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# ANALYSIS OF STUDIES IN THE FIELD OF WASTEWATER POLLUTION BY PHARMACEUTICAL CONTAMINANTS

The analysis of recent studies of surface waters pollution problem by pharmaceuticals and their derivatives was performed. The information about the sources of contaminated effluents formation, especially their negative impact on the elements of the environment, purification at municipal wastewater treatment plants was systematized. Measures of environmental pollution reduction were considered. The authors made the conclusions about the study degree of this problem and ways of this solving.

**Keywords**: wastewater, pharmaceutical contaminants, purification, ecotoxicology

**Самойленко Н. М., Єрмакович І. А. АНАЛІЗ ДОСЛІДЖЕНЬ У СФЕРІ ЗАБРУДНЕННЯ СТІЧНИХ ВОД ФАРМАЦЕВТИЧНИМИ ПОЛЛЮТАНТАМИ**

Проведено аналіз останніх досліджень актуальної проблеми забруднення поверхневих вод фармацевтичними препаратами та їх похідними. Систематизовані відомості про джерела формування забруднених стоків, особливості їх негативного впливу на елементи навколишнього середовища, очищення на муніципальних очисних спорудах. Розглянуто заходи щодо зниження забруднення навколишнього середовища. Авторами статті зроблено висновки про ступінь дослідженості даної проблеми і про напрямки її вирішення

**Ключові слова**: стічні води, фармацевтичні забруднювачі, очищення, екотоксикологія

**Самойленко Н. Н., Ермакович И. А. АНАЛИЗ ИССЛЕДОВАНИЙ В СФЕРЕ ЗАГРЯЗНЕНИЯ СТОЧНЫХ ВОД ФАРМАЦЕВТИЧЕСКИМИ ПОЛЛЮТАНТАМИ**

Проведен анализ последних исследований актуальной проблемы загрязнения поверхностных вод фармацевтическими препаратами и их производными. Систематизированы сведения об источниках формирования загрязненных стоков, особенностях их негативного влияния на элементы окружающей среды, очистки на муниципальных очистных сооружениях. Рассмотрены мероприятия по снижению загрязнения окружающей среды. Авторами статьи сделаны выводы о степени исследованности данной проблемы и о направлениях ее решения

**Ключевые слова**: сточные воды, фармацевтические загрязнители, очистка, экотоксикология

## *Introduction*

Nowadays, scientists around the world have been studied uncontrolled and continuous releasing pharmaceuticals into the environment and the consequences of their impact on the natural living organisms for decades. Recent data suggest that this leads to negative changes in its components and violate the natural processes in the ecosystem sustainability. The greatest concern is the pollution of wastewater containing pharmaceuticals and their derivatives. According to this, the prevention of the release of these compounds into environment is extremely relevant point, mostly in the developed countries [1].

**The purpose of the research:** to define the level of the studied problem related to environmental pollution by pharmaceutical residues coming into wastewater as well as trends of it solution.

**Problem Statement:** -to identify the degree of influence of pharmaceutical pollutants on the environment, in micro- and nano- quantities based on the analysis of modern publications by foreign authors;

- to make conclusions about the available results and trends for the further research.

## 1. The main sources of pharmaceuticals pollutants in wastewaters

The quantity of drugs consuming by the population is extremely large. Only in 2013, the Ukrainian pharmacies sold 1.3 billion of medicines packages, which is 28 units of such packages per an Ukrainian citizen [2]. There are nonsteroidal anti-inflammatory drugs among them (NSAIDs) which are daily worldwide used by more than 30 million of consumers. At the same time, for example, in the United States only more than 1 billion of NSAID of recipes is prescribed annually [3].

Insufficiently treated wastewaters from hospitals, pharmaceutical companies, domestic sewage and wastewater veterinary clinics and livestock farms are considered as the main sources of pharmaceuticals entering into the surface waters.

