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CHEMICAL KINETICS OF OZONATION AND OTHER PROCESSES USED FOR THE TREATMENT OF WASTEWATER CONTAINING PHARMACEUTICALS: A REVIEW

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ABSTRACT

In the last decade, considerable interest has developed regarding the presence of pharmaceuticals and threat due to their presence in the water but comparatively little has been studied to understand and counter the potential effects of these pharmaceuticals. A number of reports about the ozone treatment of pharmaceutical wastewater have been published over the years but no comprehensive review has been published, especially during the last decade. Thus the aim of this paper is to present a review of treatment of wastewater containing pharmaceuticals by ozone and other advanced oxidation processes. An attempt has been made to assess the effect of ozonation and kinetics of different chemical reactions taking place during the treatment of wastewater mainly containing pharmaceuticals. It was observed that rate of degradation of some of the pharmaceuticals, especially antibiotics, is affected greatly by pH i.e. ozonation rate improved at higher pH compared to low. For the processes studied, it can be concluded that high removal efficiencies for pharmaceuticals can be achieved by alkaline ozonation and O_3/H_2O_2. The study will give technical overview and useful information to the engineers and researchers who will work for the betterment of research activities in this field in future.

Keywords: Ozonation, Pharmaceuticals, Rate constants, Rate of degradation.

INTRODUCTION

Growing industrialization has given rise to the discharge of liquid, solid and gases into natural systems, which has been degrading the environment consequently. It increased the number of diseases in turn, which necessitated the production of a wide array of pharmaceuticals to combat. In order to manufacture these pharmaceuticals a huge quantity of water is required industrially which produces large amount of wastewater. Manufacturing of bulk pharmaceuticals involve a number of unit operations and unit processes including chemical synthesis, extraction, fermentation, and many other complex methods. Thus characterization of released pharmaceuticals and manufacturing industry is difficult [1]. Because of such diversity, chemical kinetics of these pharmaceuticals is complex, depends upon the type of particular pharmaceutical involved and treatment processes. Numerous studies have reported the occurrence of trace pharmaceuticals (mainly antibiotics) in aquatic environments worldwide [2-3]. Not all the pharmaceutical compounds are completely removed in sewage treatment plants [4-7].

Various technologies have been evaluated for the removal of pharmaceuticals: chlorination [8], biodegradation [9], photo-degradation [10-12], membrane filtration [13], activated carbon [14] and ozonation [15]. Many studies presented in that review reported important observations such as degree of reaction, reaction kinetics, degradation pathways and by-products of oxidation of pharmaceuticals using ozonation and advanced oxidation processes [16]. For ultimate treatment of all types of inorganic/organic impurities in

water/wastewater, ozonation and advanced oxidation treatment has become the most important treatment technique [17]. Many researchers found ozonation particularly effective in achieving over 90% degradation for a variety of pharmaceutical compounds [18-22].

Literature Review

Human drugs in the environment were first reported in the mid 1970s [23]. The research work on the application of ozonation process in wastewater treatment started in the late forties [24]. Large number of applications of ozonation in drinking water treatment, industrial wastewater treatment, biomedical waste treatment etc. has been reported in literature [25]. Many researchers have worked on pharmaceutical wastewater treatment by ozone or ozone combined with H_2O_2 and UV. Most of the research works in this area is related to the mechanism of direct or indirect reactions of ozone and calculation of rate constants [26].

In almost all the reported cases so far, synthetic samples were used and thus the results deviate when the treatment of actual samples from pharmaceutical industries, are carried out [27]. Thus, description of treatment of any wastewater containing pharmaceuticals or pharmaceutical industry wastewater treatment is complex. For ultimate treatment of a variety of organic pollutants water and wastewater, ozonation and advanced oxidation treatment has emerged as important treatment techniques [28-30]. With a focus over the past decade, given below is the review of research carried out relevant to the present paper.

Degradation of cefradine (an antibiotic) was studied using an immobilized TiO_2 photo catalyst. At an unknown pH, near complete conversion of 70 mg/lit cefradine was achieved in 2 hours. Rate of degradation was found to have increased when H_2O_2 was added [31].

