

## INTRODUCTION

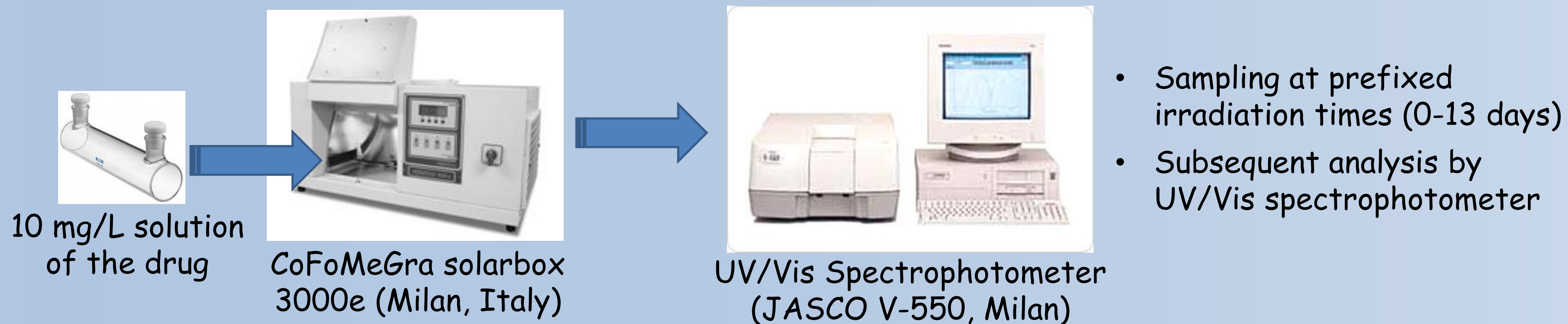
Pharmaceuticals are one of the most relevant groups of emerging contaminants in aquatic environments due to their universal use, physicochemical properties and known mode of action in aquatic organisms at low concentrations [1]. Supported by the development of highly sensitive analytical and bioassay 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 four anticancer drugs, namely, irinotecan (CPT-11), topotecan (TPT), gemcitabine (GEM) and mitomycin (MTC), has been investigated. The drugs are among the most widely used drugs in cytotoxic chemotherapy [3], used to treat colon cancer and small lung cancer like irinotecan, ovarian cancer, small lung cancer and cervical cancer like topotecan, cancer of the bladder, pancreas, ovary and breast, and non-small lung cancer like gemcitabine, and cancer of the breast, pancreas, stomach, anal, lung and liver like mitomycin.

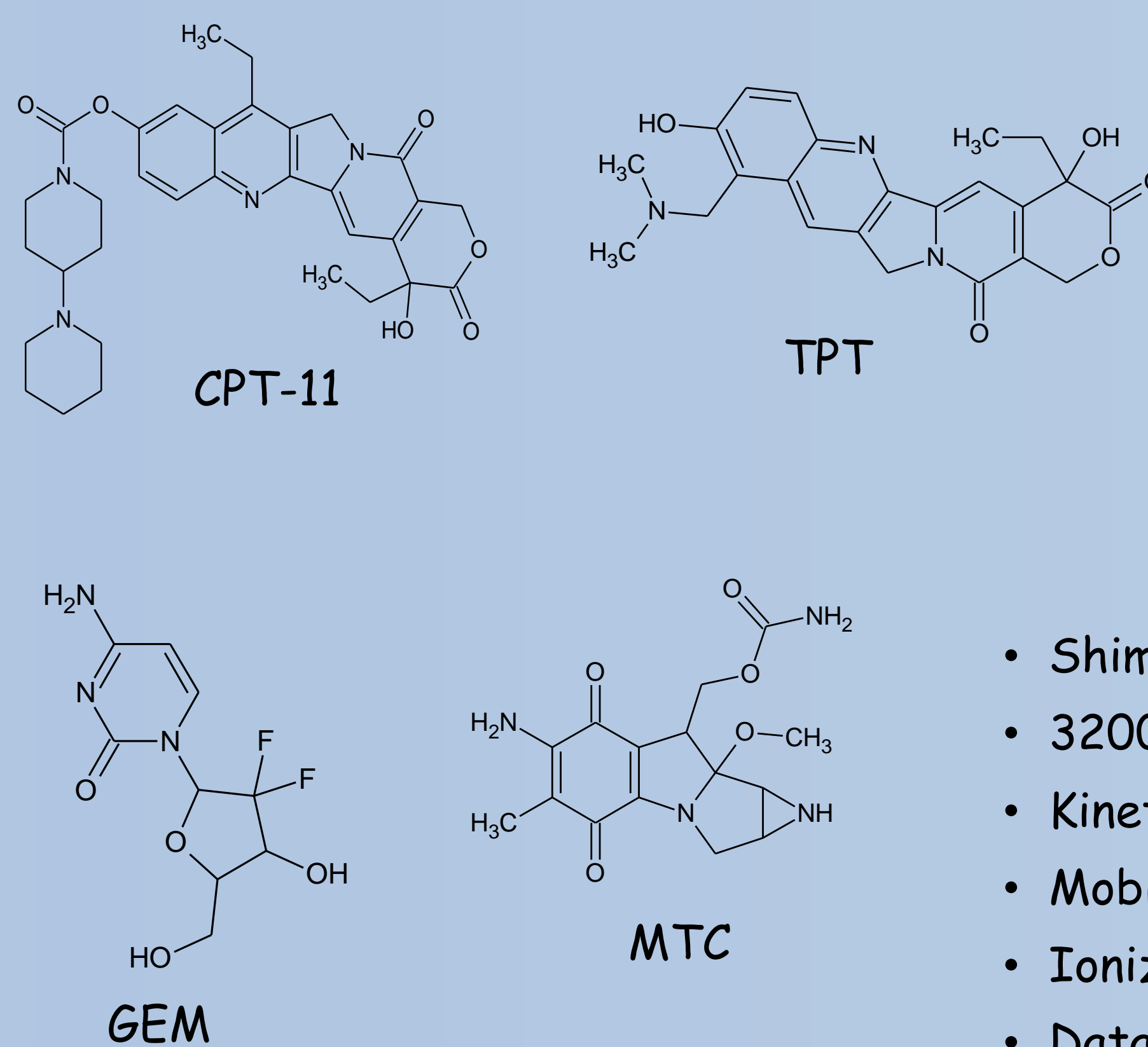
Several studies have indicated that an amount between 20% and 63% of the administered anticancer agents is excreted as parent drug by the human body [4-6]; an amount that typically enters the sewerage system ultimately reaching ground and surface waters. For this reason, our study was focused on the possible presence of CPT-11, TPT, GEM and MTC in the aquatic system and investigation of their fate in water upon interaction with sun light radiation. Here, we presented the photodegradation study of the selected compounds and in particular the development of a rapid and sensitive UHPLC-MS/MS method suitable for the identification of CPT-11 and its photodegradation products (PDPs) in water.