Unfortunately, only a small part of the unused expired or substandard drugs is gathered to be disposed or incinerated. However, a large part, in the form of original drugs or metabolites, is discarded to waste disposal site or flushed down via toilet into municipal sewer in excrement (removing with urine, feces and sweat). For example, the annual consumption of drug Diclofenac by some EU residents could be 78 579 kg/year (Germany, 2010), 22 640 kg/year (France, 2010) [4].

Obviously, the source of the formation and entering of such pollutants into municipal wastewater are is? accounted for hospitals. Literature data indicate that the hospital wastewaters have 15 times higher potential ecotoxicity than general municipal ones. For example, in Germany there are more than 12 000 tons of drugs that are disposed through the toilet or in the form of general household waste [5, 6]. The data of the concentrations of some pharmaceuticals in different types of wastewaters is shown in Table 2.

**Table 2**

**Concentrations of priority pharmaceuticals in hospital wastewaters**

| Name of the drug | Concentration in effluent hospitals in Europe, µg/l | Concentration in effluent hospitals in Sweden, µg/l | Calculated concentration in effluent hospitals in Ukraine, µg/l | Concentration of entering wastewater into MSTP in Europe, µg/l |
|---|---|---|---|---|
| Diclofenac | 70 | 0,38 | 2,2 | 10 |
| в-estradiol | 0,23 | 0,017 | n.d. | 0,114 |
| Atenolol | 122 | 1,2 | 0,325 | 0,800 |
| Furosemide | 21,48 | *n.d. | 6,2 | 2,214 |
| Cefurotoxime | >125 | *n.d. | 64,23 | 0,125 |

*n.d.

## 2. Pharmaceutical pollutants effect on environment

### 2.1 Effect of pharmaceuticals mix

The most of the scientific publications concerning pharmaceuticals influence on living organisms deal with only one drug, losing the summation effect, which has a negative impact. However, the study [7] indicates that the micro pollutants of multicomponent pharmaceutical mixture may interact with each other. Thus, this provides an integrated toxicity on organisms. For example, the study of diclofenac, ibuprofen, naproxen and aspirin interaction in water demonstrates a synergistic toxicity.

Most number of recent studies show that the pharmaceuticals and their derivatives, including many of therapeutic groups such as antibiotics, analgesics, anticancer, contraceptives and antidepressants has a sufficient environmental toxic effect [8].

### 2.2. Ecotoxicological effect

Pharmaceuticals could also cause negative effects on organisms living in the soil, such as bacteria, fungi and others earthworms through the sewage sludge, which is often used for fertilization [9].

The most bright example of failed using of diclofenac for treatment animals was shown in study [10] where 99,9% of the vulture population in the Indian subcontinent had died by 2008. The mechanism is presumed to be renal failure, a known side effect of diclofenac. Vultures eat the carcasses of livestock that have been administered veterinary diclofenac, and are poisoned by the accumulated chemical, as vul-

tures do not have a particular enzyme to break down the diclofenac.

Five different antibiotics such as ciprofloxacin, norfloxacin, ofloxacin, sulfamethoxine, and sulfamethoxasole were detected during the research of sludge from sewage treatment plant in Lithuania. Some of them were also found mainly in carrots and potatoes in 10-100 times lower concentrations than in the soil [11]. Ofloxacin and sulfadimethoxine were also detected in wheat. Ofloxacin was accumulated 5 times in the wheat seeds compared to the concentration in the soil. According to the experiments, it was made the conclusion that there is a real risk of antimicrobials uptaking into crops and the exposure to humans [12].

The study of a diclofenac, ibuprofen, naproxen and acetylsalicylic acid acute toxicity mixture to the crustacean *D.magna* as well as green algae *D. subspicatus* in a 48 h test was shown in [13]. The main conclusion of this study is that the single compound does not have any significant concentration effect. The negative effect is observed only when these substances are mixed.