Ozonation experiments of 4-chlorophenol were conducted in a homogeneous system and reactions of chlorophenol mixtures were performed in a heterogeneous system [32]. The overall rate constant for the reaction between ozone and chlorophenols were also evaluated. The second order rate constants increased (i.e. from 10^3 to 10^9 lit/mol.s) with increase in pH. It was concluded that experimental results obtained for k_{O3} at pH = 2.5 agree satisfactorily with the theoretical values calculated.

Conversion of sulfachlorpyridazine (a variety of sulfonamide antibiotics) by ozonation was reported. At pH value of 7.5 and ozone dose of 0.3 mg/lit, more than 95% of initial sulfachlorpyridazine was converted in 1.3 minutes [33]. For the reaction between hydroxyl radicals and sulfachlorpyridazine and some other sulfonamide antibiotics, the second order rate constants were been reported [34].

Presence of carbamazepine, an anti-epileptic drug, in sewage treatment plant effluents as a result of its low biodegradability was reported and analysis was carried out for its removal by ozonation process through the kinetics assessment [35]. Low degree of mineralization was observed after 60 min of ozonation treatment and it was concluded that ozonation is suitable for carbamazepine reduction even at the process conditions.

Slow degradation of diazepam (an anti-anxiety agent) by molecular ozone with a second-order rate constant of 0.75 M^{-1} s^{-1} at 20^0C was analyzed. The analysis revealed that the diazepam degraded mostly through hydroxyl radical reactions with rate constant 7.2 x 10^9 M^{-1} s^{-1}. Degradation of any intermediate or by-product formed was not determined [36].

Industrial wastewater treatment by ozonation in a gas-induced reactor with chemical coagulation pretreatment was investigated [37]. Kinetic investigations were also made using a proposed complex kinetic model, which revealed that adsorption of organic pollutants onto granulated activated carbon is a faster and more important step than liquid-phase oxidation of these

pollutants. It was concluded that final effluent after chemical coagulation and combined granulated activated carbon adsorption/ozonation treatments was free from any color and had a COD concentration much lower than 100 mg/l which was recommended to be considered for non-potable use.

Fast reaction of lincomycin (an antibiotic) towards ozonation was investigated using a stopped flow technique. For both protonated and neutral form, the absolute second-order rate constants were calculated as 3.26×10^5 and 2.43×10^6 $M^{-1}s^{-1}$ respectively [38]. It was concluded that the degradation of lincomycin by ozonation is pH dependent and no significant role of hydroxyl radical reactions was reported.

Advanced oxidation studies of the pharmaceutical diclofenac (a widely used anti-inflammatory drug) with ozone and UV/H_2O_2 were carried out. For kinetic experiments, ozonation runs were carried out at three different pH values (5.0, 5.5 and 6.0). After 90 minutes of treatment, 32% degree of mineralization for ozonation and 39% for UV/H_2O_2 was observed. To prevent radical oxidation, tert-butyl alcohol (a radical scavenger) was also used. Under the conditions studied, both ozonation and UV/H_2O_2 showed good degradation efficiencies but further investigations were recommended for the prediction of kinetics and intermediate products formation [39].

Ozone treatment of antibiotics producing wastewater mainly containing amoxicillin from chemical and kinetic point of view was carried out. Chemical investigations showed that the ozonation process is characterized by low degree of mineralization even for longer treatment times [40]. The observed low degree of mineralization and structures of intermediates and products of amoxicillin ozonation strongly suggested the need of further investigations in order to assess their eco-toxicological behavior.

Assessment of the potential of chlorine dioxide (ClO_2) for the oxidation of pharmaceuticals during wastewater treatment for the determination of rate constants was carried out [41]. Experiments performed at µg/L to ng/L levels proved that the rate constants determined in pure water could be applied to predict the oxidation of pharmaceuticals in natural waters. It was reported that compared to ozone, ClO_2 reacted more slowly and with fewer compounds, it reacted faster with the investigated compounds than chlorine. In conclusion, the results indicated that ClO_2 will only be effective to oxidize certain compound classes such as the investigated classes of sulfonamide and macrolide antibiotics, and estrogens.

