# DETERMINATION OF SELECTED NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN THE AQUATIC ENVIRONMENT

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## INTRODUCTION

Over 3000 different drugs are registered on the European Union pharmaceutical market. The increase in the production of pharmaceuticals is associated with the lengthening of human lifespan related to advances in diagnosis and treatment of diseases and the wide availability of drugs, particularly those available over the counter. This results in the continuous release of those chemicals and their metabolites to the environment. The presence of pharmaceutical compounds in the aquatic environment is a potential threat to these ecosystems and thus to human health. Among pharmaceuticals diclofenac and ibuprofen are the most common in the water environment.

The quantification of pharmaceutical compounds in the environment is a difficult procedure because of their low concentrations within the range of tens of µg/l to several ng/l, and the coexistence of pharmaceutical active compounds from different treatment groups.

The identification of individual compounds may also be impeded by the presence of other organic micropollutants. The challenge is therefore to develop an analytical procedure which is characterized by high sensitivity and accuracy, allowing the determination of the largest possible number of pharmaceutical micropollutants and by-products of their decomposition during the treatment of water streams.

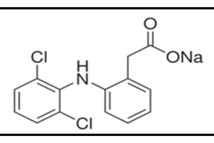
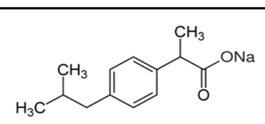
## AIM OF THE WORK

The poster presents a comparison of two analytical procedures of selected non-steroidal and anti-inflammatory drugs: diclofenac (DCL) and ibuprofen (IBU). The presented methods are based on the isolation of analytes from water samples by means of solid phase extraction (SPE) and their determination using HPLC (UV) as well as GC-MS (EI) method.

## WATER SAMPLES

During the study of the extraction proces, two aqueous solutions were prepared using deionised water and IBU and DCL standards at a concentration of 0.5 mg/l and 1 mg/l. The pH was adjusted to pH 7 with 0.1 M HCl or 0.1 M NaOH.

Table 1. Physicochemical characteristics of selected pharmaceuticals

| Pharmaceutical compound | Diclofenac sodium salt | Ibuprofen sodium salt |
|---|---|---|
| Structural formula |  |  |
| Molecular formula | $C_{14}H_{10}Cl_2NNaO_2$ | $C_{13}H_{17}O_2Na$ |
| Molecular weight, g/mol | 318.13 | 228.26 |
| Solubility in water, mg/l | 50 | 100 |

