Abstract of the PhD dissertation

"PHARMACEUTICALS AND THEIR TRANSFORMATION PRODUCTS IN WATERS – ANALYTICS, HYDROLYTIC STABILITY AND THEIR ADSORPTION ONTO MULTI-WALLED CARBON NANOTUBES"

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The main aim of this thesis was to develop novel and sensitive analytical methods for the determination of selected pharmaceuticals and their transformation products in aqueous environmental samples and apply them in the comprehensive analysis of these compounds in different matrices, during hydrolytic studies and in the evaluation of their removal with multi-walled carbon nanotubes - MWCNTs (which included investigation of the regeneration methods and the performance of the adsorbent after such treatment as well as application of MWCNTs/chitosan membranes) from water. The analytes investigated in this research included various representatives of different therapeutic groups, such as antiepileptic, non-steroidal anti-inflammatory drugs (NSAIDs), beta-blockers, antibiotics, opioid analgesics and anticancer drugs as well as their selected TPs.

The analytical methods based on the application of HPLC-UV/Vis technique have been successfully developed for 17 single compounds and applied in model experiments on hydrolytic stability and on the adsorption studies with MWCNTs. Furthermore, the analytical methods with the LC-MS/MS equipment were developed. First, the LC-MS/MS with ion trap analyser was used for the method development and selection of the best SPE conditions for the extraction of the analytes from water samples. The method was evaluated in terms of the matrix effects, extraction efficiency and absolute recovery. Afterwards, the analytical method has been transferred to another, more sensitive and faster LC-MS/MS with triple quadrupole analyser. It was evaluated, fully validated, and finally, applied for the determination of the investigated compounds in various environmental water samples, such as wastewaters and surface waters. Based on the obtained results it was proved that not only pharmaceuticals could be detected in the analysed samples but also their transformation products, including metabolites at the level from hundreds ng/L to even several μg/L in the case of wastewaters or even up to 90 ng/L in the surface water. However, it must be highlighted that in general, surface waters were much less polluted with these compounds and their concentration levels were one, two or even three orders of magnitude lower than in the wastewaters. Nevertheless, carbamazepine was found in almost all analysed samples. Presented

data is crucial in terms of their future risk assessment in Poland, as the state of the knowledge on this problem (mainly for pharmaceuticals' transformation products) is still very limited.

Taking into account the obtained results on their inevitable presence in the aquatic environment and still limited data on their stability in the environment, investigations of the hydrolytic stability of 17 pharmaceuticals and their transformation products have been performed according to the standardized guideline OECD 111. It was proved that most of the selected analytes may be classified as hydrolytically stable under environmental conditions (their $t_{1/2}$ > 1 year at 25 °C). Only cyclophosphamide, ifosfamide, carbamazepine-10,11-epoxide, hydroxymetronidazole and 4-hydroxydiclofenac have been evaluated as unstable; however, at the environmentally relevant temperatures (20 °C and less) almost all of them could be recognized as persistent. Only carbamazepine-10,11-epoxide at pH 4 was degraded quite quickly with the half-life of around 8 days at 20 °C. The presented data is crucial in their future risk assessment, as the state of the knowledge on their fate in the environment is still not sufficiently known.

Furthermore, special attention has been paid to the assessment of the potential application of selected type of the MWCNTs for the removal of such pollutants from water samples. This aspect included the evaluation of the possibility of their regeneration and reuse as well as possibility to use them in combination with chitosan as MWCNTs/chitosan based membranes. As a result, it was shown that thermal regeneration of MWCNTs can be successfully performed at 300 °C and no influence was observed on the adsorption of three anticancer drugs – cyclophosphamide, ifosfamide and 5-fluorouracil after treatment. The Freundlich and Langmuir isotherm parameters indicated that the adsorption capacity after such treatment even increased. However, after the chemical regeneration with HNO_3 or HCl there was a decrease in adsorption level of cyclophosphamide, but it was also proven that these acids efficiently remove metals from MWCNTs. Additionally, membranes with MWCNTs and chitosan were evaluated in different setups (type of MWCNTs, pH, number of membranes) for the elimination of pharmaceuticals and their TPs from water in quick process. It was observed that the removal was sufficient only for selected analytes (for example diclofenac, 4-hydroxydiclofenac, N^4-acetylsulfamethoxazole). Therefore, the composition with chitosan as a membrane should be further investigated to find a more efficient way of their performance. Nevertheless, such combination with the MWNCTs/chitosan based membranes was investigated for the first time for the removal of the mixture of different pharmaceuticals and their transformation products.