ҚАЗАҚСТАН РЕСПУБЛИКАСЫ БІЛІМ ЖӘНЕ ҒЫЛЫМ МИНИСТРЛІГІ
Л.Н. ГУМИЛЕВ АТЫНДАҒЫ ЕУРАЗИЯ ҰЛТТЫҚ УНИВЕРСИТЕТІ

ЕУРАЗИЯ ҰЛТТЫҚ УНИВЕРСИТЕТІ

ЖАС ҒАЛЫМДАР КЕҢЕСІ

Студенттер мен жас ғалымдардың «ҒЫЛЫМ ЖӘНЕ БІЛІМ - 2016» атты XI Халықаралық ғылыми конференциясының БАЯНДАМАЛАР ЖИНАҒЫ

СБОРНИК МАТЕРИАЛОВ XI Международной научной конференции студентов и молодых ученых «НАУКА И ОБРАЗОВАНИЕ - 2016»

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2016 жыл 14 сәуір
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The proceedings are the papers of students, undergraduates, doctoral students and young researchers on topical issues of natural and technical sciences and humanities.

В сборник вошли доклады студентов, магистрантов, докторантов и молодых ученых по актуальным вопросам естественно-технических и гуманитарных наук.

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грибным фитопатогенам исследуемые штаммы микромицетов проявляли низкую активность относительно бактериальных, зоны подавления которых составляли 10,0-16,0 мм (табл. 2).

Нами было установлено, что 9 штаммов подавляли рост *Fusarium culmorum* (зоны от 14,0 до 60,0 мм) и *Cladosporium gerbarum* (зоны от 11,0 до 30,0 мм); 7 штаммов с разной степенью активности задерживали рост таких фитопатогенов как *Aspergillus niger* (зоны от 18,0 до 60,0 мм) и *Agrobacterium tumefaciens* (зоны от 11,0 до 22,0 мм). Некоторые штаммы обладали способностью задерживать рост *Fuzarium oxysporum, Xanthomonas campestris, Fuzarium moliniforme* и *Clavibacter michiganensis* (зоны от 11,0 до 52,0 мм). Для *Pseudomonas syringae pv lachymans* и *Alternaria alternata* удалось обнаружить только один штамм, который показал четкую зону задержки роста этих тест-культур диаметром 30,0 мм и 36,0 мм.

Таким образом, проведенные исследования по изучению антагонистического влияния почвенных микромицетов показали, что у 4-х штаммов антифунгальный спектр составляет в отношении 4-6 тест-культур, у 3-х штаммов антибактерицидное действие проявилось к 3 тест-культурам. Были также обнаружены штаммы, которые почти полностью подавляли рост *Aspergillus niger* и *Fuzarium culmorum*, а также культуры, которые активно задерживали рост фитопатогенов.

Полученные результаты позволяют рассматривать выделенные из чернозема обыкновенного микромицеты как перспективные штаммы-антагонисты для получения биопрепаратов против грибов и бактерий – возбудителей болезней сельскохозяйственных растений.

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3.2 Экология

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PRIORITIZATION OF PHARMACEUTICALS IN THE SURFACE WATER OF KAZAKHSTAN

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Recent years studies have showed that pharmaceuticals enter to the environment as contaminants [1-2]. Many studies have reported the occurrence and fate of different classes of pharmaceuticals in the environment. It was found that surface waters, sewage effluents and freshwater sediments have the different concentration of drugs [3-6]. However, there is still

insufficient data, as ecotoxicity assessment was carried out only for several hundreds of pharmaceuticals from thousands of them [7]. Initially drugs constructed to treat human body and their interaction with the natural environment and biological species are poorly studied. In most cases, they have common properties as dangerous pollutants, because they can enter to the membranes and be persistant and in some cases their impact to the environment can be worther than agricultural pollutants [8-9].

Pharmaceuticals mostly excrete via urine and feces unmetabolized, then discharge to wasterwater treatment facilities (WWTF) and enter to the surface water [10-11]. Due to the various composition of each drug and including the fact that not all WWTF are capable to remove compounds of pharmaceuticals, it is impossible to predict their side effect to the environment and biological species. Therefore, active pharmceutical ingredients (APIs) can be classified as toxic pollutants to aquatic environment [12].

Currently, there is less than 1% of APIs ecotoxicity data is available in literature and ecotoxicological database and still insufficient information on risk assessment of pharmaceuticals. Ecotoxicological study of each 3000 API will require a lot of time and money [9-10]. Therefore, it is important to establish a ranking system of pharmaceutical in order to detect those compounds and to prevent danger that they can pose to the environment and living organisms [13]. It is important to implement ranking of pharmaceuticals in Kazakhstan. Currently, pharmaceutical market in Kazakhstan is growing, in 2012 551.38 mln packages of drugs were sold in the country [14]. There are over 14000 objects of pharmaceutica activities, that is the highest percentage of private pharmaceuticl structures in CIS [15-16]. A number of researchers have reported various prioritization approaches of APIs [17-18]. However, a major of studies require annual pharmaceutical usage data. The following methods cannot be applied to Kazakhstan, because until recently no studies have been found on pharmceuticals hazard to the environment.

The aim of this study was to explore the main pharmaceuticals can pose hazard to the aquatic environment of Kazakhstan. APIs with the highest quantity of products were assumed as used oftenly and enter to the surface water. The study highlighted the widely used drugs that could lead to the risk in Kazakhstan. Vitamins and vaccines were excluded as they do not have a big effect to the aquatic environment or species. The paper describes 238 APIs that are used in Kazakhstan. It included antibiotics, antidepressants, non-steroidal anti-inflammatories (NSAIDs), blood lipid-lowering agents, hormones, tuberculosis (TB) and antitumor drugs.

