CleanMed Europe 2018

Creating Healing Environments

Health Care Without Harm

Radboudumc university medical center

D4 & E4: MEDUWA-Vecht(e)

D4: **Alfons Uijtewaal,** The EU INTERREG-VA MEDUWA-Vecht(e) project, a general introduction, post@huizeaarde.nl

D4: **Ad Ragas,** Estimation and prioritization of hospital pharmaceutical (API) emissions, a.ragas@fnwi.ru.nl

E4: **Paul Leenders**, Plasma Activated Water Treatment, paul.leenders@vitalfluid.nl

E4: **Martien Graumans,** The use of plasma activated water and UV/H2O2 for the degradation of cyclophosphamide in wastewater, martien.graumans@radboudumc.nl

CleanMed
Creating Healing Environments
Europe 2018

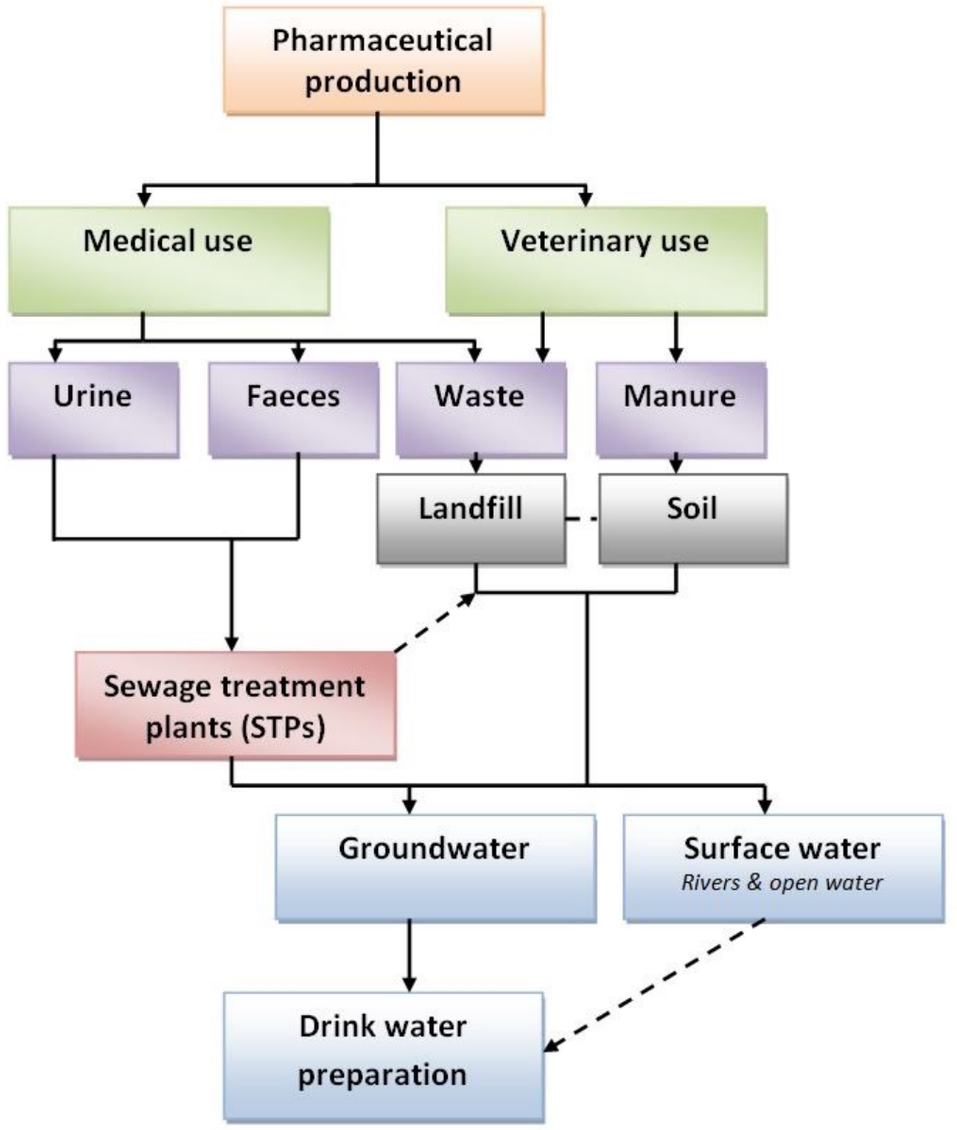
Using Plasma-activated water and UV/H_2O_2 treatment for the oxidation of persistent pharmaceuticals

