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Advance Techniques for Diclofenac Removal from Pharmaceutical Wastewater: A Review

Amir Khan[1], Mohsin Anwer[2]
[1]Research scholar, Dept, of Civil Engineering, ZHCET, AMU Aligarh , UP , India
[2]Research scholar, Dept, of Civil Engineering, ZHCET, AMU Aligarh , UP , India
amirkhan.amu94@gmail.com[1]

Abstract

Diclofenac is an anti-inflammatory, non-steroidal drug used to treat pain and inflammatory disorders such as gout. Since diclofenac is not fully absorbed in the body, it is apparent that a part of it is defecated and enters the aqueous system. Diclofenac may also be fed to the natural environment by waste from the pharmaceutical industry. Diclofenac 's presence in nature may have adverse effects on living organisms. In reality, human life and the health of natural ecosystems can be widely jeopardized. Therefore, various remediation techniques, like advanced oxidation processes, membrane filtration, biological treatment, electro-coagulation etc., are reviewed and contrasted in this review paper in order to eliminate diclofenac from the waste water or reduce its life to a minimum. Though, currently, many conventional techniques are being used for the removal of such persistent compounds but more advanced techniques should be introduced to mitigate the environmental and human health risk.

Keywords: Pharmaceutical compounds, Diclofenac, Emerging technology, Removal efficiency.

1. Introduction

In the last twenty years, pharmaceuticals have gained immense attention for the bioactive chemicals in the environment [1]. These pharmaceutical compounds in water supplies are known as emerging contaminants because they remain unregulated or are currently undergoing a regularisation phase, while the directives and other regulatory frameworks are still not in placeThese compounds are increasingly released into the environment and are present in small quantities that may affect water quality as well as the possible effects on the supply of drinking water, the ecosystem and human health[2][3-8].While pharmaceuticals have been present in water for decades, only recently have their environmental levels begun to be quantified and recognised as a potential threat to ecosystems. Among the various pharmaceuticals, Diclofenac sodium, a non-steroidal pharmaceutical, is becoming a major issue as it is commonly found in the aquatic environment and is widely used with anti - inflammatory effects to treat rheumatoid arthritis.Usually, DCF is removed from the waste water during treatment process is about 21 percent to 40 percent. DCF, along with the synthetic hormone 17 a-ethinylestradiol, is one of the few pharmaceutical compounds that have been shown to be ecotoxic, affecting both aquatic and terrestrial environments.In this context , different methods for the removal of DCF and other pharmaceuticals present in aqueous media have been suggested and examined in the present study, such as membrane filtration, advanced oxidation processes, and activated carbon adsorption. The aim of this review is to provide a short insight in the field of emerging techniques and their applicability forremoving of DCF from the water for the benefit researchers, industry society as whole. After the profound literature review, it has been found that though the diclofenac residue can remove, somehow, by natural process but possible small quantity of DCF and toxic metabolites still present in the environment which have the potential toxic effects on many species. In order to better analyse toxicological effects of diclofenac and its metabolites, further studies are needed and the potential association of diclofenac with other pollutants must be considered in order to establish an appropriate and economical method of treatment for diclofenac and transformation products. More modern and advanced methods of treatment, such as advanced oxidation process, irradiation process, membrane process, electro-coagulation process, must be fitted with the tertiary treatment system, which is proven to be successful for many pollutants, including DCFs.

2. Diclofenac (DCF) and its properties

Diclofenac is an anti-inflammatory, non-steroidal drug used to treat pain and inflammatory disorders. DCF is given topically or orally and in the human body undergoes almost complete biotransformation. The DCF 's fundamental chemical structure is shown in Fig. 1. It was discovered that topical gel adsorption was 6-7% [4] is either the cleaned from the skin or remain stuck on to the garments. Dose ingested orally (as parent drug or metabolites) are excreted from urine in between65 and 70 percentand it about 20–30 percent in fece. Most DCF is metabolised in the human body and only b1 per cent of the oral dose is excreted as unmetabolized DCF. As a result of phase II metabolism, glucuronide and sulphate conjugates of DCF are formed, including glucuronic acid and taurine.. These conjugates constitute up to 11 per cent of the dose givenA regular intake of 100 mg has been specified for diclofenac by the World Health Organization. Below 1 mg of this dose is derived from the human body as DCF and around 11 mg as conjugates of DCF.

