Archives of Waste Management and Environmental Protection

Archiwum Gospodarki Odpadami i Ochrony Środowiska
ISSN 1733-4381, vol. 14, issue 1 (2012), p. 11-18

http://awmep.org

THE ESTIMATION OF THE TOXICITY OF PHARMACEUTICAL PRODUCTS IN SOLID FORM AS COMPONENTS OF MEDICAL WASTES

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Abstract

Pharmacological waste, particularly dangerous for human and animals, makes considerable environmental stress after it gets in treatment facilities. The given article is devoted to the research in the sphere of evaluation of the toxical effect of waste pharmaceutical products having the solid form. For the discussion we have used the names of pharmaceutical products taken from the nomenclature used in Russia.

Keywords: Pharmacological waste, Dangerous waste

Streszczenie

Ocena toksyczności produktów farmaceutycznych w postaci stałej jako elementów odpadów medycznych

Odpady farmakologiczne, szczególnie te, które są niebezpieczne dla ludzi i zwierząt, powodują znaczne obciążenie dla środowiska i problemy w oczyszczalni ścieków. Artykuł został poświęcony badaniom w dziedzinie oceny wpływu toksyczności stałych produktów farmaceutycznych. Do dyskusji wykorzystano nazwy produktów farmaceutycznych zgodnie z nomenklaturą używaną w Rosji.

Słowa kluczowe: odpady farmakologiczne, odpady niebezpieczne.

1. Introduction

The group of highly dangerous wastes includes physiologically and biologically active pharmaceuticals, whose influence is directed at humans and animals. The active drugs ingredients and their metabolites from the wastewater of hospital sanitations, pharmaceutical companies, pharmaceutical wastes treatment plants cause the significant exogenous chemical effect on the environment. The content of pharmaceuticals in the morphological composition of medical wastes is less than 1% (Orlov, 2010). During the process of purification of waste water not eliminated and not biodegradable pharmaceuticals may migration and even into the drinking water supply system. There are four main routes of pharmaceuticals in the environment (Global water research ..., 2004): 1) cities waste water from treatment plants, 2) health care facilities and people, 3) manure containing veterinary drugs, 4) industrial waste water and solid waste production of pharmaceuticals. They are recognized pollutants of soil and groundwater due to the potential danger to health and environment (Discussion Paper on ..., 2005).
This fact determines their potential effects on human health (Boxall, 2004). Waste pharmaceuticals are sometimes considered as pseudostable organic environmental pollutants (Daughton, Ternes, 1999).
It is believed that companies have to develop the technologies of recycling or destruction for their drug products. So it is assumed that the descriptional articles of pharmaceutical products should include a section about the technology of their recycling or destruction at the stage when they become wastes (Rusakov, 2009).

Phytotesting is a common method to determine the toxicity of wastes (MR 2.1.7.2297-07). Garden cress *Lepidium sativum* is one of the most commonly used test objects for the biotesting of water, soil sediments, natural and synthetic substrates, testing on the radiation effect as well as the effects caused by synthesized chemical substances and their mixtures.

We have analyzed the possibility of using biotesting methods to determine the phytotoxicity of expired drugs as a type of medical wastes. We have used pharmaceuticals in various forms (ointments, tinctures, pills, lotions, suppositories, injection solutions, drops, etc.). They contain a pharmaceutically active substance and at least one pharmaceutical excipient. We have investigated the toxicity of solid pharmaceuticals commonly used in Russia.

2. Material and methods.

The study was conducted between November 2010 and May 2011 at the room temperature. The degree of phytotoxicity includes the following properties of cress: germination, (%), the average length of the germ (L, mm), the average seedling dry weight (W, mg). Investigations were carried out by laying 30 seeds of cress on a sheet of filter paper on the bottom of Petri dishes. The List of pharmaceuticals is presented in Table 1.