Some 25 pharmaceuticals, hormones & fragrances were treated and pseudo first-order degradation kinetics was observed for all compounds. After experimental evaluations, compounds could be divided into different classes according to their rate constant and persistence in wastewater (i) for $k_{biol}<0.1$: no removal, (ii) for $0.1< k_{biol}<10$: partial removal and (iii) for $k_{biol}>10$: transformation by more than 90% . It was concluded through an overview of k_{biol} values that biological degradation in studied wastewater treatment contributed only to a limited extent to the overall load reduction of pharmaceuticals [42].

In ozonation and kinetics study of bezafibrate (a lipid regulator largely used for the treatment of hyperlipidaemia), BOD_5 measurements indicated that a 0.5 $mmolL^{-1}$ aqueous solution of bezafibrate was not readily biodegradable. Second-order kinetic constants were estimated; for the ozone attack at pH 6.0, 7.0 and 8.0 in the range between 2.7×10^3 and 1.0×10^4 $Lmol^{-1}$ s^{-1} with absolute method and 1.5×10^3 & 1.3×10^4 $Lmol^{-1}$ s^{-1} with the competition method [43]. It was concluded that ozonation is a suitable technique to improve the biodegradability and reduce the toxicity of waters containing bezafibrate, although it was recommended that the optimal ozone dose needs to be determined according to the effluent composition.

Pharmaceutical compound sulfamethoxazole from wastewater was subjected to different oxidation processes involving ozonation, photolysis and catalysis under different experimental conditions [44]. All treatment processes were compared with respect to removal rates of sulfamethoxazole and total organic carbon (TOC). Conclusions drawn from the study were as follows: ozonation allowed fast removal of sulfamethoxazole in water and the use of combined ozone systems were reported appropriate to reduce the reaction time needed for total disappearance of sulfamethoxazole. Photocatalytic oxidation (O_2/UVA/TiO_2) allowed significant elimination of sulfamethoxazole but it was observed that it needs some higher reaction time than the O_2/UVA/TiO_2 system. Ozone alone could remove only 10% TOC (total organic carbon), while O_3/UVA/TiO_2 system gave highest TOC removal rates. To eliminate the toxicity of the water, photocatalytic oxidation systems with oxygen or ozone were reported to be the most appropriate technologies. It was concluded that the mechanism of photocatalytic ozonation mainly involves direct ozone reaction with sulfamethoxazole, and for TOC elimination, free radical oxidation & surface reactions were the main mechanisms of oxidation.

Ozonation of naproxen and carbamazepine during catalytic and non-catalytic semi-continuous oxidation experiments at 25^0C in the pH range 3-7 was carried out. The catalyst TiO_2 increased the mineralization compared to ozonation without catalyst and also enhanced it in both acidic & neutral solutions. Second order kinetics was assumed between organic compounds and ozone. It was observed that catalyst promotes ozone decomposition under acidic conditions, while it behaved as an ozone decomposition inhibitor at neutral pH. When the pH was increased, the rate constant of the first mineralization period also increased and the rate of mineralization was found decreased when the concentration of hydroxide was increased. Experiments carried out in the absence of ozone indicated that the adsorption of intermediates could not reduce dissolved organic carbon during the ozonation reaction [45].

Ozonation of an effluent from a wastewater treatment plant was performed using alkaline ozone and a combination of ozone and hydrogen peroxide. Application of alkaline ozone resulted in some degree of mineralization but complete mineralization could only be achieved after adding hydrogen peroxide. The measured organic matter as TOC and the hydroxyl radicals produced from the peroxide-induced ozone decomposition was fitted into a second order reaction kinetics model [46]. Over 99% removal efficiencies were observed after 5 minutes for most compounds irrespective of the use of hydrogen peroxide. It can be concluded that for reducing the total charge of pollutants (in bio-treated effluents) both alkaline and hydrogen peroxide ozonation are a promising alternative.