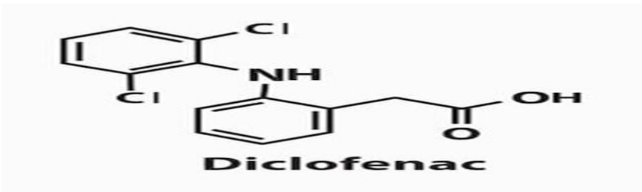

Fig.1 Chemical structure of diclofenac ($C_{14}H_{10}C_{l2}NO_2$)

Table 1: Physio-chemical properties of DCF

Important Parameters	**Value**	**Reference**
Solubility in water	2.37 mg/l	[5]
pKa	4.15	[5]
logKow	4.5	[5]
logKd (primary sludge)	2.7	[6]
	2.3	[7]
logKd (secondary sludge)	1.2	[6]
	2.1	[7]
logKd (MBR)	2.3-2.5	[7]
logKd (Sludge digested	1.3-2.2	[8]

Table 2: Percentage of diclofenac removal in different bioreactor membrane post treatment systems [9]

Treatment	**Diclofenac removal percentage**
Reversed osmosis	99.5
UV/H2O2-system	88.0
Combination of Ozone unit and GAC	99.5
Ozone unit and H2O2 addition	99.5
Ozone unit	99.5
Granular activated carbon (GAC)	95.0

3. DCF occurencein portable water, wastewaters, effluents and environment

In previous research, overall quantities of DCF in municipal wastewater ranged from 0.44 to 7.1 µg / l and average values ranged from 0.11 to 2.3 µg / l respectively.As per Vellinga et al [10], the mean concentrations reached 6.88 µg / l in hospital wastewater and 203 µg / l in South Korea in wastewater from pharmaceutical manufacturers. In municipal waste water, these ranges are substantially more than usually found. Zorita et al [11], on the other hand, calculated equivalent quantities (around 0.2 µg / l) in both municipal waste water and hospital in Sweden.Concentrations of municipal wastewater reflect the residents' use of DCF in the specific sewage system. The rates of consumption differ significantly between countries and within countries as well. This makes the typical amounts of waste water difficult to assess. DCFs Annual intake, per inhabitant, has been found between 195 and 940 mg of indifferent countries in municipal wastewater treatment plant effluents, with DCF among the pharmaceuticals most frequently detected. The fig 2 shows the entry of DCF through various routes in the environment.

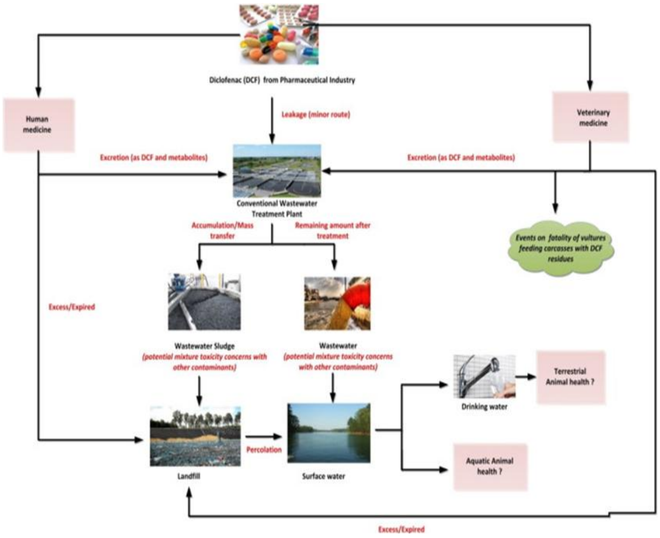

Fig.2.Entry routes of diclofenac to the environment.

Owing to its incomplete removal during treatment, when analysed using LC-MS / MS or GC / MS, concentrations of effluents seldom falldown the limits of detection of a few nano grammes/litre. According to the results, maximum effluent concentrations range from 0.12 to 4.7 µg / l and average concentrations of effluents range from 0.002 to 2.5 µg / l. In the secondary effluent of municipal wastewater treatment plants, DCF had the 8thhighest mean mass charge (240 mg/1000 inh), according to, out of the 73 pharmaceuticals examined. Additionally, DCF metabolites can also release to the atmosphereby effluents from the waste water treatment effluents.