INTERREG Deutschland Nederland
www.deutschland-nederland.eu
Europäische Union
Europese Unie
MEDUWA

Radboudumc
university medical center

Introduction

- Widespread usage of pharmaceuticals
  - *Veterinary and human use*
- Discharge via direct and indirect routes
- Sewage treatment plants (STPs)
  - *Filtration*
  - *Biodegradation*



Selection of priority substances

- MEDUWA consortium -> Taskforce
  - Shortlist as guidence

- Selection criteria:
  - *Measurements in Vechte basin*
  - *Consumption*
  - *Biodegradation*
  - *Toxicity*

- Shortlist: ***Antibiotics, anti-epilepticum, cytostati***
  synthetic hormone and anti-diabatic

Aim of the research study

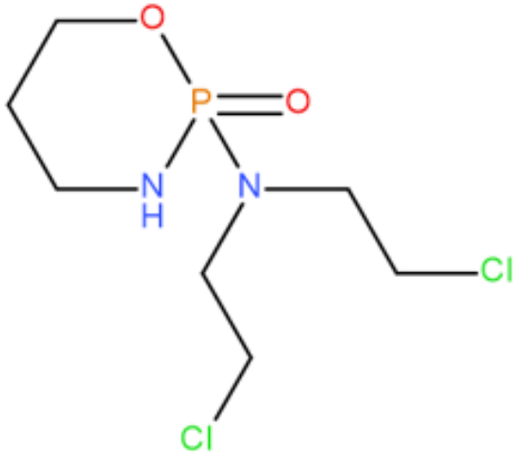
- **Prevention of contamination**

- **Oxidative degradation of pharmaceuticals**
  - Plasma Activated Water (PAW)-laboratory simulation
    - Test different matrices e.g.; tap water, urine, sewage water

- **Toxicity Assays**
    - Formation of harmful components?

Cyclophosphamide

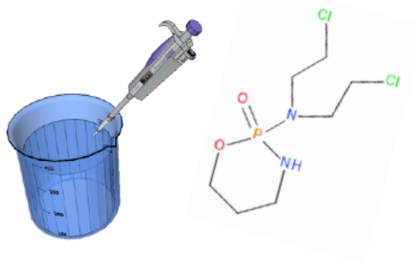
Compound, ***class*** and structure	Molecular weight (g/mol)
$C_7H_{15}Cl_2N_2O_2P$; Cyclophosphamide ***Antineoplastic agent***	260.02



- Carcinogenic and mutagenic
- Not easily removed by STPs
- Dutch River water: < **0.3 – 4 ng/L**
  - *2010 - 2017*
- Study simulation concentrations:
  - **4 µg/L: 'Low' conc.**
  - **1 mg/L: 'High' conc.**

Applied laboratory methodology

1) Spiking Cylcophosphamide

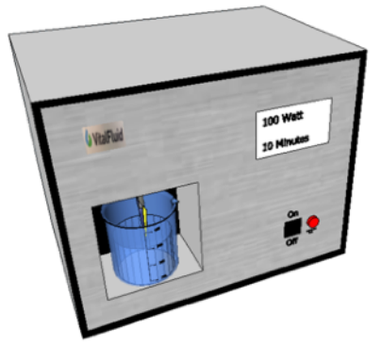


$C_7H_{15}Cl_2N_2O_2P$

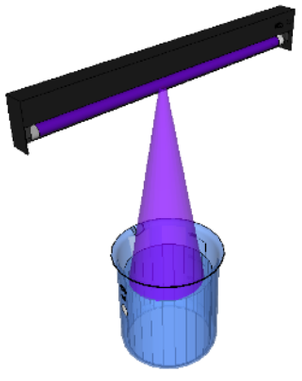
261.08 (g/mol)

