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Ultrasonic aiding of selected pharmaceuticals removal from wastewater

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ABSTRACT

In the paper, the problem of water pollution risks with pharmaceuticals was discussed. The results of the investigation from different countries are shown. Polish results are presented as well. Particular emphasis was put on water pollution with non-steroidal anti-inflammatory and psychoactive drugs. The need for additional disinfection of drinking water has been highlighted. The aim of this study was to evaluate the ultrasonic (US) process on the degradation of pharmaceuticals. For testing non-steroidal anti-inflammatory and analgesic drugs were selected. The tests were performed using Malvern Mastersizer 2000 particle size analyzer with a sonotrode. The samples were exposed to an ultrasonic field with parameters 250 W and 20 kHz. During the experiment, sonication time was altered and it was equalled to 30, 60, 120, and 240 s. Based on the results, the relationship between the ultrasonic field, length of its duration, and particles' diameters was determined. Particle sizes were strongly correlated with the intensity and time of the ultrasonic field exposition. The largest particles were obtained for unmodified samples and they amounted to even 479 μm. The smallest particles were obtained for samples modified for 240 s and amounted to 0.724 μm for ketoprofen.

Keywords: Ketoprofen; Diclofenac; Ultrasonic field; Wastewater

1. Introduction

A growing number of people are using various products created by many branches of chemical industry. This industry, developed in the twentieth century, currently responds to ever-larger and wider consumer demands. One of the branches of this industry, the pharmaceutical sector, has become the answer to all human health problems; from cancer to attaining a slim figure, and deficiency of vitamins in one's diet. An interesting and potentially dangerous phenomenon is the rapidly growing sale of non-prescription medicines, which currently represents 34% of the pharmaceutical market [1]. The amount of pharmaceutical substances (substance which brings the therapeutic effect) is impressive and is approximately 200,000 preparations around the world.

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It is estimated that the amount of drugs at domestic markets varies between 5,000 and 10,000 depending on the size of the country, population, and market characteristics [2]. Such a large selection of medicines, the relatively low price, and wide availability of drugs without a prescription at any point of trade contributes to a systematic increase in the consumption of drugs. Frequent cases of excessive use lead to numerous cases of addiction. Going further, excessive consumption of pharmaceuticals can have a significant influence on the changes concerning the qualitative and quantitative composition of the wastewater and the quality of surface water and drinking water [3,4]. It should be noted that drugs are digested by the human body only in small amounts and their byproducts from urine spread to sewages [5]. The main contributors to water pollution by pharmaceuticals are mainly households, pharmaceutical concerns, and hospitals [6]. Conducted in 1998, the research led by Thomas Ternesturned the whole world's attention and the public eye toward the mass scale of this phenomenon in many countries, not only in Europe but all over the world [7]. So far, scientists have examined about 500 different medicinal substances occurring mainly in surface water, showing their harmful impact on animals and micro-organisms [2].

1.1. Non-steroidal anti-inflammatory drugs

Anti-inflammatory drugs and analgesics are the most common and most widely used drugs. Most of them are salicylic acid derivatives, propionic acid derivatives, and phenylacetic acid derivatives. They are used to relieve rheumatic pains, headache, menstrual pain, fibrositis and other pains of various origins. They are used to treat injuries, muscles pain, and during and after surgery; due to their medical effect they are used as antipyretics. On one side, this group of medications works much weaker than narcotic painkillers (opioids) and does not cause addictions. On the other side, they are consumed in excessive amounts and are not inert to the body. Like all synthetic medicines, they have side effects. Non-steroidal anti-inflammatory drugs are a very wide group of pharmaceuticals, and they are very different in their structure [8]. There have been many studies to investigate this phenomenon (Table 1); for example, the first studies of water in Germany showed that in the rivers and surface water there are more than 32 drugs belonging to different groups [7,9,10].

1.2. Psychoactive drugs

Psychoactive medications, such as anxiolytics, sedatives, sleeping pills, and antidepressants, are one of the most widely prescribed pharmaceuticals in the world [17]. These drugs are so widely used that they can be found in all environmental conditions: in the sewers, on the ground, drinking water, soils, and sediments. The most common psychoactive medications are diazepam, tetrazepam, lorazepam, oxazepam, and nordiazepam. Antidepressants: fluoxetine, norfluoxetine, citalopram, fluvoxamine, sertraline, norsertraline, paroxetine, venlafaxine, duloxetine, and bupropion [17]. Due to such wide availability of psychoactive drugs and the fear of long-term effects of consuming even small amounts of these substances around the world, scientists started to invest in specialized research describing the scale of the threat accurately [18,19].

In comparison to the other countries, Spain has a high level of consumption of pharmaceuticals, and Madrid is one of the most densely populated areas in Europe; in such conditions the risk of undesirable substances entering the drinking water and surface water is extremely high [20]. In the vicinity of the major Madrid's rivers, scientists performed research on 10 wastewater treatment plants that discharged treated effluents into the rivers [20]. In all samples the presence of pharmaceuticals were observed: fluoxetine (80% of the samples), citalopram (60%), venlafaxine (100%), nordiazepam (90%), oxazepam (80%), and carbamazepine (70%) [20].