Studies of the kinetics and mechanism of p-chloronitrobenzene (pCNB-is a toxic, not readily biodegradable compound used in the production of pharmaceuticals, pesticides, antioxidants etc.) degradation by ozone were conducted. Nitrobenzene and chlorobenzene were taken as reference compounds and reaction rate constants of pCNB with O_3 and •OH were observed as 2.6 x 10^9 L mol^{-1} s^{-1} and 1.6 L mol^{-1} s^{-1} respectively for reactions between pCNB and •OH/O_3. Increased concentration of chloride and nitrate ions observed during ozonation, was reported to be almost equal to the reduced concentration of pCNB. It was concluded that the radical scavengers (CO_3^{2-}/HCO_3^-) prohibited the carboxylic acids to mineralize further into CO_2, thus the TOC of the water sample decreased very slowly at the latter period of pCNB ozonation [47].

Chemical, photochemical and surface reactions control the photocatalytic ozonation of sulfamethoxazole and the kinetic regime of ozonation corresponds to fast reaction [48]. Hydroxyl radical and photocatalytic reactions

were reported to contribute mainly for the removal of total organic carbon.

Ozonation of some pharmaceuticals in the pH range between 2.5 and 9 and the rate constants for the reactions between ozone and the selected compounds were studied. Simultaneous ozonation of the pharmaceuticals in different water matrices was also carried out. The influence of the operating conditions such as initial ozone dose, nature of pharmaceuticals and type of water on the pharmaceuticals elimination efficiency was established. A kinetic model was proposed for the evaluation of the partial contribution to the global oxidation of both, the direct ozonation reaction and radical pathway [49].

During the ozonation study of various pharmaceuticals, endocrine disrupting compounds and pesticides, second-order rate constants for the reactions of selected compounds were determined. Bench-scale experiments were also conducted with surface waters spiked with 16 target compounds to assess removal by oxidation using ozone. The second-order rate constants for direct molecular ozone reaction were determined as 650±22, 601±9, 558±9, 2215±76 and 1427±62 M^{-1} s^{-1} in ultrapure water buffered to pH 8.10, respectively. Variation in pH did not affect the kinetics. It was observed that ozone is effective for removing trace organic contaminants from water and could be concluded that over 80% of caffeine, pharmaceuticals and endocrine disruptors were removed by ozonation [50].

Treatment studies of heterogeneous catalytic wet peroxide oxidation systems using a nano-composite (Fe_2O_3/SBA-15) catalyst were conducted to analyze wastewater [51]. The pH of the reaction medium was reported to have critical influence in Fenton-like reactions and a pH between 3 and 4, optimum for advanced oxidation processes (AOPs). The effect of the reaction temperature showed that a temperature of 80^0C is necessary for total organic carbon degradation. Increase in temperature from 80 to 100^0C resulted in a slight increase in TOC conversion, especially at final reaction.

Survey of over seventy individual pollutants (mainly pharmaceuticals and personal care products, as well as some metabolites) in a sewage treatment plant was conducted over one-year period from sewage treatment plant. The ozonation results showed that paraxanthine, caffeine and acetaminophen were the main individual pollutants usually found in concentrations over 20 ppb. Ozonation with doses lower than 90 μM allowed the removal of many individual pollutants including some of that more refractory to biological treatment. The kinetic analysis allowed the determination of second order kinetic constants for the ozonation of pollutants in its wastewater matrix and ozonation treatment yielded high removal efficiencies of most individual pollutants detected in treated wastewater [52].

Three tertiary-treated wastewater effluents were analyzed to determine the impact of wastewater quality on ozone (O_3) decomposition and subsequent removal of some organic contaminants including pharmaceuticals, endocrine disrupting compounds, and personal care products. The O_3 dose was normalized based on total organic carbon and nitrite to allow comparison between the different wastewaters with respect to O_3 decomposition. The decomposition of ozone occurred at different rates in the three wastewaters [53]. Advanced oxidation using ozone and hydrogen peroxide did not increase the net production of hydroxyl radical compared to ozone under the conditions studied. Trace contaminants greater than 95% were removed with second order reaction rate constants with O_3 (k_{O3}) > 10^5 M^{-1} s^{-1} and with OH (k_{OH}) > 10^9 M^{-1} s^{-1}.

