Classification of antibiotics contained in urban wastewater

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Abstract. The article is devoted to the study of available information about identification of groups of antibiotics in urban wastewater. At the same time, results of research conducted in Tunisia, Spain, the United States, China and other countries were examined. The comparison showed that wastewater contains a specific set of antibiotics of a country, which is aroused by special veterinary medicine and pharmaceutical industry in the country. However, there are common antibiotic types of urban wastewater in all countries, because of their high applicability and effectiveness of treating bacterial infections. The question of learning the composition of urban wastewater in Russia remains unstudied.

1. Introduction
An analysis of the literature shows that for stopping the onset of bacteria, it is important to search for new medicine and at the same time introduce strict measures to control the release of drugs into the environment and using antibiotics so as not to "kill" those drugs that are still used today [1-2].

One of the main source of releasing antibiotics into the environment is a man. Human antibiotics used for treatment inevitably fall together with feces into municipal wastewater. Monitoring their concentrations in sewage treatment plants will help to develop a technology for their complete removing and prevention of further contact with the water body. [3-5].

2. Theoretical basis
For the first time, the term “antibiotic” which means “against life” was proposed in 1942 by an American microbiologist, a native Russian, a specialist in soil microbiology, Zelman Waxman [6]. Nowadays, more than 30,000 types of antibiotics of only natural origin are in the world, which are synthesized by living creatures from various taxonomic groups. But it does not mean that all existing antibiotics are produced by living cells. Chemists learned how to improve and enhance the antibacterial properties of natural substances, modifying them by using chemical methods. Antibiotics, obtained this way, are semi-synthetic [7]. Figure 1 shows the classification of antibiotics according to the main features (figure 1).
Figure 1. Classification of antibiotics according to the main features.

180 from the 30,000 currently known antibiotics have been found active in human treatment and are included in the classification of antibiotics “Access, Watch, Reserve – AWaRe” developed in 2017 by the World Health Organization (WHO). The classification database “AWaRe” divided antibiotics into three groups: Access, Watch and Reserve. Classification is an antibiotic management tool at local, national and global levels to reduce resistance. In the summer of 2019, WHO launched an overall campaign urging governments to use this classification. WHO recommends to provide Access antibiotics at all times to treat a wide range of common infections. This group includes, for example, amoxicillin, an antibiotic widely used to treat infections such as pneumonia. The Watch group includes antibiotics recommended as first and second choice drugs for treating a limited number of infections. The third group “Reserve” includes antibiotics such as colistin and some cephalosporins, which should be considered as “last hope” medicines and used only in the most severe cases [8-15].

3. Materials and methods

Wu M, Que C, Tang L, Xu H, Xiang J, Wang J, Shi W and Xu G [8] research results show that the greatest danger to the nature is represented by almost uncontrolled sources of antibiotics that are produced by animals, and mainly by us – people who use pharmaceutical drugs for medical purposes. According to [10], scientists have found that antibiotics after injection do not totally collapse and do not lose their original properties, but almost completely retain their biological activity. It comes to the fact that a molecule of the active substance is released unchanged during physiological secretions or through the skin and is able to influence the environment.

Nowadays wastewater treatment plants remove about 80% of pharmaceuticals and their remains. Even the best cleaning methods do not remove pollution completely, so up to 10% of drugs remain in the treated wastewater. Besides, sometimes, the concentration of pharmaceuticals after treatment facilities increases, due to biological processes, interactions with metal ions during time, decomposition of products and metabolites are formed, which leads to the ability of the studied substances to multiply, for example, during the interaction of antibiotics with chlorine ions.

The most widespread antibiotic types in the world used to treat people [16-21]:

- penicillins;
- macrolides;
- cephalosporins;
- fluoroquinolones;
- tetracyclines;
- aminoglycosides;
lincosamides.

They are acting against majority of bacteria. That is why, studies of the composition of antibiotics in urban wastewater from different countries (Tunisia, Spain, USA, China) included the detection of these groups. According to the results of studies conducted in these countries, more than 10 different antibiotics were found in samples of urban wastewater. The largest concentrations of antibiotics are characterized by the group of fluoroquinol: enrofloxacin, ofloxacin, ciprofloxacin (figure 2). The last of them, ciprofloxacin, was included in the classification group Watch, which calls for a sharp reduction of its using to fight against drug resistance. It was established that the level of antimicrobial resistance is close to critical level nowadays.