Table 1 - The List of pharmaceuticals in solid form

	Name	Form
1	Amoxicillin	Tablet
2	Apaurin	Tablet
3	Afobazol	Tablet
4	Acetylsalicylic acid	Tablet
5	Validol	Tablet
6	Glycine	Tablet
7	Diphenhydramine	Tablet
8	Corvalolum	Tablet
9	Laevomecitinum	Tablet
10	Mildronate	Capsule
11	Isosorbide mononitrate	Capsule
12	Paracetamol	Tablet
13	Ranitidin	Tablet
14	Troxevasin	Capsule
15	Ultop	Tablet
16	Furosemide	Tablet
17	Hartil	Tablet
18	Cholenzym	Coated tablets
19	Chondrlonum	Capsule
20	Enalaprilum	Tablet

The tablet or the capsule powdered in a porcelain mortar and dissolved in 100 ml of distilled water (fallopian solution) is the stock solution. There are also solutions in a twofold, fourfold, eightfold, and sixteen fold dilution. The filter paper is moistened with solutions of different concentrations of pharmaceuticals. As a control liquid we have used the water from city water system. The experiment was repeated three times.

The experiment lasted for seven days. Conclusions were drawn considering the percentage of germinated seeds, seedling length, dry weight, and the ratio between the length and the dry weight of seedlings.

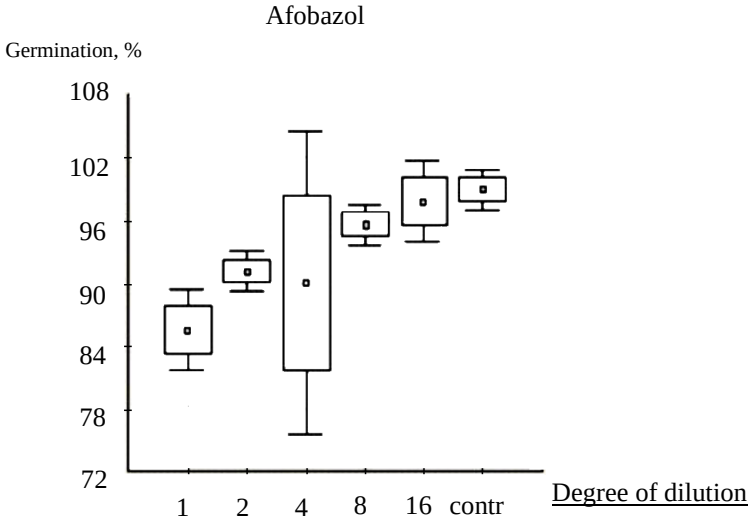
Statistical data processing was performed by standard methods of the program «Statistica-5.0 for Windows». The evaluation of the relevance of the difference of the average parameters was done with the help of the t-criterion by Student.

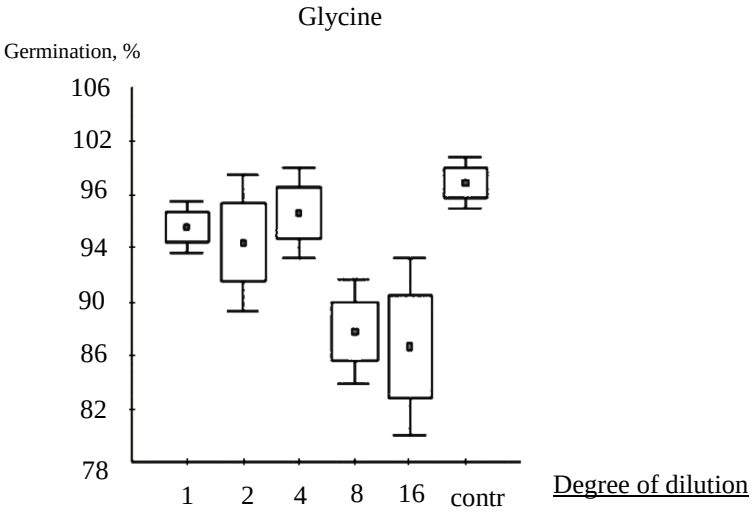
3. Results and discussion

The changes between the length and the dry weight of seedlings are given in Table 2.