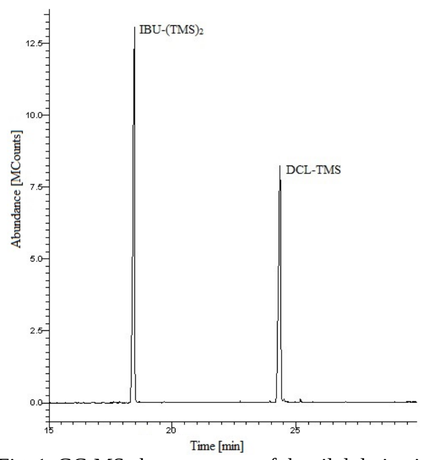



Fig. 1. GC-MS chromatogram of the silyl derivatives of ibuprofen and diclofenac

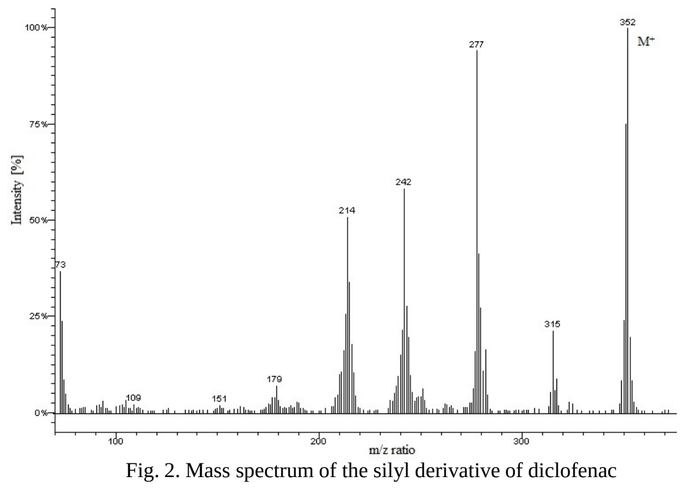



Fig. 2. Mass spectrum of the silyl derivative of diclofenac

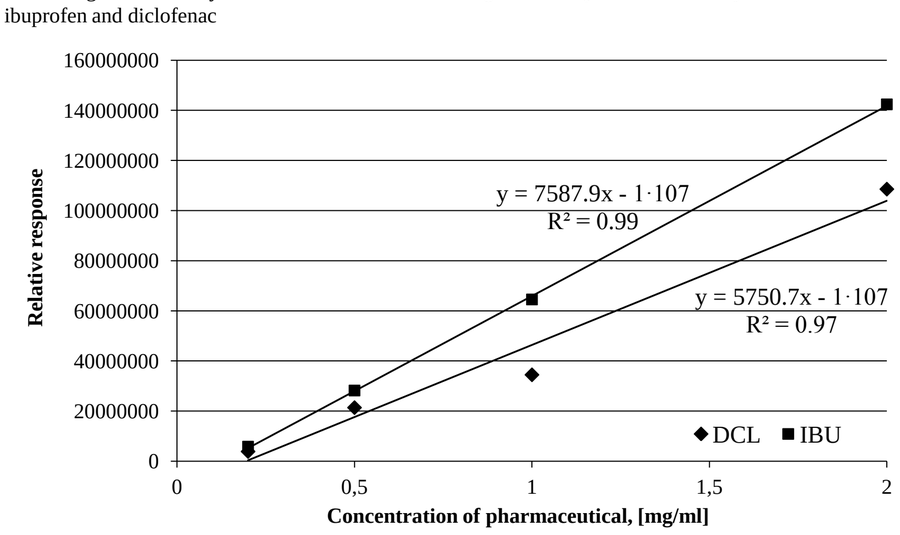



Fig. 3. Calibration curve of DCL and IBU determination by the GC-MS (EI) method

## ANALYTICAL PROCEDURE

| HPLC (UV) method | GC-MS (EI) method |
|---|---|
| - Solid phase extraction (SPE) in cartridges with octylsilane ($C_8$) packing,<br>- Drying of eluents under a stream of nitrogen and their dissolution in methanol,<br>- Quantitative and qualitative analysis of pharmaceuticals. | - Solid phase extraction (SPE) in cartridges with octylsilane ($C_8$) packing,<br>- Derivatisation of eluents with a silylating reagent – MSTFA,<br>- Quantitative and qualitative analysis of pharmaceuticals. |

Table 2. Parameters of the qualitative analysis

| Method | Compound | Characteristic ions, m/z | Retention time, $t_R \pm SD$ (n = 5)*) | CV, % (n = 4) | IDL, ng/µl |
|---|---|---|---|---|---|
| HPLC (UV) | IBU | - | 3.190 ± 0.010 | 0.08 | 5 |
| | DCL | - | 2.150 ± 0.010 | 0.02 | 2 |
| GC-MS (EI) | IBU-$(TMS)_2$ | 350, 263, 234, 161, 117 | 18.429 ± 0.059 | 2.82 | 2 |
| | DCL-TMS | 352, 277, 242, 214, 179 | 24.319 ± 0.063 | 1.50 | 11 |

*) n - number of replicates

Table 3. Precision of the detector response

| Method | Compound | Concentration, µg/µl | | | |
|---|---|---|---|---|---|
| | | 0.2 | 0.5 | 1 | 2 |
| | | CV, % (n = 5) | | | |
| HPLC (UV) | IBU | 3 | 2 | 0.1 | 0.1 |
| | DCL | 1 | 1 | 0.1 | 0.1 |
| GC-MS (EI) | IBU | 1 | 1 | 6 | 3 |
| | DCL | 1 | 2 | 1 | 2 |

Table 4. Repeatability of tested analytical methods in the determination process of analytical standards of drugs

| Compound | Concentration in model water | | | |
|---|---|---|---|---|
| | 0.5 mg/l | | 1 mg/l | |
| | Recovery, % (n = 5) | SD, % | Recovery, % (n = 5) | SD, % |
| IBU | 55 | 4 | 60 | 9 |
| DCL | 78 | 3 | 85 | 4 |

Table 5. Limit of quantification (LOQ) of proposed methods for analytical standards of IBU and DCL

| Compound | Method | |
|---|---|---|
| | HPLC-UV | GC-MS (EI) |
| | µg/l | ng/l |
| IBU | 2.8 | 16 |
| DCL | 0.8 | 44 |

## CONCLUSIONS

- Presented analytical procedures allow for separation and quantification of mixtures of two non-steroidal anti-inflammatory drugs present in water at a concentration of 1 mg/l and 0.5 mg/l with satisfactory accuracy and repeatability. The GC-MS (EI) technique has a higher sensitivity than HPLC (UV).
- Values of the degree of recovery enable full control over the quantification of the studied pharmaceuticals in water samples.
- Analytical procedure based on the HPLC (UV) technique can be used for screening of tested compounds. Furthermore, determination of the studied pharmaceuticals in the environment at low concentration levels is possible by the procedure employing the GC-MS (EI) chromatography.