Ozonation of the quinolone antibiotic levofloxacin at different pH revealed strong influence of pH on levofloxacin degradation rate as well as reaction pathways whereas addition of different H_2O_2 amounts (concentrations 2-100

μM) had only limited effect. At pH 10, the tertiary amine at the piperazinyl substituent was found unprotonated leading to fast ozonation and high concentrations of the N-oxide degradation product. At pH 7, degradation at the quinolone moiety was also observed, probably mediated by reaction with hydroxyl radicals. It was concluded that degradation was about 2 times faster at pH 10 compared to pH 3 and 7 explained by direct ozonation [54].

Investigations on the aqueous degradation of two cytostatic drugs (cyclophosphamide and methotrexate) by ozone were made [55]. The second-order rate constant, for the reaction of cyclophosphamide with molecular ozone and hydroxyl radicals, was also determined as 3.3±0.2 $M^{-1}s^{-1}$. The study showed that ozone is very effective to oxidize methotrexate and it was found that high contact time would be required to remove cyclophosphamide in natural water matrix. Further research was recommended to examine the ozonation efficiency for the removal of relevant cyclostatic drugs and their byproducts.

Degradation study by advanced oxidation techniques were carried out by selecting some commonly used pharmaceuticals and personal care products in laboratory bench scale experiments. The research was conducted to find the appropriate treatment technique out of seven advanced oxidation methods in laboratory batch experiments. Physicochemical properties of the compounds and solution pH showed substantial effect on the removal of pharmaceutical compounds [56]. Based on kinetic analysis and removal profiles, ozone/UV treatment was found to be most appropriate method.

Oxidation studies of hydrochlorothiazide by ozone, UV radiation and hydroxyl radicals were performed. Influence of some operating variables on the degradation process was determined and kinetic parameters were also evaluated. By using competition methods of kinetics, the values obtained for the second-order rate constants varied from 91.3 $M^{-1}s^{-1}$ at pH = 3 to 16 400 $M^{-1}s^{-1}$at pH = 9. A kinetic model was proposed for the prediction of the elimination of the selected pharmaceutical, which could reproduce experimental data well [57].

Ozonation runs were made to determine rate constants for direct reaction between ozone and benzotriazole at pH values ranging from 2 to 10.2. The behavior of benzotriazole was predicted in ozonation and advanced oxidation processes. The second order rate constants were determined by two different methods [58]. The rate constants were found to vary from $1.7x10^{10}$ M^{-1} s^{-1} at pH 2 to $6.2x10^{9}$ M^{-1} s^{-1} at pH 10.2. Further investigations for the identification and quantification of byproducts formed and also for the evaluation of toxicity and biodegradability were suggested.

Degradation characteristics of sulfamethoxypyridazine (pharmaceutical-antibacterial agent) through oxidation experiments by ozonation and photocatalysis were studied. Sulfamethoxypyridazine followed pseudo first-order kinetics. At pH 6, sulfamethoxypyridazine degraded almost completely within 7 hrs in UV/TiO_2. At the same pH the reaction rates for its decomposition in water were observed as highest compared to runs at pH 3 and pH 11. Ozonation was concluded to be superior to photo-catalysis for the removal of selected compound [59].

Catalytic ozonation studies of some pharmaceutical compounds were performed and a two-step first order kinetic model was proposed. The compounds were observed to be removed completely in less than 10 minutes through fast direct reactions with ozone with or without the presence of catalyst (Al_2O_3 or Co_3O_4/Al_2O_3). By using the same catalyst, chemical oxygen demand (COD) and total organic carbon removal efficiency were found to have improved by single ozonation process [60]. It was concluded that the presence of catalyst does not rapidly improve the removal of pharmaceutical compounds but they

affect the mineralization of these pharmaceutical compounds.