Table 2 – Examples of the acute phytotoxicity of pharmaceuticals

Name	Degree of dilution				
	1	2	4	8	16
Acetylsalicylic acid					
Diphenhydramine					
Hartil					





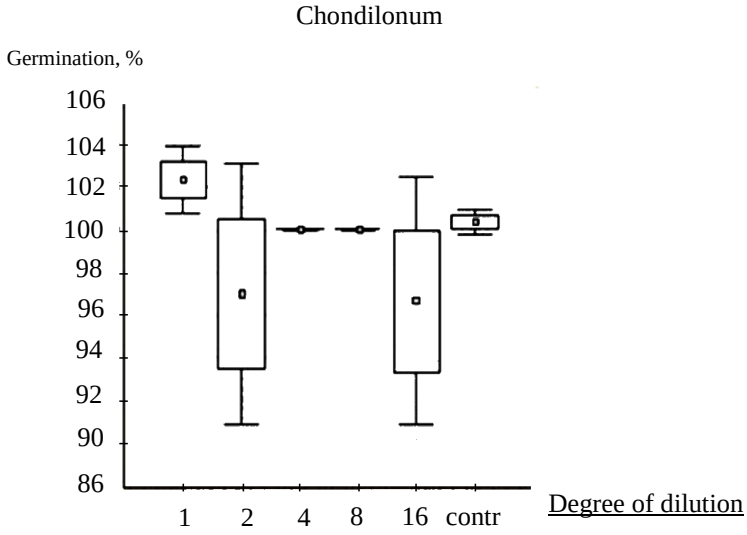


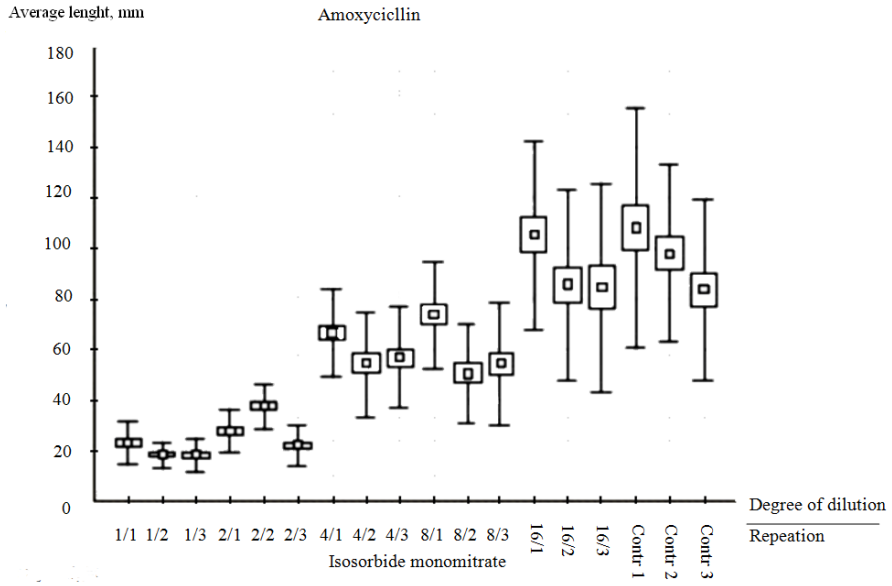
Fig.1 – Examples of various changes in germination, % (mean, standard error, standard deviation)

There are three types of changes in germination with increasing dilution:

a) The germination significantly increases with dilution (Afobazol);

b) The germination significantly decreases with dilution (stimulation effect) (Glycine). The similar dependence is observed in cases with eutrophic waters (Seifert, 2010);

c) The germination does not change (Chondrlonum). This type of dependence indicates that this product is the least toxic.