In another investigation of the freshwater the amphipod *H. Azteca* was exposed by 0,2 μg/L mixture concentration of seven pharmaceuticals such as paracetamol, diclofenac, gemfibrozil, ibuprofen, naproxen, salicylic acid and triclosan [14]. The main criteria were survival, mating, body size and reproduction. All of them were negatively influenced by the mixture.

In the research of biomarker cytogenotoxic effects [15], freshwater bivalve *D.polymorpha* was investigated with different concentrations 1.5, 9, 13 μg/l of the diclofenac, ibuprofen and paracetamol mixture for 96 h. The results demonstrated that all 3 concentrations produced a considerable destabilization of the lyzosomal membranes and cellular stress in 72 h. DNA fragmentation increasing was observed in 24 h.

### 3. The treatment contaminated effluents at the MSTP

The main reason of getting pharmaceuticals and their derivatives into the surface waters is the lack of an effective biological treatment at the MSPT. Table 3 shows the cleaning data at wastewater treatment plants containing these contaminants.

**Table 3**

**The purification factor of the sewage at MSTP containing pharmaceutical pollutants**

| Name of the drug | Concentration of entering wastewater into MSTP in Europe, μg/l | Purification factor at MSTP, % |
|---|---|---|
| Diclofenac | 10 | 34 |
| в-estradiol | 0,114 | 30 |
| Atenolol | 0,800 | 71 |
| Furosemide | 2,214 | 42 |
| Cefurotoxime | 0,125 | n.d.* |

*n.d.- no data

The authors [16] explain such a low rate of treatment by two factors. Firstly, the concentration of the mostly detected pharmaceuticals is extremely low. This leads to the fact that microorganisms of the activated sludge are not able to catch molecule of the chemical compounds of the drugs. Secondly, annually new types of medicines that belong to the new group of pharmaceuticals are getting on market, to which the microbiota of activated sludge cannot adapt.

Chemical substances of pharmaceutical pollutants can poison the living community of activated sludge at MSTP. The study of the activated sludge microorganisms reactions to the pharmaceuticals toxic effects allows forecast negative changes in biological nature. Hence, it may have the impact to the wastewater treatment results. It becomes especially relevant during any flu epidemic, when the number of pharmaceutical pollutants getting into municipal sewage significantly increase. The paper [17] highlights the destabilization risk of the activated sludge when it is exposed to this period of biologically active pharmaceuticals. The investigation of activated sludge from treatment facilities helps to establish the degree of the degradation of hormonal substances that are contained in effluent. Thereby, the paradoxical fact was established. It determined that the products of its biodegradation can be even more harmful (dangerous) than the "parent" original compound [18].

Now, pharmaceuticals are considered as emerging microcontaminants in the treated wastewaters and as storages in the activated sludge. According to the research [19] water and sludge from biological treatment should not be used in agriculture, especially if these waters contain antibiotics. Pharmaceutical contaminants and their derivatives have a variety of negative effects on activated sludge. Some of them slow down oxygen consumption of activated sludge and reduces its productivity while others could be the food for them. The formed conglomerates of the sludge with pharmaceutical pollutants can effect on the rate of oxygen uptake and negatively affect its condition.

The chemical composition of pharmaceuticals varies significantly during their interaction with activated sludge. Particularly, this is expressed by example of drug "hardness" that is connected with the complex chemical formula (for example, carbamazepine, diclofenac and others). Furthermore, it is an important biological effect of the drug on the biocenosis and sludge, the presence of active chlorine molecules in it.

## 4. Measures for the pharmaceuticals pollution reduction in environment

### 4.1 Legislative level

Taking into account the existing problem connected with the fact that the European Commission of the EU Water Framework Directive has put 3 pharmaceuticals in the list of priority substances with controlling discharge into environment [20] (table 3).