## EXPERIMENTAL PART

### The Photodegradation Workflow



- Photo-irradiation of samples
- Solarbox conditions: irradiance = 600 W/m<sup>2</sup> and Temperature = 35 °C
- Soda-lime glass UV-filter



### UHPLC-MS/MS Analysis



- Shimadzu Nexera LC 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 Experiments

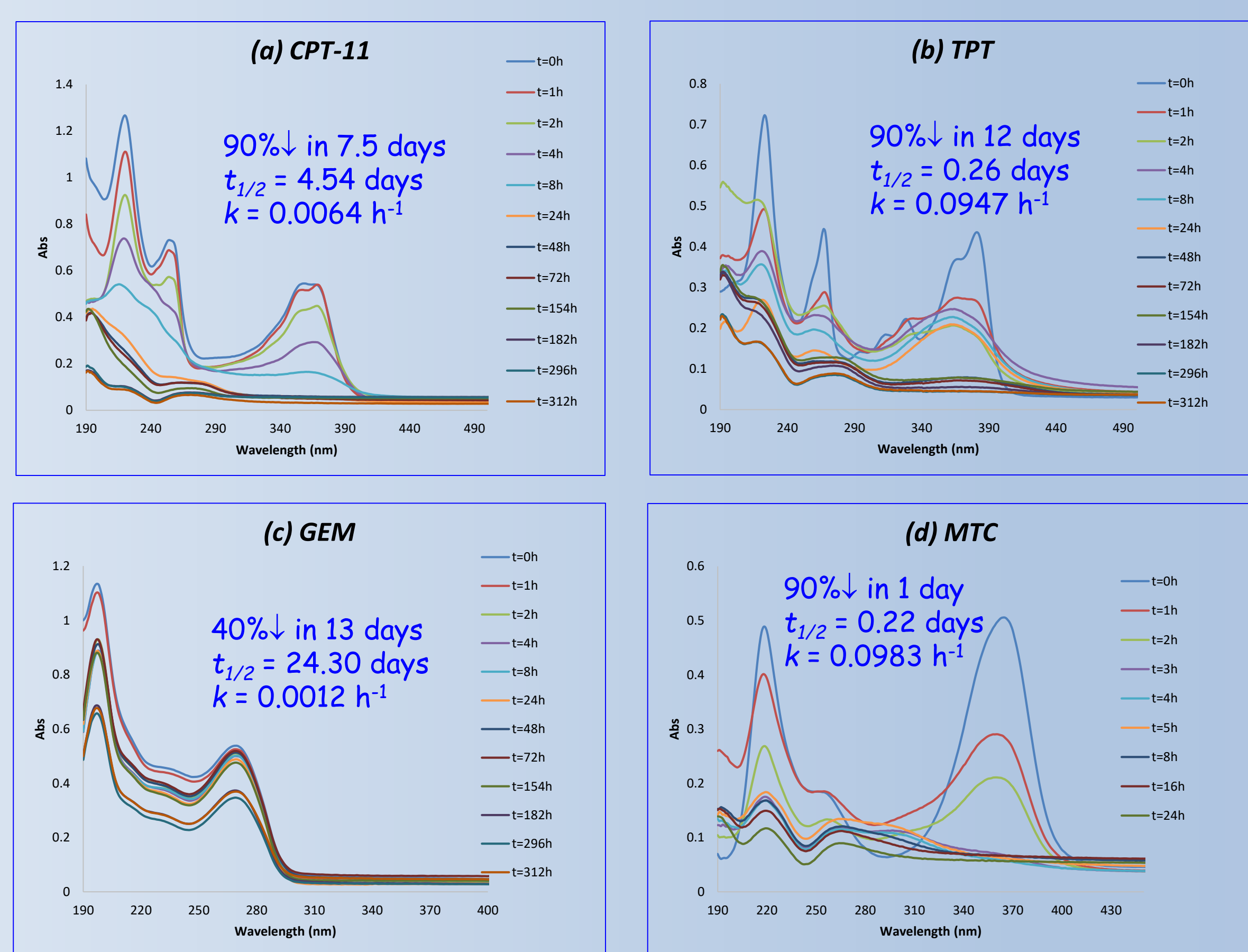
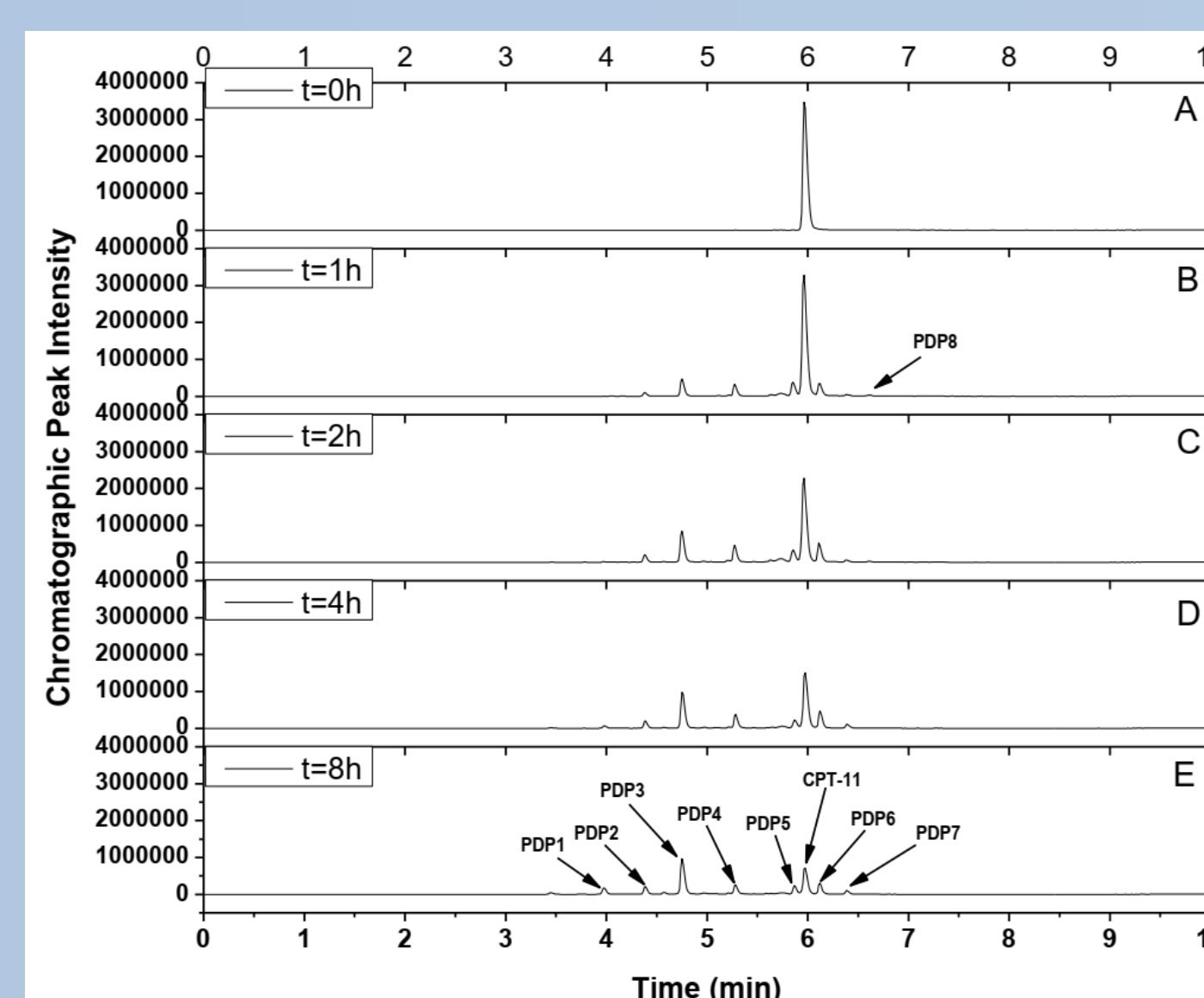
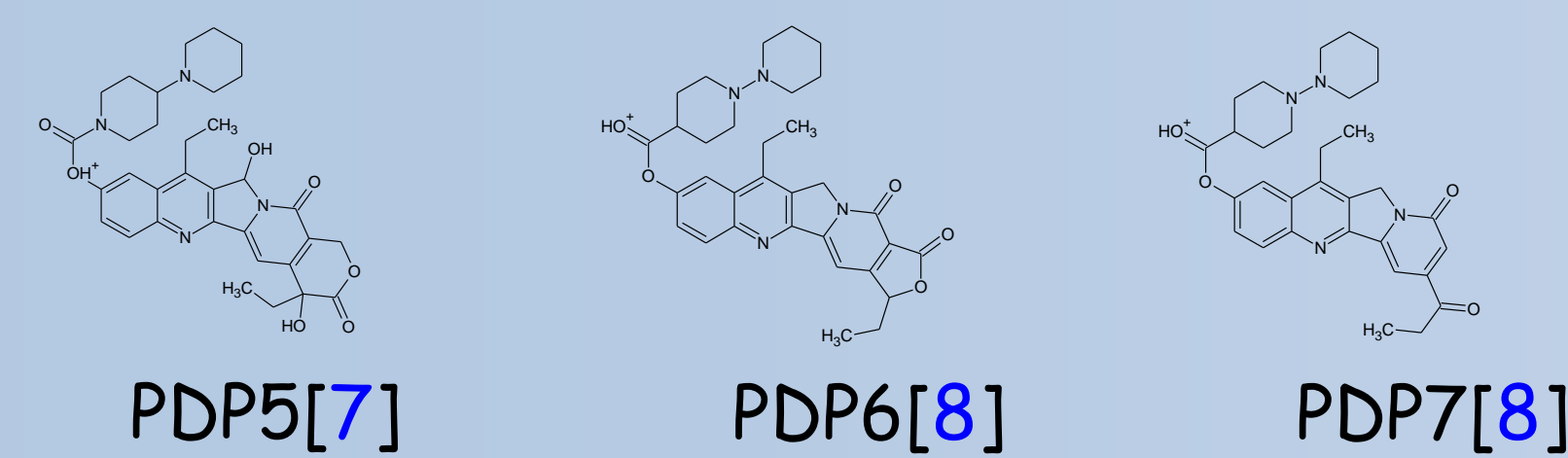