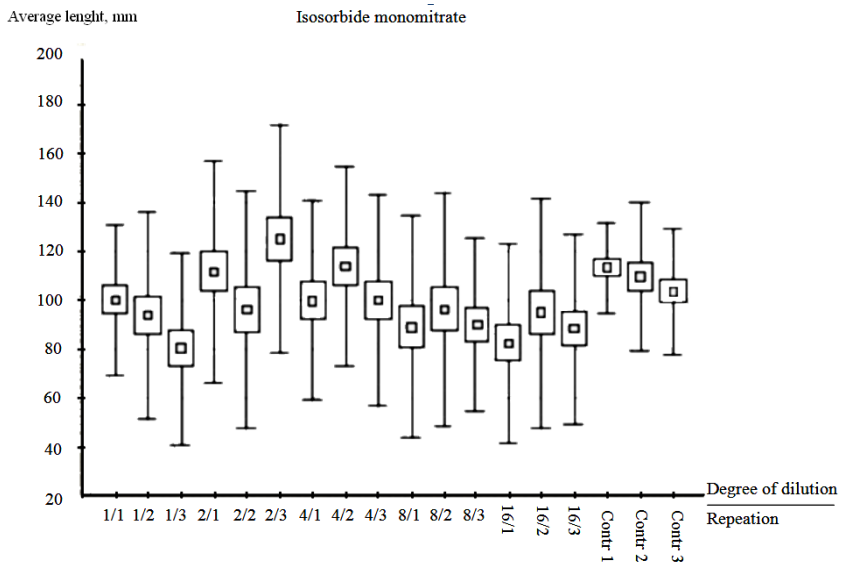
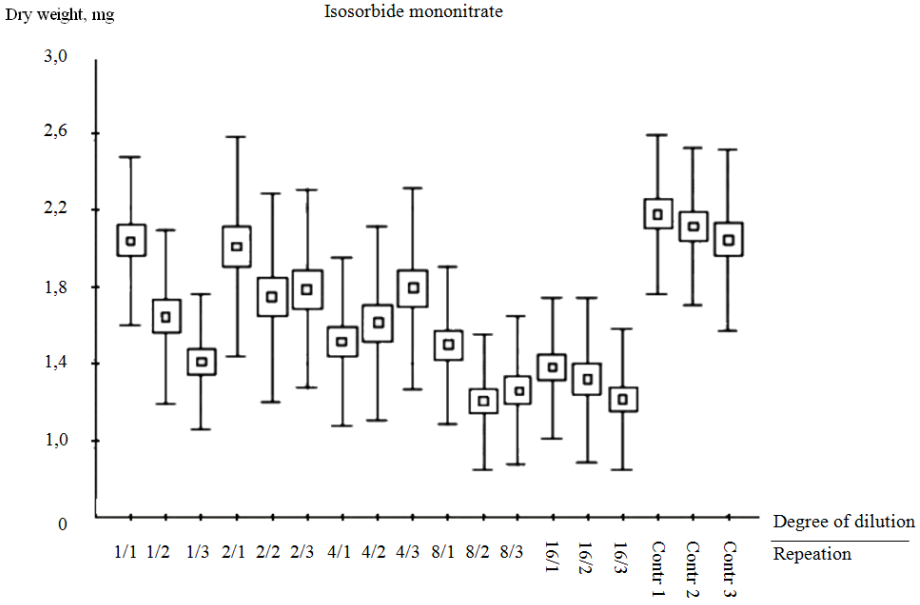


Fig. 2 – Examples of various changes in average length, mm (mean, standard error, standard deviation)

There are two types of changes in the average length of seedlings with increasing dilution:

a) The average length significantly increases with dilution (Amoxicillin);

b) The average length does not change (Isosorbide mononitrate).



