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Catalytic Ozonation of Aqueous Solution of Paracetamol

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Abstract—The catalytic properties of iron ions in the oxidative destruction of the active pharmaceutical ingredient paracetamol, in the presence of hydrogen peroxide have been investigated. It was found that in the presence of a homogeneous catalyst, the oxidation degree reaches more than 98%. The dependence of the oxidation efficiency on the concentration of the catalysts (hydrogen peroxide and ferrous ions) has been determined. A scheme for the treatment of pharmaceutical effluents is proposed, including the stages of homogeneous ozonation, coagulation of oxidative destruction and filtration products, and adsorption on activated carbon. The concentration of paracetamol and the chemical oxygen demand in the model solutions after treatment does not exceed the maximum permissible levels.

Keywords: catalytic ozonation, paracetamol, pharmaceutical effluents, ferrous sulfate, hydrogen peroxide

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INTRODUCTION

Undoubtedly, over the past decade, the production of pharmaceuticals has increased significantly not only abroad, but also in Russia [1]. The emergence of new dangerous infections (in particular SARS-CoV-2) has contributed to an increase of the pharmaceutical market share of new, highly effective biologically active substances, analgesics, antibiotics, antiseptics, etc. Along with the development of the pharmaceutical industry, the problem of proper pharmaceutical waste disposal has also arisen.

Paracetamol is one of the widely used antipyretic analgesics. Abundant evidence is available on the presence of paracetamol in waste and natural waters all over the world, which leads to a conclusion that the present treatment technologies are unable to reduce the concentration of paracetamol to a safe level. Paracetamol, compared to other active pharmaceutical ingredients (APIs), is most commonly found in natural waters, in about 75% of cases, due to its persistence in the environment and ubiquitous use [2]. Paracetamol has also been found in drinking water in the USA, France, Spain, and Canada at concentrations ranging from 0.0003 to 0.298 mg/L [3].

The reasons for the environmental pollution with APIs are incomplete wastewater treatment and improper disposal of expired or spoiled medicines. As a result, APIs enter ground and surface waters from dumpsites. Gradually, they accumulate in the environment and, consequently, in plants and animals, which can lead to disturbances at the organ and cellular levels [4–5].

In recent years, active research has been carried out in the field of modern destructive oxidative methods of water purification from pharmaceutical compounds, since, together with high efficiency, they are also more environmentally friendly compared to chemical purification methods and much less time-consuming that biological methods. Advanced oxidation processes (AOPs) provide an extremely promising wastewater treatment technology for pharmaceutical companies.

Advanced oxidation processes were developed in the 1980s as a new way to remove toxic pollutants. The process involves the formation of active hydroxide radicals ($^{\bullet}OH$), and they effectively oxidize organic compounds. The high oxidizing power and high rates of reaction of these radicals with APIs make it possible to almost completely decompose organic compounds

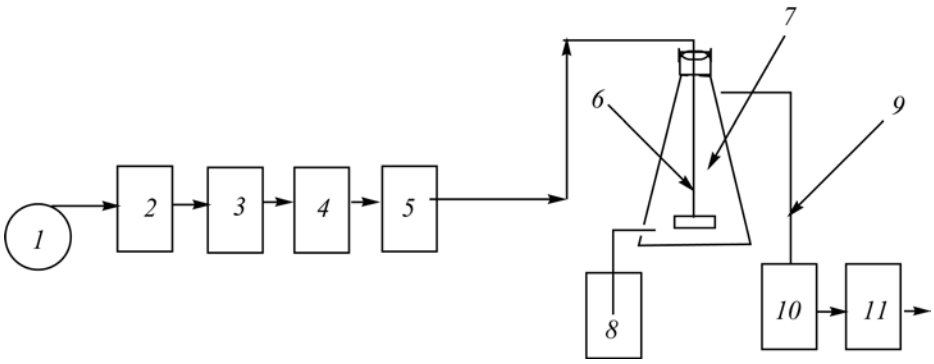

Fig. 1. Scheme of the laboratory paracetamol ozonation plant: (*1*) compressor, (*2*) oxygen concentrator, (*3*) rotameter, (*4*) ozone generator, (*5*) ozonometer, (*6*) ozone distributor, (*7*) reactor, (*8*) sampling flask, (*9*) residual ozone outlet , (*10*) vessel with hopcalite for ozone decomposition, and (*11*) water-jet pump.

into harmless inorganic compounds (carbon dioxide and water) [6].