2. Aim of the study

The aim of the conducted study was to evaluate the impact of sonication on the particle size distribution in pharmaceutical solutions. For the research a group of non-steroidal anti-inflammatory drugs was chosen. The choice of parameters and active substances was made after reviewing the available literature related to the subject of research [21].

The specific objectives of the study were:

(1) Examining the effects of sonication time extension on the particle size.
(2) Checking if the ultrasonic degradation affects the concentration of the tested substance in solution.
(3) Checking the efficiency of the process and determining the smallest particle size which can be obtained.
(4) Answering the question whether the experiment could be performed on a wider range of drugs and whether the results are repeatable?

3. Experimental section

3.1. Chemicals

Ketoprofen (Fig. 1) is one of the propionic acids belonging to the class of non-steroidal

Table 1
Concentration of selected pharmaceuticals in surface water ($\mu g L^{-1}$) [7–9,11–16]

	Ibuprofen	Naproxen	Ketoprofen	Diclofenac
Finland	4.00	2.00	0.80	1.30
Brazil	0.10	0.20	0.20	0.20
Germany	0.20	0.22	0.20	0.70
Great Britain	3.08	0.10	no data	0.42
Poland	0.10	0.02	0.02	0.50

anti-inflammatory drugs (NSAID) with analgesic and antipyretic effects. It acts by inhibiting the body's production of prostaglandin. Diclofenac (Fig. 1) is a NSAID which reduces inflammation and as an analgesic reduces various pains. It works by inhibiting cyclooxygenase [22,23]. Both substances were obtained from Galenic Laboratory Olsztyn, Ltd., Poland. The test samples were in the form of white powder with high purity, ready for chemical analysis. Purified filtered water and ethyl alcohol were used in experiments.

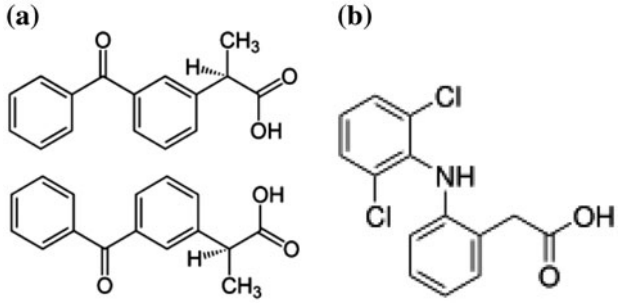

Fig. 1. The structural formulas of investigated NSAIDs (a) ketoprofen and (b) diclofenac [22,23].

3.2. Apparatus

The method used to measure an aggregate size in the solution was particle size distribution determined using Malvern Mastersizer 2000 particle size analyzer with a sonotrode. The Mastersizer 2000 uses the technique of laser diffraction to determine the size of the particles. It does this by measuring the intensity of light scattered by particles while passing through the sample. Large particles scatter light at narrow angles with high intensity, whereas small particles scatter light with wider angles but with low intensity. The instrument was equipped with a large volume manual sample dispersion unit suitable for wet samples. The dispersion mechanism consisted of a centrifugal pump, a stirrer, and an ultrasonic probe. Sampling port was designed to be used with 0.6–1.0 L standard laboratory beakers [24]. After each experiment the reactor was rinsed three times with distilled water.

3.3. Experimental procedure

During the study a synthetic solution was used designed to create more repetitive conditions than in the sewage from treatment plants. By using a solution of pure samples of NSAIDs in ethyl alcohol, the same conditions for all samples tested were obtained. Natural effluent has low repeatability of qualitative and quantitative composition, except that the substances present in it may have an impact on the results of research and transparency. It should be noted that the medium in the samples was ethanol instead of water, which prevented the dissolution of active ingredients in the solution. Tests were performed using Malvern Mastersizer 2000 particle size analyzer with a sonotrode. Each medication was tested at various concentrations and subjected to the variable field of ultrasound at different time intervals. Pharmaceuticals were gradually added to the measuring cuvette with a capacity of 0.6 L in order to obtain the desired concentration (0.05% vol). Then, the prepared solution was treated with an ultrasonic field whose parameters were 250 W and 20 kHz [25]. During the experiment, sonication time was altered and it was equalled to 30, 60, 120, and 240 s. Ultrasonic field parameters were chosen on the basis of the data available in literary review sources [26–28]. Each sample was tested 1, 5, 8, 10, and 12 min after sonication. The results were analyzed and compared with the computer program compatible with the test apparatus.

4. Results and discussion

Pure pharmaceuticals are insoluble in ethanol and sediment rapidly. When powder was added to the liquid suspension was obtained. Based on the analysis of particle diameters, the size distribution was determined depending on the ultrasonic field. Firstly, primary particle size distribution of the drug was measured. For diclofenac a single peak was obtained with particle diameter of 60–150 μm (Fig. 2). The particle size distribution for ketoprofen has a wider range and ranges from 70 to 210 μm.