4. Treatment methods:

4.1 Physio-chemical methods

In the treatment of waste water, physiochemical techniques such as ion exchange, precipitation, coagulation and flocculation, adsorption, chemical reduction, frothing and electrochemical methods, as well as combinations of other separate treatment processes, are mostly used from preliminary treatment to finally controlling theirtoxic concentrations accumulated in various wastewater at different levels[9-14].The efficacy of such conjugate treatments resides in their success when, due to their inefficiency in the extraction of dissolved COD and the introduction of complex chemicals into the system, direct physical or chemical treatments are not suitable for the handling of medicinal waste water.Although many techniques like precipitation-air floatation display more efficiency of removing COD over the process of coagulation-precipitation, it has been observed that the latter requires less operational costs (almost 25 percent) than the former.

4.2 Advance oxidation process

Advanced Oxidation Processes (AOPs) are of various of various techniques including heterogeneous and homogeneous,ultraviolet (UV) or solar visible irradiation based photo catalysis, electrolysis, ultrasonic,ozonation, wet air oxidation and treatment by Fenton. The other emerging technologies include microwave- and pulsed plasma-subject ionising radiation and treatment. In degrading the pharmaceutics compounds (PhACs), the AOPs use unique features of the oxidising agents. Some research studies have shown that, especially in the treatment of persistent contaminants or drugs such as diclofenac, these AOPs can be very successful. Mechanisms of degradation of such compounds can differ from treatment to treatment [12]. For example, the lytic activity of ozone is used to simultaneously digest and remove personal care products in the advanced oxidation process based on ozone. On the other hand, the stabilising ability ofreagents of Fenton and the degradation and mineralization potential of photo catalysis are used in the removal of pharmaceuticals compounds (PhACs) in the Fenton process. The effectiveness of ozonation in the treatment of effluent from wastewater treatment plants (WWTP) containing bio-refractory and/or hazardous materials, such as PhACs, has been well known in some studies. Fenton 's treatment greatly increases the biodegradability of pharmaceutical wastewater. In subsequent downstream biological treatment, the BOD to COD ratio is always enhanced by 3 to 5 times, making it easy to removethe waste. The general observation is that the process of Fenton alone can reduce wastewater COD by approximately 50 percent and only when combined with downstream processes such as aerobic biological degradation can the efficiency of COD removal increase to 98 percent.

4.3 Biological treatments

The use of microbes to degrade and transform pharmaceutical wastes into either harmless or usable forms has been a significant part of research. The proposed pathways are composting, vermicomposting, anaerobic and aerobic methods and their mixture of each of which has produced helpful co – product[13-17].It is acceptable for anaerobic processes due to the increased COD loads of pharmaceutical contaminated water. In an up-flow anaerobic stage reactor (UASR), studies have shown the biodegradability capacity of antibiotics, resulting in a 70 to 75 percent reduction in COD on antibiotic residues. Many researches show that when a hybrid system is applied to the treatment of waste water in a hybrid upstream anaerobic sludge blanket reactor combining the anaerobic sludge blanket and a filter, it gives a very significant increased Organic Loading Rate (OLR)i.e. 8 kg COD / m^3 d with a high COD removing efficiency of about 72 percent.

4.4 Electro-coagulation

Electro-coagulation increases speeds of the conventionally used coagulation process by introducing electric current. This is characterised by the production of OH ionsand provide a large surface area for the adsorption of organic ions and colloidal particles from the substrate, with subsequent separation of the flocks (insoluble) by electro-floatation.. Processes involving electro-coagulation for the removing the pharmaceutical from waste water have become a popular approach due to changes in which the processes are driven by renewable energy sources. The anode dissolves in electro-coagulation because of the application of electric potential yielding active coagulant precursors.Electrocoagulation was applied to real waste water containing pharmaceutical by Deshpande et al[14], where COD loadings decreased substantially by 72 percent and the BOD to COD ratio increased from 0.18 to 0.3. They showed the importance of saving of energy , high efficiency over a relatively short period of time, and overall increase in biodegradability of waste water..