The aim of this work was to realize oxidative destruction of paracetamol in model solutions by catalytic ozonation in combination with hydrogen peroxide oxidation, as well as to propose a process scheme involving consecutive stages of physicochemical and oxidative treatment.

EXPERIMENTAL

The object for study was a model aqueous solution of paracetamol ($C_8H_9NO_2$) with an initial API concentration (C_{init}) of 0.23 g/L. To prepare a solution of a solid API, a tablet of paracetamol was ground in an agate mortar, and a required amount of the powder was weighed on an analytical balance, mixed with water, and stirred on a magnetic stirrer for 15 min until it completely dissolved. A 100-mL aliquot of the model solution was subjected to oxidative ozonolysis on an XR-ZJ-1GT laboratory ozonizing plant with a power of 10 W (Fig. 1). Plant performance 1000 mg/h, mains voltage 220 V (frequency 50 Hz), and measured air capacity 7 l/min and 2.5 mg O_3 per 1 liter of air per minute.

The ozonation time was varied from 0 to 15 min. To intensify the ozonation process, hydrogen peroxide ($[H_2O_2]$) with various concentrations in the sample from 0.06 to 0.48 g/L and iron ions (Fe^{2+}) from 0.1 to 2 mg/L were added to the treated paracetamol solutions. Quantification of paracetamol before and after oxidative destruction was performed via nitration to obtain a nitro derivative, whose alkaline solution has a yellowish orange color. The main regulated parameter characterizing the content of organic matter in water (COD) was determined according to [7]. After catalytic ozonation, the solution was coagulated with adding aluminum oxychloride of a concentration of 40 g/L (0.8 mL per 100 mL of treated water). Adsorption was carried out on activated carbon BAU (1g per 100 mL of treated water).

The process rate was calculated by the formula:

$$v = -dC/dt,$$

where v is the process rate, mmol/L s; C, substrate concentration, mmol/L; and t, process time, s. The experimental dependences were approximated by curves of the form:

$$y = a \cdot \exp(-x/b) + c,$$

where a, b, and c are constants.

The initial process rate (v_0) was calculated as a derivative of these functions at $t = 0$. The rates of paracetamol destruction were found by processing the kinetic curves of the decomposition of the starting compound using the Origin 8.0 software package.

RESULTS AND DISCUSSION

The concentrations of the main catalytic compounds (in our case, hydrogen peroxide and ferrous ions) play a decisive role in the oxidation of any organic compounds [8]. Figure 2 shows the dependence of the amount/dose of the homogeneous Fe^{2+} catalyst on the efficiency of the ozonation process in the presence of 0.48 g/L of hydrogen peroxide.

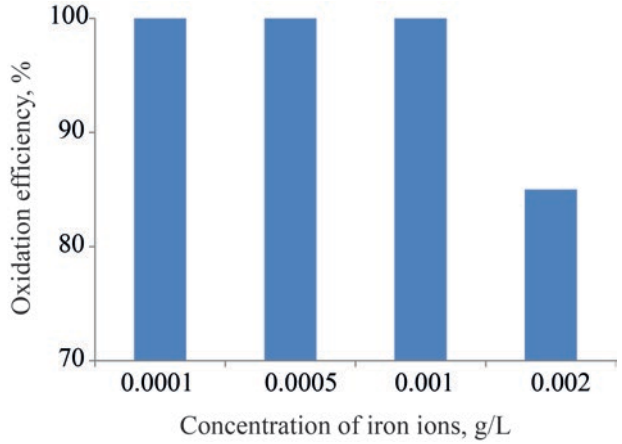

Fig. 2. Dependence of the efficiency of homogeneous catalytic ozonation on the concentration of iron ions.

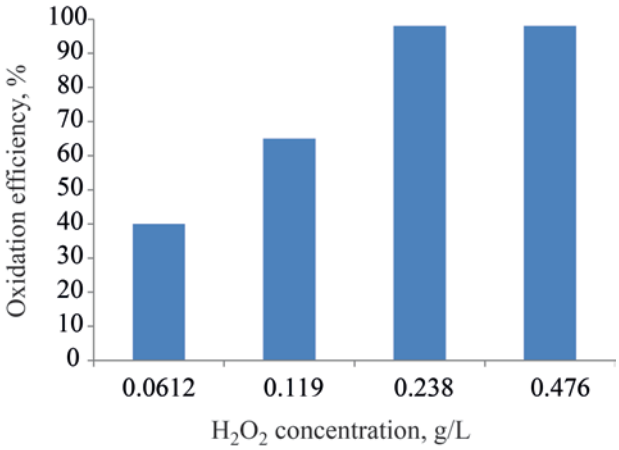

Fig. 3. Dependence of the efficiency of homogeneous catalytic ozonation on the concentration of hydrogen peroxide.

