Review on Physicochemical, Chemical, and Biological Processes for Pharmaceutical Wastewater

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Abstract. Due to the needs of human life and health, pharmaceutical industry has made great progress in recent years, but it has also brought about severe environmental problems. The presence of pharmaceuticals in natural waters which might pose potential harm to the ecosystems and humans raised increasing concern worldwide. Pharmaceuticals cannot be effectively removed by conventional wastewater treatment plants (WWTPs) owing to the complex composition, high concentration of organic contaminants, high salinity and biological toxicity of pharmaceutical wastewater. Therefore, the development of efficient methods is needed to improve the removal effect of pharmaceuticals. This review provides an overview on three types of treatment technologies including physicochemical, chemical and biological processes and their advantages and disadvantages respectively. In addition, the future perspectives of pharmaceutical wastewater treatment are given.

1. Introduction
Pharmaceutical industry has been developed so rapidly in the past few decades that a large amount of pharmaceuticals is being used in many fields such as agriculture, poultry farming, fishery and human health [1]. Pharmaceuticals can be divided into three categories according to their production methods: extraction pharmacy, biopharmacy and chemical pharmacy [2]. Among them, chemical pharmacy is the main trend at present [3]. Although the use of pharmaceuticals has brought people a lot of benefits, also caused great harm to the environment due to its structural stability and non-biodegradation [4].

Pharmaceuticals as an emerging contaminant have been reported to be present in different environmental compartment such as soil, surface waters or even in drinking water [5], which might potentially cause negative effects on the environment and the human health [6]. A large amount of water is consumed due to the requirement of the pharmaceutical process, at the same time, some harmful drugs are secreted in the process and then merge with the water [7], resulting in a great production of wastewater, which has arisen the global occurrence of pharmaceuticals in aquatic solution as a serious problem. The main characteristics of pharmaceutical wastewater are as follows: (a) high concentration of organic contaminants, large concentration fluctuation and complex composition [8]; (b) high BOD value and COD value and large difference of BOD/COD value in wastewater [9]; (c) high NH$_3$-N concentration and chroma [10]; (d) high suspended solids concentration and salinity [11]. Therefore, pharmaceutical wastewater is difficult to be treated by wastewater treatment plants (WWTPs) which use conventional physicochemical and biological treatments. In this paper, three types of technologies including physicochemical, chemical and biological treatment for pharmaceutical wastewater are reviewed, aiming to offer a brief introduction of treatment of this refractory industrial effluent.

2. Technologies for pharmaceutical wastewater
2.1 Physicochemical processes

2.1.1 Coagulative precipitation Coagulation precipitation technology is currently widely used at home and abroad, because of its economic reliability which is the first choice of physical-chemical treatment technologies due to its economy reliability. Under the effect of charge neutralisation, bridging and netting by adding chemical agents [12], the stability of the colloids in wastewater is destroyed, resulting in colloidal coalescence, bonding, and precipitation under the action of gravity, thereby being separated from wastewater. Coagulants in common are divided into two categories: a. inorganic salt coagulant, mainly aluminum (aluminum sulfate, alum, etc.) and iron salts (ferric chloride, ferrous sulfate and ferric sulfate, etc.) b. polymer coagulants which can be divided into inorganics (PAC, PFS, etc.) and organics (polyacrylamide, etc.). By adding coagulants, it can not only play a role of adsorption and flocculation in wastewater, but also improve the biodegradability. However, this process has a low removal rate of dissolved substances and generates a large amount of chemical sludge, meanwhile, it is difficult to completely remove pathogens and toxic trace substances in wastewater. Therefore, it is often used as a pretreatment in sewage treatment.

2.1.2 Flotation Flotation process is an effective solid-liquid and liquid-liquid separation method, through accessing to a large number of micro-bubbles in the water to make it adhere to the concentration of similar pollutants in the wastewater, thereby floating to the water surface, so as to achieve the purpose of separation and removal of pollutants [13]. According to different ways to produce micro-bubbles, flotation process can be divided into the electro-flotation, induced air flotation and dissolved air flotation. Flotation process is commonly used for the separation of small particles whose density is close to or smaller than that of water, with the advantage of less investment, low energy consumption, simple process, easy maintenance and so on.

