

## O1 EAC2

### DEVELOPMENT AND VALIDATION OF A UHPLC-MS/MS METHOD FOR THE IDENTIFICATION OF IRINOTECAN PHOTODEGRADATION PRODUCTS IN WATER SAMPLES

M.H. Belay, F. Gosetti, E. Robotti, E. Marengo

*Dipartimento di Scienze e Innovazione Tecnologica, Università degli Studi del Piemonte Orientale "Amedeo Avogadro", Alessandria, Italy*

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 anticancer drugs and their transformation products have been the focus of recent research on water pollution [2]. Irinotecan (CPT-11) is a water-soluble anticancer drug widely used to treat several types of cancer such as colon, small lung, ovarian, brain, gastric, cervical and pancreatic cancers. Studies have indicated that not all administered CPT-11 drug is metabolized, but an amount around 45-63% is excreted as parent drug by the human body [3] and enter the sewerage system ultimately reaching ground and surface waters. Even if the metabolites of CPT-11 are well-known and investigated, very limited information is present in the literature about the formation of photodegradation products that can naturally originate from sunlight irradiation when the drug is released in aqueous systems.

In the present study, CPT-11 solutions at  $10.0 \text{ mg L}^{-1}$  were irradiated for a maximum of 13 days by simulated sunlight through a solar box (Co.fo.me.gra 3000e, Milan, Italy) utilizing Xe lamp at  $600 \text{ W m}^{-2}$  and temperature of  $35 \text{ }^\circ\text{C}$ . In the course of the photodegradation process, sample aliquots of about 3 mL were withdrawn after irradiation at prefixed time intervals. In order to monitor the progress of the photodegradation process, the sample aliquots were subsequently analysed by UV-Vis spectrophotometer (Jasco V-550, Milan, Italy). The intensity of CPT-11 decreased by 90% after 7.5 days of irradiation and no significant reduction of absorbance values was observed after 12 days.

A sensitive UHPLC-MS/MS method was developed employing a hybrid triple quadrupole/linear ion trap mass spectrometer (Nexera UHPLC-MS/MS, Shimadzu, Tokyo, and 3200 Qtrap, Sciex, Canada), that is able to work in data-dependent acquisition mode, in order to automatically obtain information about the unknown species formed by irradiation and to build a reaction monitoring method with the MS/MS fragmentation pattern of the species previously investigated. The method was validated obtaining for CPT-11 LOD and LOQ values of  $0.02$  and  $0.05 \text{ ng mL}^{-1}$ , respectively and MDL and MQL in river water of  $0.03$  and  $0.10 \text{ ng mL}^{-1}$ . Eight photodegradation products were identified and five of them for the first time. The total ion chromatogram (TIC) given in Fig. 1 shows the formation of the photodegradation products for the first five irradiation time points. The chemical structures of the unknown species formed in the photodegradation process were proposed on the basis of the following data: (i) the molecular mass identified by the quasi-molecular ion in

## O1 EAC2

the MS, (ii) the isotopic pattern through the ER mode, (iii) the assignment of even or odd number of N atoms corresponding to an even or odd molecular mass, and (iv) the result of the MS/MS fragmentation analyses through the EPI mode. Hydrolysis experiments were also carried out on the same solutions preserved in the dark, but no formation of other species was highlighted. The method was applied to several real samples (river water, groundwater, well water before and after chlorination and samples collected close to a depurator outlet), but neither CPT-11 nor any of its photodegradation products were found. The outcomes of this study may be useful for updating the pollutant screening in water samples.

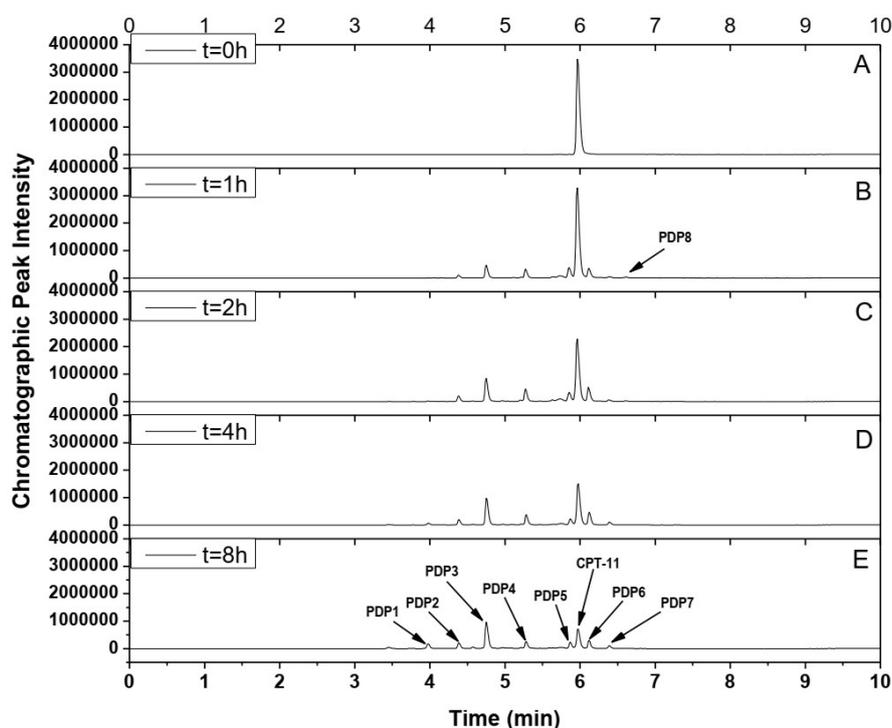


Figure 1. TIC for irradiated irinotecan solutions from time 0 to 8 h.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 765860.

### References

- [1] Nannou, C. I., Kosma, C. I., & Albanis, T. A., *International Journal of Environmental Analytical Chemistry*, 2015, 95, 1242-1262.a.
- [2] Isidori, M., Lavorgna, M., Russo, C., Kundi, M., Žegura, B., Novak, M., Filipič, M., Mišić, M., Knasmueller, S., de Alda, M.L., Barceló, D., Žonja, B., Česen, M., Ščančar, J., Kosjek, T., Heath, E., *Environmental Pollution*, 2016, 219, 275-287.
- [3] Slatter, J. G., Schaaf, L. J., Sams, J. P., Feenstra, K. L., Johnson, M. G., Bombardt, P.A., Cathcart, K.S., Verburg, M.T., Pearson, L.K., Compton, L.D., Miller, L.L., Baker, D.S., Pesheck, C.V., Lord, R.S., *Drug Metabolism and Disposition*, 2000, 28, 423-433.