4.5 Membrane Separation

As is evident in comprehensive studies,The emerging system based on membrane can be very lightweight, environmentally sustainable, small, scalable, economically viable, easy to mount, operate and maintain. These plants are recognized for their high separation degree, due to the high selectivity of the applied membranes, but polarisation concentration and fouling of membrane can sbe hinder in the way of sustainable operation unless it is managed with some appropriate module. In so many few certain tests, the reusability of the water recovered after membranebased on filtration has been shown. In a novel approach Bloetscher et al [15-20], The design of a LEED approved water treatment plant has been shown to result in the integration of a third stage reverse osmosis device with two-stage nano filtration systems.Taking into account the mentioned researches , the application of the technologies based on membrane to directly treat waste waterpharmaceutical has demonstrated concrete evidence of its effectiveness and highly diverse benefits. The high separation potential of membrane processes, along with all the objectionable persistent compounds, can act as an effective method for separating the organic load. They are suitable candidate technologies due to their modular nature,high flux, cost of maintenance is low and most important of the friendly of nature. Processes such as Ultrafiltration, Nanofiltration are feasible options as a potential secondary approach for dealing with residues of medicines present in municipal industrial effluent sludge.

4.6 Irradiation process

There are several pharmaceutically active compounds (PhACs) that can be extracted successfully with the application of gamma ray irradiation techniques or ionising irradiation, such as, hormones,antibiotics and X-ray contrast agents, antineoplastic drugs, and anti-inflammatory drugs. The main benefit of ionising irradiation is that the high removal efficiency exceeds almost 100 percent. However, the application of an irradiation procedure needs the utmost caution whenapplying an appropriate dose of radiation. Anumber of intermediate by- products, as result , are also produced at low doses ,where identification and even analysis becomes very difficult. And such several intermediates are even more harmful than the originally existing pharmaceutical. For full degradation, radiation doses over 1kGy need to be used without leaving the possible risk of creating more harmful intermediates. Combined treatment with gamma irradiation using H_2O_2 or TiO_2 can be more effective [16]. The study explained in great detail that irradiation techniques with a high degree of efficiency at a high radiation dose can remove pharmaceutical ingredients from various pharmaceutical waste streams. Nevertheless, there has been no standardised treatment method focused on irradiation method with faith scale-up. The table 3 shows the occurrences of DCF in waster bodies in different countries.

Table.3. Recent occurrences of DCF in various water bodies in different countries

Water bodies	Concentr-ations in mg/l	Country	Reference
Seawater	19.4	Brazil	[17]
River	230	China	[17]
River	34-145	Argentina	[17]
River	6.2	German	[18]
River	195	United Kingdom	[18]
River	18-50	Canada	[19]
River	2-3	Finland	[20]

Conclusions

Literature indicates that Diclofenac is one of the world's leading PhACs with a wide variety of applications. Diclofenac residues are present in land, ground and drinking water worldwide. Although the residue is removed by natural processes, such as photo oxidation, diclofenac is removed. The possible toxic metabolites and diclofenac are still present in the area. Diclofenac is found at lower concentrations in the environment, such as nanograms per litre to micrograms per litre, and it is clear from the available ecotoxicological evidence that these lower concentrations are capable of causing acute toxic effects on many species, such as mussels. There are less risks of acute toxicity at lower measured concentrations. However, persistent toxicological effects can result from repeated exposure to lower concentrations. In the case of diclofenac, the residue of DCF in the atmosphere is accelerated by constant entry into the setting due to the year-round use of medications. In order to better assess the fate and toxicological effects of diclofenac and its metabolites, further studies are needed and the potential association of diclofenac with other pollutants must be considered in order to establish an appropriate and economical method of treatment for DCF and transformation products. In addition, DCF metabolites must be recognized as another emerging contaminant along with DCF, and treatment approaches must also priorities metabolites. More modern and advanced treatment methods, such as advanced oxidation process, irradiation process, membrane process, electro-coagulation process, must be fitted with the tertiary treatment system, which is proven to be successful for many pollutants, including DCFs.

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