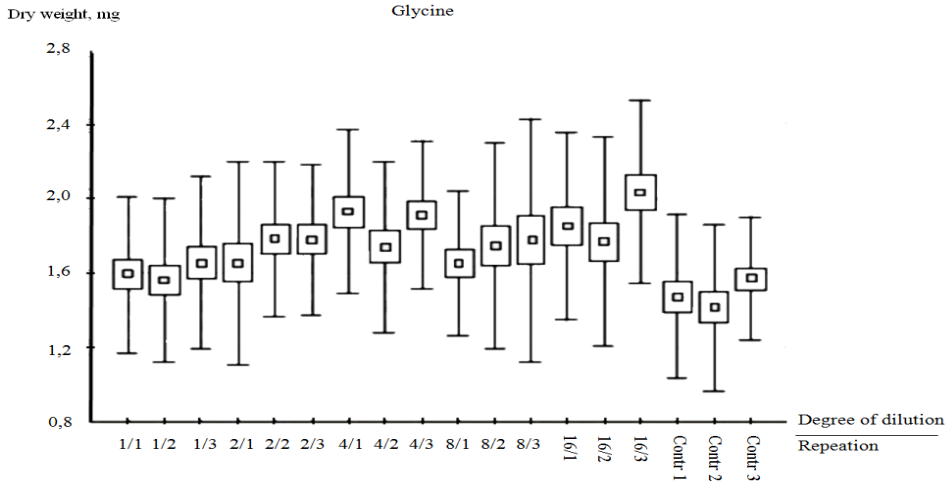


Fig.3 – Examples of various changes in the average dry weight, mg (mean, standard error, standard deviation)

There are two types of changes in the average dry weight of seedlings with increasing dilution:

a) The average dry weight of seedlings is significantly different from the control parameter (Isosorbide mononitrate). In this case we can argue about the toxicity of the tested drugs.

b) The average dry weight equals the control value (Glycine).

The most serious level of phytotoxicity is observed in 3 types of pharmaceuticals. In case of the acetylsalicylic acid the highest phytotoxicity appears at eightfold dilution.

The results of other cases were fixed considering the changes in germination (Figure 1), changes in the average length of seedlings (Figure 2) and changes in the average dry weight (Figure 3).

The differences between the length and the dry weight of seedlings are shown in Table 3 and 4.

Table 3 - Correlation between the length and the dry weight of seedlings (1)

Enalaprilum			
	1	2	3
1	-0,16	-0,07	0,20
2	0,18	0,16	0,45
4	0,44	-0,22	0,25
8	0,47	0,29	0,38
16	-0,02	0,35	0,60
control	0,53	0,52	0,51
Corvalolum			
1	0,12	0,03	0,12
2	-0,09	0,23	0,19
4	-0,30	-0,06	0,18
8	0,04	-0,30	0,01
16	0,12	0,35	0,13
control	0,30	0,16	-0,07

Table 4 - Correlation between the length and the dry weight of seedlings (2)

Diphenhydramine			
	1	2	3
1	-	-	-
2	-	-	-
4	-0,11	-0,05	-
8	-0,25	-0,64	-0,12
16	0,07	0,36	-
control	0,30	0,16	-0,07
Hartil			
1	-	-	-
2	**0,62***	**-0,56***	**0,54***
4	**0,61***	**0,66***	0,32
8	0,16	**0,40***	-0,06
16	0,17	0,23	-0,02
control	-0,14	-0,21	0,05

*- The value is significant under P=0,95

Nowadays the development of technical regulations for handling of medical wastes needs deep improvement. It is also important to develop indicators and risk assessment criteria for them. Development of organizational and administrative documentation is one of the priorities of modern research (Rusakov, 2009). This article describes the three identified types of effects of investigated pharmaceuticals: the manifestation of toxicity, the manifestation of stimulation and lack of expression of these effects. Apparently, for other pharmaceuticals will be revealed similar types of effects, the differences will be determined only by the degree of severity (Seifert, Shkrebel, 2012). In comparison with the currently used methods we proposed a method combining both low cost and sufficient solubility. We have tested a tiny number of available pharmaceuticals. But there are a lot of differences in toxicity even between the tested pharmaceuticals. This fact shows that drug wastes should be separately collected and sorted according to the degree of their toxicity and disposal methods. This is one of the ways to reduce the costs of their treatment.

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