Log $P_{(Octanol/Water)}$: 0.10

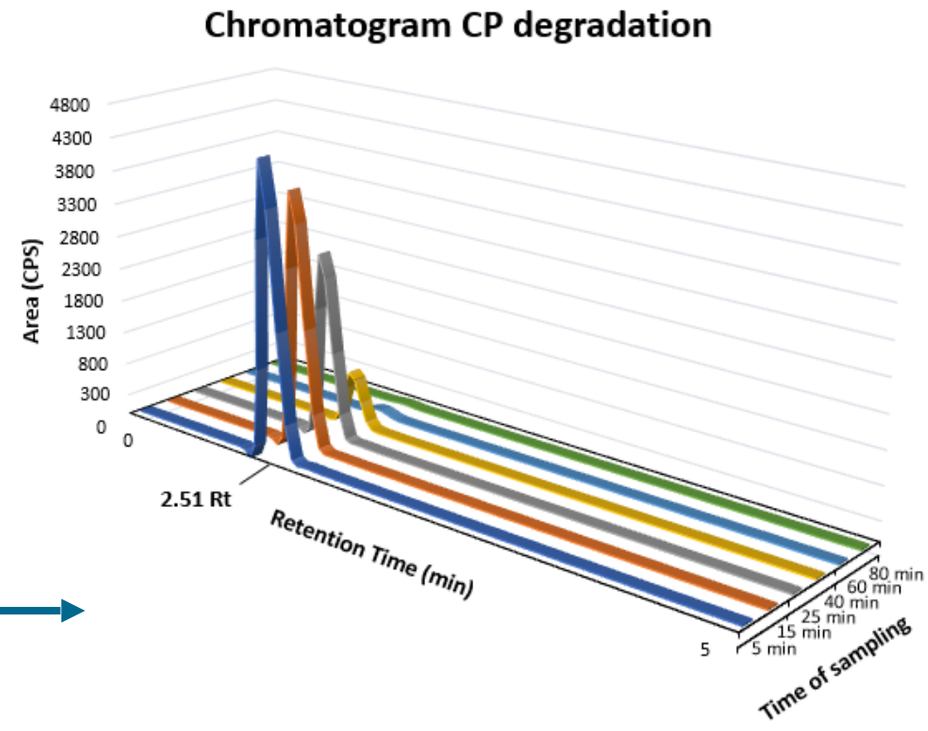
2a) PAW Treatment



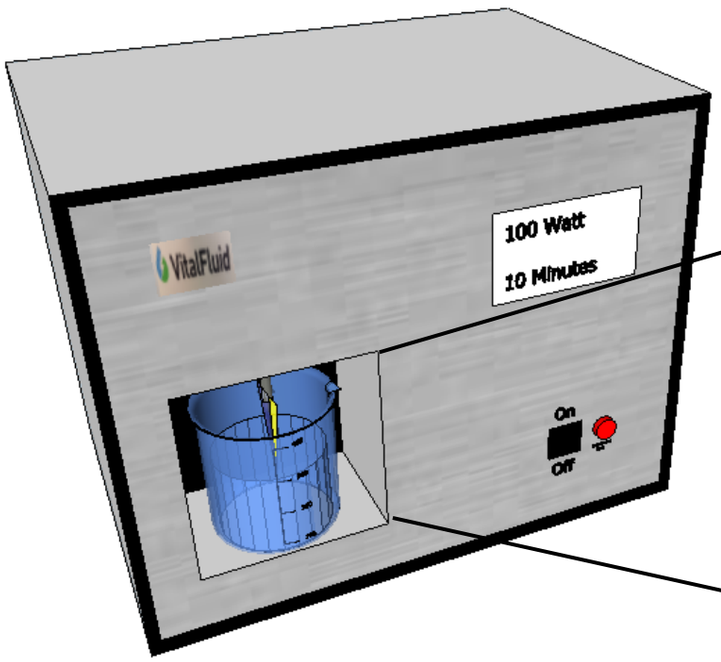
2b) UV/H_2O_2