Concentrations of different antibiotics in the treated sewage of Tunisia are:

- enrofloxacin: 400.20 ng/l;
- ciprofloxacin: 330.33 ng/l;
- ofloxacin: 175.01 ng/l.

A higher concentration of antibiotics of the floroquinol group was found in Spain:

- ciprofloxacin: 639 ng/l;
- ofloxacin: 529 ng/l;
- enrofloxacin: haven’t found.

The high level of enrofloxacin (a veterinary agent) in Tunisia can be attached to the presence of certain veterinary activities and a specific pharmaceutical industry. In the United States, concentrations of the same group of antibiotics are:

- enrofloxacin: 270 ng/l, (2006);
- ciprofloxacin: up to 100 ng/l;
- ofloxacin: 10 ng/l, this antibiotic was even discovered in the world ocean.

In second place in terms of concentration in wastewater is the oldest group of antibacterial drugs sulfonamides (sulfapyridine, sulfamethoxazole), which have lost their significance in recent decades and have very limited indications for use. However, their concentrations detected as a result of the studies are also significant. (figure 3).

The levels of sulfapyridine and sulfamethoxazole were also high according to the results of all sampling and reached up to 365.50 and 126.70 ng/l.
These results were below than in other countries, for example, in Korea and the Czech Republic, where sulfapyridine was found in the amount of 921 ng/l and 660 ng/l. Sulfamethoxazole was found at high concentrations in China, up to 959.13 ng/l and in Spain, up to 417.4 ng/l. An antibiotic, lincomycin, with a concentration of 100-150 ng/l was found in wastewater. These indicators significantly exceed the concentration of a similar antibiotic found in Greece – 66.7 ng/L (2016), but much lower than in Australia, up to 500 ng/L.

The concentration of cephalexin varies from 23.30 to 33.33 ng/l. Tetracycline and metronidazole were found in some cases during sample tests, but were always below the limit, probably due to its low consumption in Tunisia. In contrast, a higher concentration of macrolide antibiotics, such as spiramycin and azithromycin, were found in all samples, in the amount of 690.50 ng/l and 135.45 ng/l. Penicillin group of antibiotics are one of the most widespread, but despite the high consumption of this group of antibiotics, neither penicillin nor amoxicillin were found in Tunisia’s sewage. It is most likely due to their chemical instability; they are easily transformed by hydrolysis. There are also another results of scientific studies about antibiotic concentrations in wastewater from other countries and they are presented in table 1 [8].

Table 1. Concentrations of antibiotics in wastewater at different countries.

| Title             | Concentration, ng/l | Country   |
|-------------------|---------------------|-----------|
| Ciprofloxacin     | 418.8 – 667.1       | Portugal  |
| Norfloxacin       | 90-300              | Sweden    |
|                   | 72-174              | Sweden    |
|                   | 179-1760            | Taiwan    |
| Sulfamethoxazole  | 1000                | USA       |
|                   | 402                 | Italy     |
| Oxytetracycline   | 0.3-7               | Luxembourg|
| Tetracycline      | 46-234              | Taiwan    |
| Trimethoprim      | 330                 | USA       |
|                   | 240                 | Serbia    |
| Ofloxacin         | 11-77               | China     |
| Erythromycin      | 137                 | South Korea|

Concentration of antibiotics in wastewater in different countries vary dramatically. This is because countries use different antibiotics.
4. Results
Because of the lack of an overall regulatory framework on permissible concentration of antibacterial agents in surface and wastewater, we can only state the presence of the above drugs in wastewater and the need to pay attention to the following groups of antibiotics: fluoroquinols, sulfonamides, macrolides. Their detection is the main goal of the chemical analysis of urban wastewater and it will allow the development of technology for absolute removal.

5. Conclusions
Using antibiotics leads to their penetration into water bodies, which brings the level of resistance to antimicrobials closer to maximum. To solve the problem of removing antibiotics from wastewater, including urban sewage, and to improve the existing classical treatment scheme, taking into account the best available technologies, we have to conduct a study in Russia about the content of fluoroquinolones, sulfonamides, macrolides in urban wastewater.

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