Initially, the study considered approximetly 2640 pharmaceuticals. Then, the list of APIs was made by using the online directory pharmaceuticals in Kazakhstan [19]. The each of APIs also contain the information of the daily intake, therapeutic class, concentration and number of products and as a result 841 substances were picked for the study. The lack of annual usage and sales data for the pharmaceuticals in Kazakhstan did not allow to generate the top usage pharmaceuticals. Therefore, it was decided to rely on the number of products of each APIs. The number of products of all APIs were obtained from the same directory Vidal pharmaceuticals. All compounds with less than 3 products were eliminated from the list.

Predicited environmental exposure was estimated based on products number, daily dose and metabolism. The data for the following assessment was obtained from the peer-reviewed papers and available online datasets [20-21].

The calculaton of predicted no-effect concentrations (PNEC) was based on experimental or estimated aquatic ecotoxicity data. The data included EC50 and LC50 for fish, daphnia and algae with acute and chronic toxicity. All these data were collected from several database [22] and peer-reviewed papers. Estimation of PNEC based on relations of concentration of the most sensitive ecotogicological data to safety factor. The calculation of safety factor was performed based on Technical guidance document on risk assessment proposed by European Commision [23].

There were some substances with no experimental data of toxicity. In order to fill the gap of them, QSAR Toolbox was used with read across approach of the Organisation for Economic Co-operation and Development.

In order to estimate the hazard of compounds in fish, we used fish plasma model (FPM) which was proposed Hugget et al [24]. Overall, this model compares the steady state concentration in fish plasma (FssPC) with the threapeutic plasma concentrion in human (HtPC) (ratio of HtPC/FssPC). The information of HtPC was obtained from online databases [20, 25] and peer reviewed papers. FssPC was calculated by multiplying aqueous phase and and fish arterial blood partition coefficient (Pbw) to exposure amount.

Totally, the study characterised 238 APIs for the prioritization. All compounds were highlighted by disease classes, which have been registered in health care institutions of Kazakhstan [16]. Each substance was considered based on predicted environmental exposure (Exposure:PNEC).

Table 1 provides information on drugs that pose the risk to the environment and have danger to the fish. The highest number of pharmaceutical products were found in the class of infectious and parasitical diseases (60 products). Overall, it was detected that paracetamol and hydrochlorothiazide had the top-notch number of products. However, the highest exposure was estimated on amoxicillin, clarithromycin, azithromycin, sulfamethoxazole and ketoconazole. Respiratory and cardiovascular diseases had the highest number of registered sickness rate.

Table 1. Top 20 highly ranked compounds

Ranking based on exposure	Ranking based on FssPC
Amoxicillin	Lisinopril
Clarithromycin	Orlistat
Azithromycin	Estradiol valerate
Sulfamethoxazole	Cinnarizine
Ketoconazole	**Drotaverine**
Meropenem	Estradiol
Naproxen	**Clotrimazole**
Oxytetracycline	Telmisartan
Ranitidine	Disulfiram
Diclofenac	Clemastine
Clotrimazole	Clopidogrel
Capreomycin	**Terbinafine**
Drotaverine	**Azithromycin**
Disulfiram	**Diclofenac**
Terbinafine	Montelukast
Moxifloxacin	Sertraline
Levofloxacin	Dextromethorphan
Beclomethasone	Miconazole
Clioquinol	Beclomethasone
Mycophenolic acid	Albendazole

Note: Bold highlighted pharmaceuticals show their common appearance in top ranking of drugs on exposure and FssPC

Even including the fact that ranking approach was different from previous studies, the results had some common compounds with some earlier prioritization research. Amoxicillin, clarithromycin, diclofenac and azithromycin were put in the list of high risk in ecotoxicological risk-based prioritization research by Guo et al (Table 1) [2]. Moreover, amoxicillin was identified as chemical with high hazard to aquatic ecosystem in the United Kingdom, Italy and Iran [26-28].

There are several same substances in exposure based ranking and FPM based ranking (Table 1). The majority of them are designed to treat infectious diseases and this class of disease has the highest number of products in APIs in Kazakhstan. Furthermore, several substances from the list have been concurred with previous works. For example, orlistat, montelukast, telmisartan, estradiol, clemastine and miconazole were also detected as priority chemicals in Roos et al study [29]. The highest value in FPM was estimated in Lisinopril. Previous studies did not include this substance to

the highest priority. However, Kostich et al research on measurement of concentration of APIs in effluent samples in US concluded that Lisinopril had the highest concentration value in terms of potential risks to humans [30].

Based on results it can be concluded these compounds should be considered in future research. The approach of ranking can be applied in countries with limited data to detect APIs of priority. Future research should investigate the analytical methods for these compounds and to monitor concentration.

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REDUCE OF THE ECOLOGICAL LOAD ON THE ENVIRONMENT BY THE WASTE TREATMENT

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The environment is a condition for the existence of living organisms together with human being. In order to improve the quality of life, human transforms the environment to fit his needs. This inadvertently changes the constancy of the composition of the internal environment. Thermodynamic principles and laws of conservation of energy, matter and information are closely related with each other. As an example, it is possible to consider the flow of energy and material information in the system, which should cover the entire system. Currently, there are quite a large number of calculations in a matter of improving environmental quality. For example the water flow in the biological specimen takes hours, the moisture in the atmosphere (hence in aerobiosfere) - 8 days, free continental surface water - from 16 days in rivers, and up to 17 years in lakes, groundwater is updated in 1400 years, and the ocean water in 2500 years. Similarly, the specified time of energy and metabolism transition exist in all natural systems.