Carboplatin-Degradation Products Formed Under Deliberated and Non-deliberated Laboratory Experiments: Structural Elucidation

Water Research Center
Tel Aviv University

Igal Gozlan & Adi Rotstein & Dror Avisar

Introduction:

- Pharmaceutical residues derived from human therapy (hospital wastewater) is of great concern due to their potential toxicological effects.
- Many forms of residues drugs and their by products are rarely detected, however several studies have indicated some cancerostatic platinum compounds in hospital wastewater.
- Although Carboplatin is undisputed recognition in cancer therapy and is widely used, there are no reports on its detection.

The aims of this research:

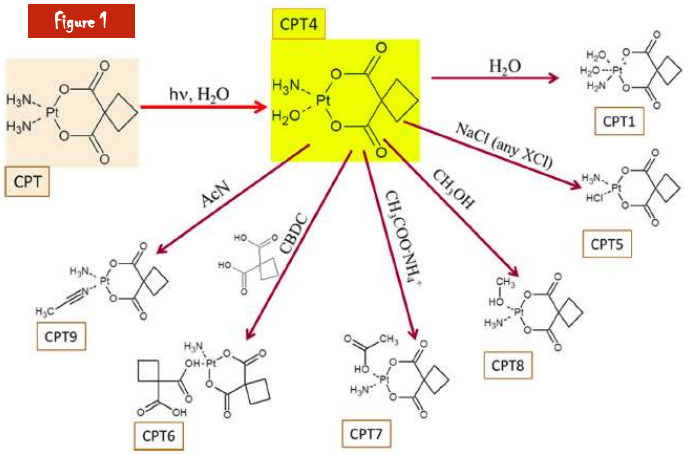
This study firstly addresses to characterize CPT together with CPT degradation products:

- Characterize the production of CPT DPs formed under controlled environmental conditions.
- Examine the kinetics behavior of CPT and CPT4
- Obtain selected CPT DPs under both deliberated (simulated environmental conditions) and non-deliberated laboratory experiments in various solutions, to verify their chemical structure.

Results and discussion

- CPT4 product was consistently obtained in the different solutions containing 100 µg/mL mostly under solar irradiation only.
- The DPs CPT6, CPT7, CPT8 and CPT9 were obtained during the laboratory experiments only in the presence of CPT4, which obtained only under solar irradiation (Figure 1).
- Informative UV spectra supported that the CPT DPs consist of a chelating dicarboxylate attached to the Pt atom (six member ring) and has a specific peak (Figure 2).
- The kinetics of the CPT degradation showed significant differences in the rates between solar irradiation compare to shade, which is probably due to decrease in CPT under photoactivity of the molecule (figure 3).

Figure 1



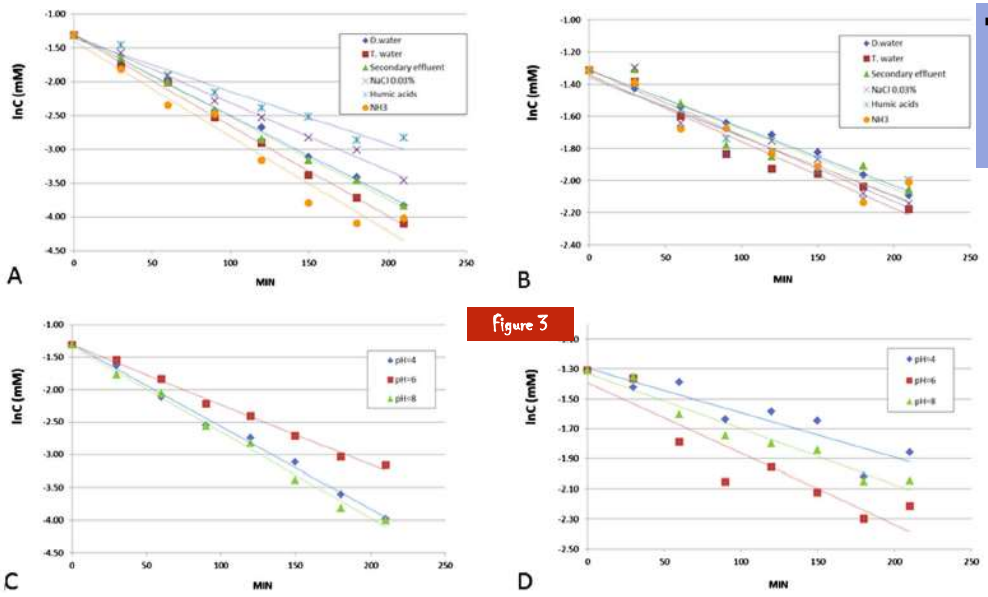


Figure 3

- CPT was relatively stable in the shade in all measured solutions, indicating by higher K_1 values under solar irradiation compare to shade.

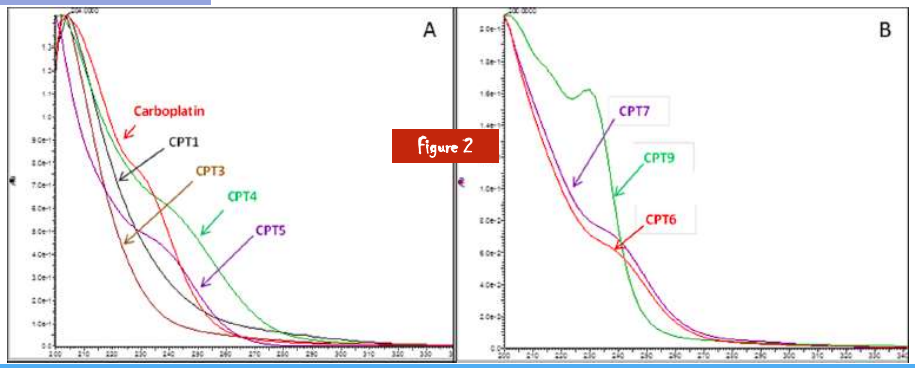
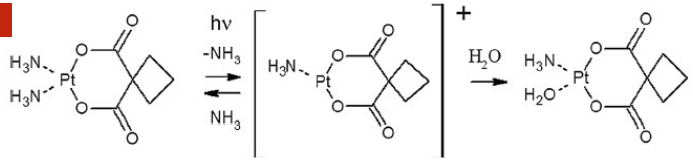


Figure 2

- CPT degradation under solar irradiation followed first order kinetics, indicating that the process occurs in two steps of NH3 group leaves the CPT and produce $[CPT - NH_3]^+$ at first and secondly nucleophilic group (e.g. H_2O) attaches to the Pt atom to form CPT4 (Figure 4).

Figure 4



Summary and Conclusions:

CPT DPs under deliberate and non-deliberate conditions were identified and characterized.
Kinetics behavior analysis of CPT and its main DP CPT4 formed under solar radiation.
Six CPT DPs: CPT1, CPT5, CPT6, CPT7, CPT8 and CPT9 were produced following exposure of CPT4 to solar irradiation in the presence of the appropriate nucleophiles.
These DPs retain the six-member ring which may increase the toxicity of these compounds to humans.
The degradation processes of CPT to CPT4 go through an intermediate product [CPT – NH3]+
The behavior of CPT under solar irradiation showed rapid but different degradation rates, while in the shade degradation rates where much lower but only minor differences in the degradation process..