Degradation studies of tetracycline (a pharmaceutical compound) by ozone at laboratory level at different pH, gas flow rate, gaseous ozone concentration, H_2O_2 concentration were carried out and pseudo-first order kinetic model was developed [61]. It was reported that the tetracycline degradation rate increased with increase in pH, gas flow rate, and gaseous ozone concentration. H_2O_2 addition or radical scavenger had little effect on the rate of removal of tetracycline. It was also observed that ozonation is a dominant process and radical contribution could be neglected.

Advanced oxidation processes (ozone, electron beam and UV) were studied to evaluate the degradation and mineralization of antibiotics (sulfamethoxazole and chlortetracycline). The oxidation efficiency of each organic compound was observed to be dependent upon the advanced oxidation process used and algal toxicity significantly reduced after each treatment. The rate constants of hydroxyl radicals and hydrated electrons for sulfamethoxazole were (8.5±0.3) x 10^9 M^{-1} s^{-1} and (1.0±0.03) x 10^{10} $M^{-1}s^{-1}$ [62], respectively, and the rate constants for chlortetracycline were (5.2±0.2) x 10^9 M^{-1} s^{-1} and (1.3±0.2) x 10^{10} M^{-1} s^{-1}[63]. The rate constant for the reaction of sulfamethoxazole with ozone was reported as 5.5 x 10^5 M^{-1} s^{-1} and the degradation of sulfamethoxazole was found to be dependent on ozone but independent of hydroxyl radicals during ozonation [64]. Electron beam process was concluded to be effective for the degradation of sulfamethoxazole and chlortetracycline, while ozone and UV were used to selectively treat the antibiotics. For detailed analysis of intermediates and products formed, further studies were suggested [65].

Kinetic study and toxicity assessment of ampicillin by ozonation were performed. Experiments were carried out to study the pH effect under different conditions (5, 7.2, and 9) on ozonation of ampicillin and degradation efficiency of ampicillin was also determined. Under the pH conditions, the second-order rate constants (2.2-5.4 x 10^5 $M^{-1}s^{-1}$) for the direct reaction of ampicillin with ozone were measured [66]. At pH 5, the acute toxicity and lower biodegradability was observed. It was concluded that higher pH conditions are required for the removal of ampicillin and toxicity of ampicillin and intermediates formed.

CONCLUSIONS

From the reviewed literature, it was observed ozone treatment alone or in combination with H_2O_2 and/or UV can remove pharmaceuticals from wastewater in less time compared to other processes but when such processes are used with a catalyst, they affect the mineralization greatly. However, addition of hydrogen peroxide does not result in complete mineralization. The presence of catalyst does not normally enhance the rate of reaction rapidly, although required time reduces when advanced oxidation processes are compared with other treatment processes. Since the hydroxyl radical concentrations depend mainly on the pH of the solution, decomposition of a substrate in ozonation processes proceeds by direct oxidation by ozone or indirect oxidation by hydroxyl radicals.

Some of the pharmaceutical compounds were reported to follow first order kinetics while majority of pharmaceutical compounds (like benzotriazole, carbamazepine, clofibric acid, chlorophenol mixtures, paraxanthine, caffeine, and acetaminophen), endocrine disrupting compounds and personal care products followed second order kinetics. In case of ozone treatment of some of the pharmaceutical compounds which follow first order kinetics, COD and TOC removal efficiencies increases comparatively. In case of pharmaceutical wastewater ozonation with or without catalyst, in the acidic to neutral pH range, adsorption of intermediates could not

reduce dissolved organic carbon during the ozonation reactions in the absence of ozone.

In some cases high removal efficiencies of pharmaceuticals were achieved by employing alkaline ozonation and O_3/H_2O_2. Degradation rate of some of the pharmaceuticals (especially antibiotics) is affected greatly by pH i.e. ozonation rate improved at higher pH compared to low pH. In case of endocrine disrupting compounds, pH variations do not affect the kinetics. To assess eco-toxicological behavior of antibiotics, further research is required. Due to the direct reaction of ozone with pharmaceutical compounds, identification and quantification of byproducts formed is still not conclusive and thus further investigations are suggested.

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