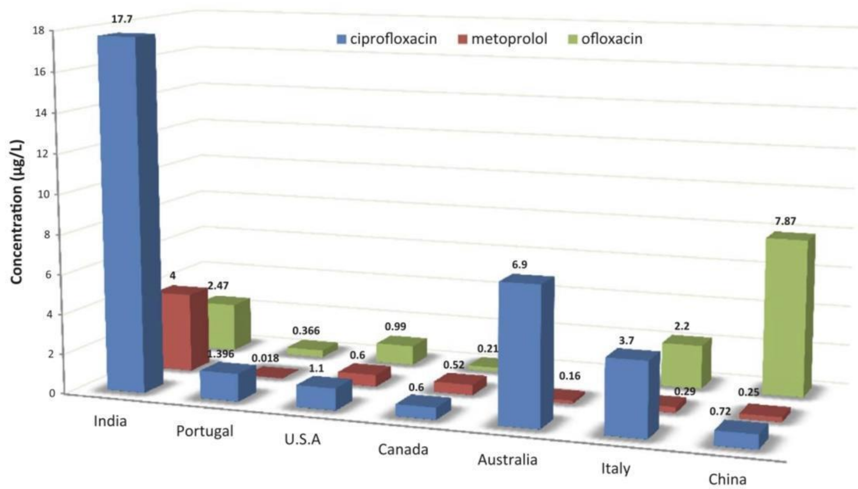

Fig. 2. Comparison of pharmaceuticals in hospital effluents in India (Adapted from Keshava et al., 2016)

Impact of pharmaceutical pollutants on water quality:

Pharmaceutical companies generate a wide range of chemical and biological components as effluents. These effluents' nature can result in changes in the water purity. Some aspects of drinking water quality indicators, comprising pH, temperature, total solids, total dissolved solid (TDS), total suspended solid (TSS), chloride, oil and grease, biochemical oxygen demand (BOD), and chemical oxygen demand (COD), revealed greater levels of contaminants in wastewater [5]. Along with other micropollutants, a broad range of medications are typically found in ambient fluids. This calls into question how dangerous these combinations are when combined. Most of the time, the cumulative toxic effect outweighs the impact of each individual compound's toxicity. It has been demonstrated that even though each drug exists in the mixture at low, individually safe concentrations, a substantial mixing effect is still possible [26]. Assessing risks in relation to pharmaceuticals presents several key challenges. Primarily, there is a scarcity of occurrence data specifically pertaining to pharmaceuticals in drinking water, the extensive variety of pharmaceuticals currently in circulation, the substantial differences in the utilisation of pharmaceuticals across different countries, the scarcity of publicly available data, and the technical limitations involved in determining risks associated with long-term exposure to low doses of pharmaceuticals and mixtures [1].

Health impacts due to pharmaceutical drugs present in fresh water and wastewater:

Even at such low concentrations of pharmaceuticals in WTPs, ranging between ng/L and µg/L, research suggests that these pharmaceutical residues can potentially impact the user's health through respiratory disorders, cancers, reproductive problems, chronic depression, and congenital problems including cognitive impairment and physical defects [5,6]. Additionally, these pharmaceutical residues can indirectly impact agricultural productivity, alter agricultural infrastructure, and contribute to significant losses in livestock and fish populations [5].

When reclaimed water and organic manures derived from sewage sludge are utilised, specific plant species have the capacity to absorb various pharmaceutical compounds. Pharmaceuticals tend to have the ability to cause bioaccumulation in fish and other aquatic organisms, resulting in unforeseen disruptions in their well-being. For instance, enlargement of livers can occur as a result of chronic exposure to estrogenic pollutants in water [6]. In earlier research, bacteria containing antibiotic resistance genes have been detected in biofilms that were exposed to drinking water bacteria. This discovery suggests that there could be a potential transfer of genes from surface and/or wastewater sources into the drinking water distribution systems. The widespread occurrence of such gene transfer could raise significant concerns regarding human health [2].

Certainly, the presence of pharmaceuticals would have a negligible impact on the health of adults with no underlying conditions. However, variations such as gender and maturation could lead to different levels of sensitivity and respond to toxicological tests for the same substances. Thus, it might be more noticeable in individuals who are young or elderly; as they might have a diminished capacity to eliminate toxic substances. In addition, people with allergy to specific compounds or those in vulnerable stages of life such as pregnancy could further exacerbate the effects [2].

Therefore, the importance of considering potential adverse effects cannot be ignored, particularly because there is limited knowledge regarding the environmental or human health risks associated with chronic, subtherapeutic levels of pharmaceutical substances or their).by-products. Furthermore, even in the absence of proven risks, the quality of drinking water will always be a major concern for consumers as it provides a direct pathway for drug compounds to enter the human body [2].

Occurrence of pharmaceuticals in drinking water:

Due to various factors and challenges many developing countries lack strict vigilance and routine testing policies for identification of pharmaceuticals and their byproducts in drinking water. The major challenges being are lack of analytical laboratories and other infrastructure, high costs and lack of standardised protocols in detecting pharmaceuticals in drinking water. A study conducted by Benotti et al in 2009 first reported the presence of high levels of meprobamate (40 ng/L) in drinking water in the USA [27]. Various other researchers reported the presence of various types of pharmaceuticals in different concentrations in tap water in countries like Germany, Netherlands and Italy in 2011 [28]. The drugs identified include anti-epileptic drugs, beta blockers, and antibiotics in traces which possess a direct risk to human health and environment. Therefore,it is the need of hour to conduct risk assessment analysis for ecotoxicological and human health in relation to pharmaceutical products and their metabolites [3,29].

CONCLUSION:

Pharmaceutical compounds, especially their metabolites, have become more prevalent in ecosystems that are both terrestrial and aquatic. Environmental pollution resulting from pharmaceutical products has drawn international attention and demands fresh laws and regulations. A major concern with regard to the purity of drinking water is the presence of micro pollutants in water supplies, such as pharmaceuticals [5]. Despite being one of the largest global manufacturers and consumers of medications, very few studies on pharmaceutical pollution in water bodies have been published in India. Various pharmaceutical residues, including psychoactives, antibiotics, analgesics, antihistamines, illegal drugs, and artificial sweeteners, have been found in sewage, rivers, and groundwater from households, hospitals, and factories. In comparison to WTPs in Europe, Japan, and Australia, domestic WTPs in India reported greater quantities of amoxicillin, ciprofloxacin, metoprolol, and ofloxacin in the treated effluents. The large variety of medications that are accessible over-the-counter in India might have led to the lack of treatment guidelines and ramifications as well as the greater amounts of drug remnants in the environment [4]. It is difficult to estimate the potential hazards to human health from exposure to trace traces of pharmaceuticals in drinking water as there is a less comprehensive, systematic surveillance research on pharmaceuticals in water, and there is also very little occurrence data accessible. Furthermore, there is no standard procedure for the analytical evaluation and sampling of medication [1]. In order to safeguard human health, the health of other organisms, and the environment from any kind of pharmaceutical-related contamination, significant investigations and research must be conducted to establish sustainable and long-term effective solutions [5].

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