According to theoretical calculations, paracetamol is oxidized by hydrogen peroxide according to the reaction:

$$C_8H_9NO_2 + 21H_2O_2 \rightarrow 8CO_2 + 25H_2O + HNO_3.$$

Thus, if the initial concentration of paracetamol in water is 0.23 g/L, to oxidize it completely requires 0.48 g/L of hydrogen peroxide (1.6 mL of 3% H_2O_2 per 100 mL of the sample).

Based on the resulting data, the efficiency of the combined process is greater that 99%, even if the lowest concentration of the catalyst of 0.0001 g/L is used. The efficiency decreases at a Fe^{2+} concentration of 0.002 g/L in view of the excess of the catalyst, which is likely to inhibit oxidative processes in the aqueous solution of paracetamol.

Figure 3 shows the results of the catalytic ozonation of the aqueous solution of paracetamol at various concentration of hydrogen peroxide and a Fe^{2+} concentration in the system of 0.0001 g/L.

It was found that increasing concentration of hydrogen peroxide in the catalytic ozonation system increases the efficiency of oxidation. For example, as the peroxide concentration is increased 7.7 times, the efficiency of paracetamol oxidation increases 2.3 times. This fact is not unexpected, since the concentration of H_2O_2 largely determines the amount of formed hydroxyl radicals, which, in their turn, rapidly react to form organic radicals, thereby triggering the mechanisms of radical chain oxidation of paracetamol. The reaction of iron(II) with hydrogen peroxide is described by the scheme:

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^{\bullet} + OH^{-}.$$

As follows from the results of the experiment (Fig. 4), first, with increasing time of ozonation, the concentration of paracetamol exponentially decreases, irrespective of the treatment technique. Second, the efficiency of oxidation in the absence of catalysts or additional oxidizing

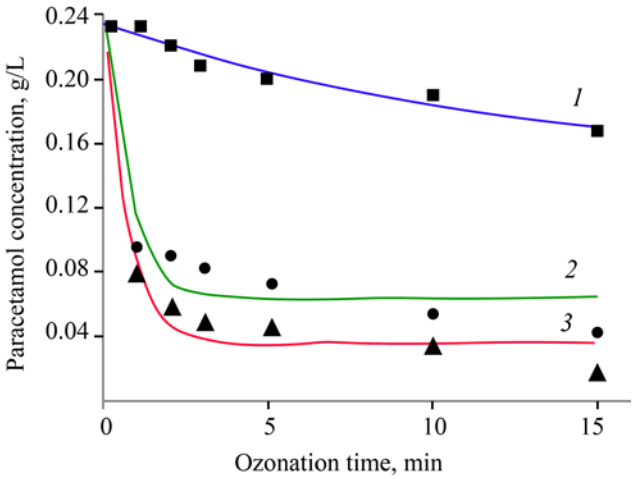

Fig. 4. Kinetics of the oxidation of the aqueous solution of paracetamol (C_{init} 0.23 g/L): (*1*) ozonation, (*2*) catalytic ozonation in the presence of iron(II) ions (O_3/Fe^{2+} method), (*3*) catalytic ozonation under the combined action of iron(II) ions and hydrogen peroxide ($O_3/H_2O_2/Fe^{2+}$ method).

Table 1. Degree and rate of the oxidative destruction of paracetamol (C_{init} 0.23 g/L)

Method	Degree of oxidative destruction, %	Rate of oxidative destruction, mol/L s
Ozonation	28.3	2.8
O_3/Fe^{2+}	81.9	90.9
$O_3/H_2O_2/Fe^{2+}$	92.9	107.6

Table 2. Concentrations of the monitoring parameters before and after treatment of the model wastewater containing paracetamol

Parameter	Before treatment	After each stage of treatment		
		$O_3/H_2O_2/Fe^{2+}$	coagulation and filtration	adsorption
Paracetamol, mg/L	173	8	< DL	< DL
COD, mg O/L	320	360	160	120

agents is as low as 30% at the longest ozonation time of 15 min, whereas the efficiency of catalytic ozonation in the presence of hydrogen peroxide reaches more than 90% (increases about 3 times).