2.1.3 Membrane separation Membrane separation process is a method, including diffusion-dialysis, electrodialysis, reverse osmosis and ultrafiltration, which utilizes outside energy or chemical potential difference as a driving force to separate contaminants from wastewater [14]. Membrane separation can deal with wastewater that is difficult to be treated by traditional methods, and the change of water quality will not have a great impact on the treatment effect. This method has the advantages of simple process, convenient operation and no change of the nature of the sewage, but at present, it is a problem that the membrane module is expensive and prone to being polluted.

2.1.4 Adsorption Adsorption process is a method which utilizes porous solids (activated carbon, silica gel, artificial pumice and so on) to adsorb contaminants in wastewater so as to recover or remove contaminants, thus purifying wastewater [15]. Adsorption can reduce the concentration of refractory organic matter in wastewater, improve biochemical and recover useful ingredients, however, the cost of adsorbent is high, and the regeneration of adsorbent needs a further study.

2.1.5 Electrolysis By applying an electric current, an array of chemical reactions will happen to change the property and structure of organic pollutants in wastewater. The contaminants in wastewater can be oxidized and reduced by the hydrogen and oxygen produced at the two level of the electrode. In electrolysis, there is a variety of mechanisms, the electrochemical role which is the most important, coupled with flotation and flocculation, so as to remove contaminants in wastewater under their respective functions [16]. Electrolysis process has the advantages of simple operation and management, stable effluent quality, impressed decolorization effect and less area-covering. But the processing cost is high due to the high energy consumption.

2.2 Chemical processes

2.2.1 Fe-C Fe-C process, ferric-carbon micro-electrolysis technology, is also known as iron reduction
method, zero-valent method. The method generally uses cast iron scrap and activated carbon or coke as the electrolytic material and causes electric erosion under acidic conditions to form a plurality of fine galvanic cells in the iron filings and between the iron filings and the carbon powder, so as to generate a sufficient amount of active hydrogen, whose strong reducibility is able to decompose macromolecule organic matter. At the same time, Fe(OH)_3 flocs which have an adsorption effect are generated by Fe^{2+} under aeration conditions.

Therefore, Fe-C process is a method comprised of oxidation and reduction, adsorption, complexation and electric flocculation, which can change the shape and structure of contaminants to remove refractory substances, and improve biodegradability [17]. Its advantages are mainly simple process, low operating costs and wide range of applications, but there may be iron sludge problems and the need for active regeneration.

2.2.2 Fenton Fenton reagent is a combination of ferrous salt and hydrogen peroxide. Ferrous salt can catalyze hydrogen peroxide to generate hydroxyl radicals (•OH) with extremely high oxidation potential to oxidize organic compounds in wastewater. •OH with non-selectivity and extremely oxidizing ability (E_0=2.8eV) can degrade a variety of contaminants [9], therefore, Fenton process is suitable for treating the wastewater of high concentration, hard-degradation and toxicity or as pretreatment before biological treatment. Fenton oxidation has advantages of simple equipment, mild reaction conditions, easy operation and the use of a wide range, however, there is a large amount of iron ions in effluent, which needs follow-up treatment.

2.2.3 Ozonation Ozone is a strong oxidant with the redox potential of 2.07V, which has the highest redox potential among commonly use chemical oxidants and strong disinfection and sterilization. There are two oxidation mechanisms, namely direct reaction and indirect reaction. Direct reaction uses the strong oxidation of ozone to directly oxidize pollutants. Indirect reaction means that ozone decomposes in water to generate •OH with highly reactivity, thereby oxidizing contaminants in wastewater. On the other hand, ozone has the function of open-loop and chain scission, which can make the macromolecular organism become biodegradable small molecule organic substances, improving the biodegradability of the wastewater [18]. Therefore, ozonation is especially suitable for the pretreatment of high concentration, hardly biodegradable wastewater or the advanced treatment of the effluent of biological treatment, which has good treatment effect on organic pollutants of high stability and refractory in wastewater. The advantages of this method are fast rate, good effect, no secondary pollution and the less remaining sludge.

