

PHOTODEGRADATION STUDY OF IRINOTECAN AND IDENTIFICATION OF TRANSFORMATION PRODUCTS IN WATER SAMPLES BY UHPLC-MS/MS

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INTRODUCTION

Pharmaceuticals are one of the most relevant groups of emerging contaminants in aquatic environments due to their universal use, physicochemical properties and known mode of action in aquatic organisms at low concentrations [1]. Supported by the development of highly sensitive analytical and bioassay methods, the persistence and toxicity of antitumoral drugs and their transformation products has been the focus of recent research on water pollution [2].

In this study, the photodegradation of the anticancer drug irinotecan has been investigated. Irinotecan, also known as CPT-11, is a semi-synthetic water-soluble analogue of the natural alkaloid camptothecin. CPT-11 is among the most widely used drugs in cytotoxic chemotherapy, reported as one of the 200 most-prescribed off-patent active ingredients in the European Union in 2013 [3]. It is mainly used to treat colon cancer and small lung cancer [4], but also for the treatment of non-small cell lung cancer, ovarian cancer, malignant brain tumors, gastric cancer, cervical cancer and pancreatic cancer [5].

The aminopentane carboxylic acid (APC), the NPC (a primary amine metabolite) and the SN-38G glucuronide are the CPT-11 human metabolites mostly detected in urine, bile and faeces. Moreover, between 45% and 63% of the administered CPT-11 is excreted as parent drug by the human body [6], an amount that typically enters the sewerage system ultimately reaching ground and surface waters. For this reason, our study was focused on the possible presence of CPT-11 in the aquatic system, given its relatively high abundance with respect to that of its metabolites. We developed a rapid and sensitive UHPLC-MS/MS method suitable for the identification of CPT-11 and its PDPs in river water samples.

EXPERIMENTAL PART

The Photodegradation Procedure



- Photo-irradiation of samples
- Solarbox conditions: irradiance = 600 W/m² and Temperature = 35 °C
- Soda-lime glass UV-filter

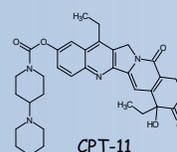
Sampling at prefixed irradiation times (0-13 days) and subsequent analysis by UV/Vis spec.



UV/Vis Spectrophotometer (JASCO V-550, Milan)

- Analysis of the measured UV spectrum and monitoring the photodegradation progress

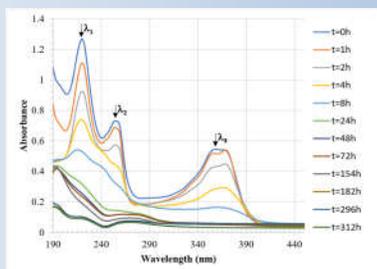
The UHPLC-MS/MS Analysis



- Shimadzu Nexera Liquid Chromatography system (Kyoto, Japan)
- 3200 QTrap™ LC-MS/MS system (Sciex, Concord, Canada)
- Kinetex XB-C18 column (3.0 mm x 100 mm; 1.7 μm)
- Mobile phase: Water + 0.1% FA (A) and Methanol + 0.1% FA (B)
- Ionization: ESI(+)
- Data processed by Analyst 1.5.2 software (Toronto, Canada)

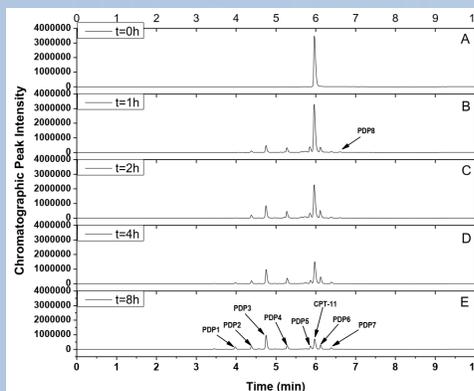
RESULTS

1. UV-Vis Spectrometric Measurements

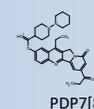
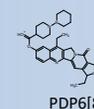
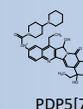


- 90% reduction of the initial peak intensities of CPT-11 after 7.5 days
- About 5% of the initial CPT-11 peak recorded after 296 h and no further significant reduction of intensity

2. Development of UHPLC-MS/MS Method and Identification of PDPs



- 8 PDPs identified.
- 3 of them were already reported; PDP5 (bile) and PDP6 & PDP7 (aqueous).
- 5 of them were identified for the first time and their chemical structures proposed.
- Hydrolysis (dark) → NO formation of other species
- Validated method: LOD = 0.02, LOQ = 0.05 ng/mL.
- River water analysis:
 - ✓ MDL = 0.03 & MQL = 0.10 ng/mL
 - ✓ Neither CPT-11 nor any of its PDPs found
- Manuscript submitted for publication.



CONCLUSION

- Photodegradation of CPT-11 in aqueous solutions relevant to surface water conditions.
- A validated, very sensitive UHPLC-MS/MS method developed for the identification of CPT-11 PDPs.
- A total of eight PDPs (PDP1-PDP8) identified and their chemical structures proposed.
- Five of them were identified for the first time and only two of them (i.e. PDP6 and PDP7) were previously detected in aqueous samples.
- The findings of the present study will be significant in updating the current knowledge about the possible formation of CPT-11 PDPs up on the excretion of the drug (in hospitals) and find the way to enter the wastewater and surface water systems.

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