**Table 3**

**List of priority pharmaceuticals in the field of water policy under the Water Framework Directive of the European Union (2000/60 / EC)**

| Name of Pharmaceuticals | CAS[2] number | Annual average ENVIRONMENTAL QUALITY STANDARDS (EQS), Inland surface waters[1], µg/l | Maximum allowable concentration EQS, other surface waters, µg/l |
|---|---|---|---|
| 17alpha-ethinylestradiol | 57-63-6 | $3{,}5 \times 10^{-5}$ | $7 \times 10^{-6}$ |
| 17beta-estradiol | 50-28-2 | $4 \times 10^{-4}$ | $8 \times 10^{-5}$ |
| Diclofenac | 15307-79-6 | 0,1 | 0,01 |

[1]Inland surface waters encompass rivers and lakes and related artificial or heavily modified water bodies
[2]CAS: Chemical Abstracts Service

Unfortunately, now in Ukraine pharmaceutical substances are not included in any normative documents for wastewater discharges. In addition, it does not carry out any monitoring or control.

### 4.2 Engineering methods

Current analysis of the information sources demonstrates that there is no universal method for purification of wastewater containing various contaminants and allowing produce their disinfection with high cleaning degree in a single process. Moreover, the efficiency of wastewater treatment by the same drug may have significant differences. For example, the removal efficiency of Diclofenac on standard treatment plants varies from 17% to 69%. Thus, at wastewater treatment plant - Collybia in Sweden, it is 22% [20].

The removal of pharmaceutical pollutants are basically regarded as purification of water from organic substances. There is a great variety of these kinds of pollutants disposal methods. Many of them are widely known and have been used for organic compounds removing from industrial and municipal wastewater for a long time. However, their purification efficiency is usually not satisfactory because even microquantities of pharmaceutical substances in the waters have a significant negative impact on the environment. Other similar methods and techniques that are relevant to the new developments usually have certain limitations or drawbacks. It holds back their implementation (Fenton - photocatalytic method, supercritical technology and etc). Existing combined processes in which the oxidation reagent and further biodegradation are applied are quite expensive from an economic point of view. A very perspective waters purification by reverse osmosis cannot be applied to wastewater containing some com-

monly used hard degradable drugs. Wastewater treatment from antibiotics, cholesterol, bisphenol A to 93-99% at MSTP leads to the fact that the concentration of contaminants is reduced to 223 ng / l. It is not enough of getting a complete effect from the treatment [21].

Publications about wastewater treatment from the mixtures of pharmaceutical pollutants are not found.

## *Conclusion*

1. Pharmaceutical contaminants, which are found in residual concentrations in the wastewaters, entering into treatment plant, passing through cleaning process, are not always completely decomposed. Moreover, they could cause negative changes into environment. The content of analysis shows that the study of pharmaceutical wastewaters pollutants impact on the environment is mostly researched by European scientists. They are performing the analytical tests of these pollutants presence both in municipal wastewaters and surface waters. Based on the results of the EU at the normative level, they are making the control of priority pollutants dumping into environment. It is appropriate to use this approach for the waters monitoring in Ukraine as well.

2. Most of the residues of pharmaceutical pollutants demonstrate the effect of summation in relation to the toxicity effects on organisms in effluents. Diclofenac, Beta-estradiol, Cefuroxime and others are the source of ecotoxicity.

3. The effect of residual drugs on activated sludge from treatment facilities can lead to poor treatment performance due to the toxicity effects on biota. It is noted that some of the products of biodegradation could be more harmful than the original contaminants are. In general, the effect of the active pharmaceutical substances on a sludge will depend on its chemical structure, as well as the presence of biological effects.

4. Modern engineering methods of wastewater treatment from residuals of medicines do not provide the required criteria. Furthermore, there are no studies performed in a single neutralization process of effluents containing pharmaceutical mixture characterized for wastewaters of medical establishments. Therefore, scientists are searching for the most effective and economically appropriate method for solving this urgent problem, which requires combining efforts of specialists from different fields.

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