2.2.4 Photocatalytic oxidation The n-type semiconductors such as TiO_2, SrO_2, WO_3, SnO_2 and so on, are used as catalysts for photochemical degradation in photocatalytic oxidation process. When these catalysts are irradiated by ultraviolet light, electron-hole pairs (h^+•e^-) will be formed and then migrate to the semiconductor surface, resulting in a strong oxidation effect to generate •OH which can oxidize contaminants in wastewater [19]. Photocatalytic oxidation process with its strong oxidizing power, no secondary pollution and mild reaction conditions becomes an effective method of treating refractory organic wastewater, which has a broader prospect, and the search for the photocatalyst of low cost and strong stability is the main research direction.

2.3 Biological processes

2.3.1 SBR Sequencing batch reactor is completely mixed on flow pattern, which is a “water injection - reaction - drainage” type of reactor. It is a kind of activated sludge sewage treatment technology operated by intermittent aeration, consisting of five basic processes: injection, reaction, precipitation, drainage and idleness. All the processes take turns in a reactor with aeration stirring device, therefore, there is no need for a separate sedimentation tank [11]. The method has the advantages of simple process, flexible operation, simple maintenance and management, strong compliance with impact resistance, stable
effluent quality, so it’s suitable for treating the wastewater with large fluctuations of water quality and amount. However, SBR process takes a long time to carry out sludge settling and separation, and when treating high-concentration wastewater, it is necessary to maintain high sludge concentration, lest high viscosity bulking happened.

2.3.2 **UASB** Upflow anaerobic sludge bed process is an anaerobic biological treatment technology, whose reactor is mainly composed of influent water distribution system, reaction zone, three-phase separator, gas chamber and treated water discharge system. At the bottom of the reactor, there is a high concentration of highly active sludge that converts most of the organic contaminants to CH₄ and CO₂ when the wastewater passes through the reactor from bottom to top. Due to the agitation of the digestive gas and the adhesion of bubbles to the sludge, a sludge suspension layer is formed above the sludge layer, which needs the three-phase separator to complete the separation of gas, liquid and solid phases [20]. UASB reactor has the advantages of compact structure, large processing capacity, no mechanical stirring, good treatment effect and low investment cost. However, it’s difficult in microbial domestication and complex in management. In the initial stage of start-up, the intermittent pulse influent needs to make up for the insufficient contact between the bacterial cells and the matrix caused by insufficient gas production.

2.3.3 **MBR** Membrane bioreactor process is a combination of membrane technology and wastewater biological treatment technology, which uses an ultrafiltration membrane instead of secondary sedimentation tank to achieve sludge solid-liquid separation. As a sewage treatment technology integrated with concentration and separation, MBR process can intercept activated sludge and macromolecular organic contaminants by membrane separation device, overcoming the problem of sludge expansion in the traditional activated sludge process. In addition, it can control hydraulic retention time and sludge residence time flexibly, increase the concentration of activated sludge in the aeration tank to improve the biological degradation rate and achieve automatic control. That not only improve the removal efficiency of contaminants, but also make the effluent in many cases can be recycled directly [21]. Membrane bioreactor has the advantages of strong microbial biomass interception ability, high operation stability and high effluent quality. However, there are still some disadvantages such as high cost, easy contamination of membrane module, limited membrane service life.

3. Conulsion
The pharmaceutical industry is one of the largest and prominent industries worldwide. At the same time, the increasingly severe pollution caused by pharmaceutical wastewater highlights the need for a sustainable treatment process. In this review, a number of treatment technologies and their advantages and disadvantages were summarized. To reach the discharge standard, a combination of different treatment technologies needs adopting. The conventional combed process usually decreases the concentration of contaminants or recycle available components in wastewater, meanwhile improving the biodegradability by physical or chemical pretreatment, and then the biological treatment is adopted to further remove the contaminants in wastewater. On the other hand, future research should focus on the treatment effect and the cost of these potential processes for pharmaceutical wastewater.

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