Fig. 1. UV absorbance measurements showing the photodegradation progress of irinotecan (a), topotecan (b), gemcitabine (c) and mitomycin (d). The photodegradation of all the four compounds obeyed pseudo-first order kinetics.

### 2. Development of UHPLC-MS/MS Method and Identification of CPT-11 and its PDPs in water



- 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 ng/mL ; MQL = 0.10 ng/mL
  - ✓ Neither CPT-11 nor any of its PDPs found

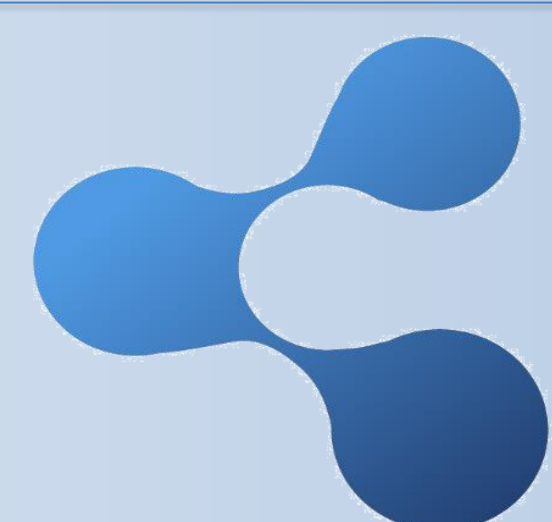


## CONCLUSIONS

- Photodegradation of four anticancer drugs in aqueous solutions relevant to surface water conditions.
- A validated, very sensitive UHPLC-MS/MS method developed for the identification of CPT-11 and its 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.

### References:

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