The calculation of the maximum degrees and rates of oxidative destruction of paracetamol (Table 1) showed that, under the combined treatment with ozone, hydrogen peroxide, and iron ions, the efficiency of oxidation at the initial moment of time is a few times higher than in the case of ozonation alone.

Spectrophotometric analysis of the model solutions of paracetamol before and after oxidative destruction, performed at a GBC Cintra 303 spectrophotometer at the Mendeleev Center for Collective Use, showed that the maximum absorption of paracetamol occurs at a wavelength of 257 nm. After oxidative ozonolysis by the combined method at the longest ozonation time of 15 min, no paracetamol maximum at 257 nm was observed. Thus, the catalytic ozonation in the presence of hydrogen peroxide ($O_3/H_2O_2/Fe^{2+}$ method) increases the efficiency of API removal up to 98%. The optimal volume of hydrogen peroxide is 0.8–1.6 mL (concentration 0.24–0.48 g/L).

In view of the fact that the catalytic oxidation of paracetamol can be accompanied by the formation of intermediate degradation products (acids, aldehydes, and alcohols), we performed experiments on the purification of the model API wastewater using other oxidative and physicochemical methods.

Figure 5 shows a flowsheet for the proposed treatment process involving a combination of reagent oxidation methods. This scheme makes it possible to achieve high degrees of purification from paracetamol due to its destruction by catalytic ozonation in the presence of hydrogen peroxide and removal of residual degradation products by sorption at the final stage.

The estimated COD of the treated model wastewater does not exceed the regulatory limit (150 mg O/L), and,

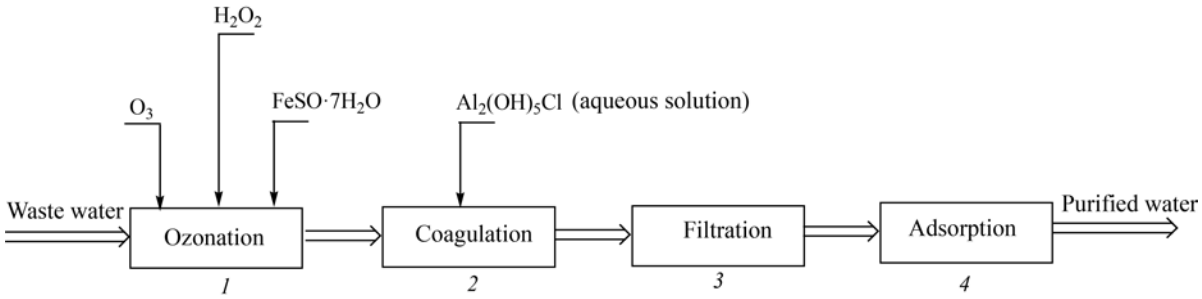

Fig. 5. Block diagram of the pharmaceutical wastewater treatment process: (*1*) ozonator; (*2*) flocculation chambers; (*3*) mechanical filters; and (*4*) adsorption filter.

therefore, such wastewater can be directed to the sewer for further biological treatment (Table 2).

Further extension of the method of catalytic ozonation to real pharmaceutical wastewater in the presence of iron sulfate and hydrogen peroxide is a quite a promising line of research. However, when passing from a model experiment to real conditions, one should expect a change in the efficiency of oxidative processes, primarily due to side reactions, which may occur, because real wastewater contains substances of various nature.

CONCLUSIONS

The example of a model pharmaceutical wastewater containing paracetamol was used to establish that a combination of ozonation with hydrogen peroxide and a Fe^{2+} sulfate homogeneous catalyst provides an effective and promising approach to oxidative destruction of paracetamol (efficiency > 98–99%). The oxidative destruction of an aqueous solution of paracetamol by the $O_3/H_2O_2/Fe^{2+}$ method was confirmed at a qualitative level. A concept scheme of the technology of wastewater treatment from paracetamol, involving a combination of reagent and oxidative methods and allowing the concentration of paracetamol and COD in wastewater to be reduced to the maximum permissible levels, is proposed.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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