Longer sonication makes it possible to obtain a much reduced particle size. For the longest sonication

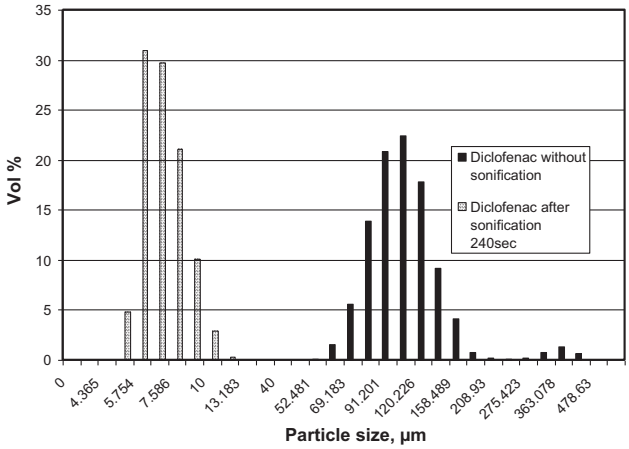

Fig. 2. Effect of ultrasonic field on the particle size distribution (diclofenac).

time, amounting to 240 s, particle sizes were less than 20 μm (Fig. 2). With the longer duration of the ultrasonic field, it was observed that the particle size decreased and participation of small particles increased.

Based on the results, the relationship between the ultrasonic field, length of its duration, and particles' diameters were determined. Particle sizes strongly correlate with the intensity and the time of ultrasonic field exposition. The largest particles were obtained for unmodified samples and they amounted to even 479 μm (Figs. 2 and 3). The smallest particles were obtained for samples modified for 240 s and amounted to 0.724 μm for ketoprofen. Based on the results from more than 200 experiments, one could conclude that the length of sonication time has a very

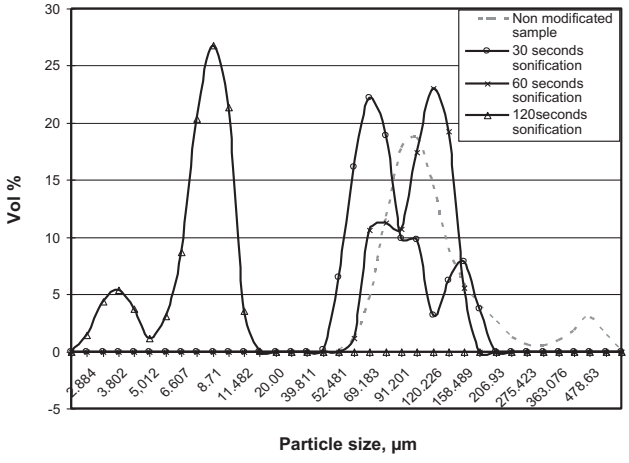

Fig. 3. Influence of sonication time on particles' size (ketoprofen).

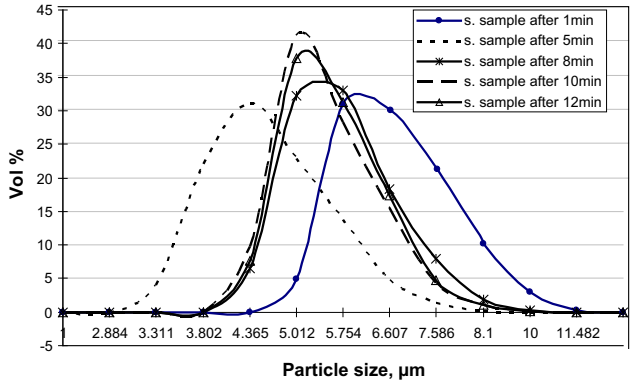

Fig. 4. Changes in size distribution of diclofenac particles in the modified sample after:1, 5, 8, 10, and 12 min.

strong influence on the results. The best results were obtained for the samples modified for 240 s, and the worst for 60 s of sonication (Fig. 3). This feature was observed for both tested drugs. The stability of the disintegrated particles was studied in the longer time intervals as well. Best results were observed for the sample containing diclofenac (Fig. 4), in which the particles did not return to the form of larger aggregates.

5. Conclusions

(1) With longer duration of sonication, the particle size reduction occurs. The longer the sonication is, the smaller and more stable the particles are. Participation of small particles was very similar even after a long time span.
(2) A decrease in the volumetric concentration of the solution was observed. For ketoprofen the concentration decreased from 0.0183 to 0.001% vol. Decrease in the concentration of diclofenac in solution was also observed. Concentration decreased from 0.0449 to 0.0005% vol. The lowest observed concentrations were 0.0001 and 0.00012% vol.
(3) The smallest particle size with diameter equal 0.724 μm was observed for the diclofenac sonicated for 240 s.
(4) The obtained results indicate the necessity to continue research with broader group of drugs, and changing the ultrasonic field parameters so that the full assessment of the process could be realized. It is worth making a practical assessment of the suitability of the observed phenomena in the process of wastewater and surface water treatments.

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