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Oxidative Inactivation of Drugs.

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ABSTRACT

There was a detailed study of some drugs oxidation with the different structures of hydrogen peroxide and the presence of iron ions (II). The comparative analysis of the system containing iron ions oxidizing ability was performed (III). The optimal conditions for the products disintegration were determined.
Keywords: Disintegration, hydrogen peroxide, pharmaceuticals, Fenton's reagent, Raff system.

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INTRODUCTION

Currently, the problem of organic compounds disposal in the environment becomes more acute. One of the most serious pollutants is pharmaceutical preparations and their production waste. It is proved that a number of pharmaceutical substances are in biologically active form even after their passing through a living body. When these substances come into a food chain, they affect living organisms, their habitats and the ecosystem as a whole [1, 2].

There are many ways of organic compounds disposal described by the literature: chemical, physical, biological, but neither of them is a universal one, cost-effective and applicable to the substances of any structure by natural object pollutants neutralization [3-5]. A separate group of isolated oxidation-destructive processes involving highly active radical elements is marked out among the chemical methods of inactivation. These methods have the prospect of water treatment technologies development, including the treatment technology from drugs.

Hydrogen peroxide is one of the most common reagents in the development of Advanced Oxidative Processes. According to the literature the most effective way to increase the oxidizing power of hydrogen peroxide is its radical decomposition in the presence of iron ions with OH and HO2 radicals formation. At the same time it was shown that the use of a combined approach, the so-called "photo-Fenton" is necessary for the full destruction of persistent pollutants [8-11]. In this article we studied the process of the active ingredient mineralization in various purpose medicines by Fenton's reagent - a mixture of hydrogen peroxide and doubly charged iron ions. The comparison of the reagent oxidizing power with the Raff system - a mixture of hydrogen peroxide and triply charged iron ions was performed.

METHODS

In this paper we studied the oxidation-destructive transformations of 14 drugs (Table). The oxidation of drugs was carried out in aqueous solutions with the active substance concentration of 0.25 mmol/l. The studied substrates are referred to the respective names of drugs, but it is only about an active ingredient concentration change. The possible transformations of drug adjuvants, included in the composition of drugs, are not discussed.

Table: Researched drugs list

№	Drug name	Active substance chemical name	Active substance gross formula	Maximum grades of destruction, %
1	Analgin	1-phenyl-2,3-dimethyl-4-metilaminopirazolon - 5-N-sodium methanesulphonate	$C_{13}H_{16}N_3O_4SNa$	88
2	Dibazol	2-phenyl methylene-1H-benzimidazole	$C_{14}H_{12}N_2$	64
3	Diclofenac	2-(2,6-dichlorophenyl) amino benzeneacetic acid	$C_{14}H_{11}Cl_2NO_2$	73
4	Dimedrol	2-(diphenylmethoxy)-N, N-dimethylethanamine	$C_{17}H_{21}NO$	51
5	Carbamazepine	5H-dibenz (b, f) azepine-5-carboxamide	$C_{15}H_{12}N_2O$	93
6	Levomizetin	2,2-dichloro-2-hydroxy-1-hydroxymethylene-2-(4 - nitrophenyl) ethylacetamide	$C_{11}H_{12}Cl_2N_2O_5$	95
7	Methyluracil	2,4-dioxy-6-methyl-1,2,3,4-tetrahydro-pyrimidine	$C_5H_6N_2O_2$	90
8	No-shpa	1-(3,4-dietoxyfenilmetilen) -6,7-diethoxy - 1,2,3,4-tetrahydroisoquinoline	$C_{24}H_{31}NO_4$	72
9	Paracetamol	N-(4-hydroxyphenyl) acetamide	$C_8H_9NO_2$	83
10	Efferalgan UPSA	N-(4-hydroxyphenyl) acetamide	$C_8H_9NO_2$	72
11	Furacilin	2-(5-nitro-2-furanilmetilen) hydrazine carboxamide	$C_6H_6N_4O_4$	97
12	Furocemide	5-aminosulfonyl-4-chloro-2-(2-furanylmethyl) aminobenzoic acid	$C_{12}H_{11}ClN_2O_5S$	84
13	Isoniazid	Hydrazide 4-pyridine of carboxylic acid	$C_6H_7N_3O$	85
14	Metronidazole	2-methyl-5-nitro-1H-imidazole-1-ethanol	$C_6H_9N_3O_3$	83

The initial pH value of the medium is in the range of 3.0-3.5 for all experiments.

The process of drugs oxidation at room temperature in an aqueous solution of 25 ml was studied in all experiments. The test solution was added with the calculated amount of hydrogen peroxide solution and iron sulfate (II)/(III). The concentration of hydrogen peroxide was varied from 4 to 16 mmol/l, the concentration of iron ions varied in the range of 0,125-0,500 mg/l. In all experiments, the reaction mixture was maintained for a long time (6-8 days) to avoid the effect of random factors. The optical spectra of medicinal substance solutions and the reaction mixtures were recorded on a SPESORD 50 device within the wavelength range from 190 nm to 450 nm with 1 nm step. The reagents concentration decrease was monitored by the change of solution optical absorption at the wavelength corresponding to the maximum absorption for each compound. The reagent concentration was determined by the calibration curves in their linear areas.

MAIN PART

The drugs of different functionality were selected for the study, from the category of potentially difficult degradable pollutants of various structures: aromatic rings, condensed aromatic fragments or heterocycles are the structural elements for the majority of these structures. The varying of the oxidizing reagents concentrations was performed to determine the effect of the components ratio. The oxidative degradation was performed with different concentrations of hydrogen peroxide at the same concentration of iron ions, and then the concentration of hydrogen peroxides maintained a constant one and the content of iron ions was changed. The drugs degradation degree was calculated from the obtained data for different concentration ratios of hydrogen peroxide and iron salts. Among the researched drugs one may distinguish the group of drugs with a high degree of degradation after 6 days, almost independent on the concentration of the oxidizing reagents: Furacilin, Levomizetin, Carbamazepine (table). These drugs are added with two more drugs with a somewhat lesser but still significant conversion degree - Metiluratsil and Furocemide. The degree of other substrates degradation depends on the concentration of oxidizing reagent to a much greater extent; one may achieve a deeper degradation by increasing the concentration of hydrogen peroxide and iron ions. There is no a strict relation between the carbon atoms content in the molecule and the required amount of oxidants, so paracetamol (C8) and no-shpa (C24) are difficult to be oxidized [12, 13].

It may be noted that all the substances in this group are resistant to oxidation medicines and are widespread in the Russian medical practice. Hence, one can predict the growth of their content in wastewaters.

The replacement of Fe2 + to Fe3 + by paracetamol oxidation improved the process characteristics: at the minimum content of oxidative reagents the degradation reached 60% within an hour, although it reached up to 30% at the most optimal ratio of reagents in the presence of iron ions (II). The rates of Fenton and Ruff are comparable at a high content of oxidizing reagents. The assumption that the mechanisms of hydrogen peroxide catalytic decomposition in the Fenton and Rapha systems have much in common is confirmed; the difference is in the initiation mechanism.

SUMMARY

The oxidative degradation may be considered as a promising method of inactivation unfit for the drugs use, as well as the way for a local wastewater treatment of the clinics and pharmaceutical plants.

CONCLUSION

The performed studies showed that many conventional drugs undergo oxidative degradation by the exposure to hydrogen peroxide in the presence of iron ions at the room temperature and atmospheric pressure.

It is established that Fe2 +, and Fe3 + use is possible as the iron source at the activation of hydrogen peroxide.

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