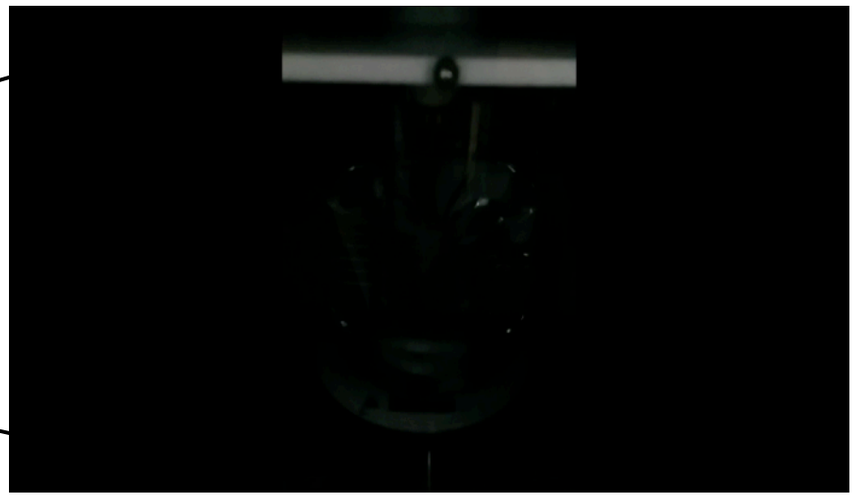


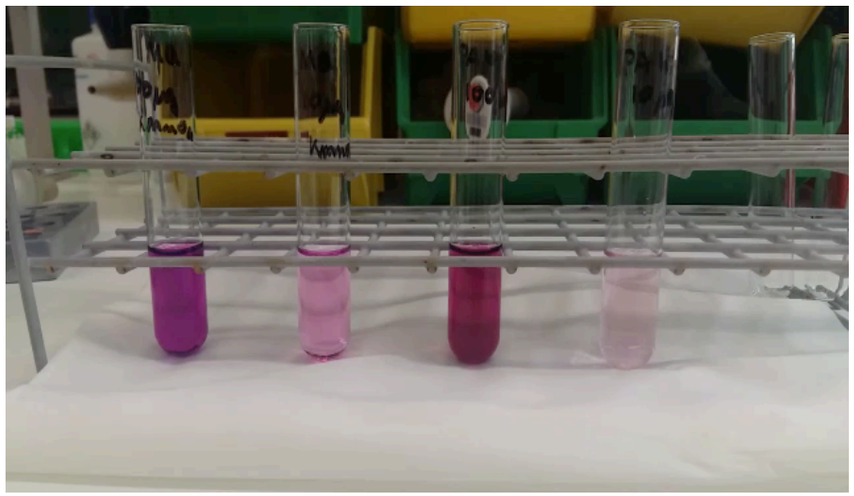
3)LC-MS/MS analysis



Plasma-activated Water (PAW)

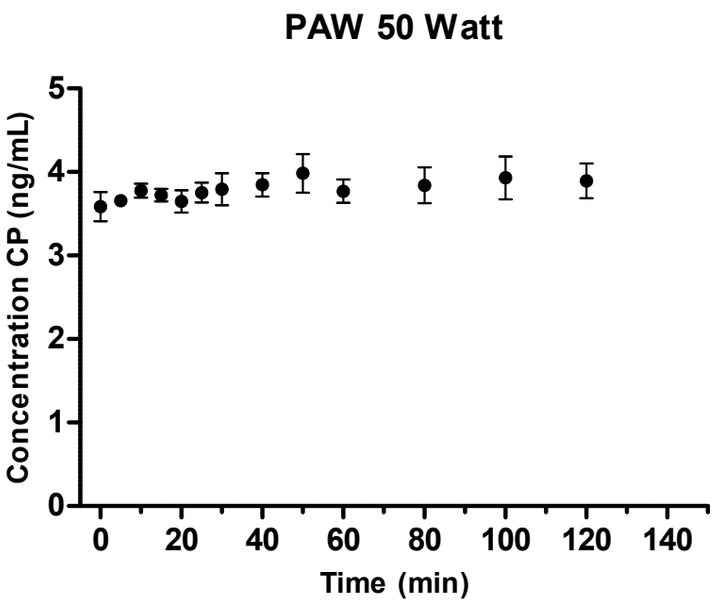


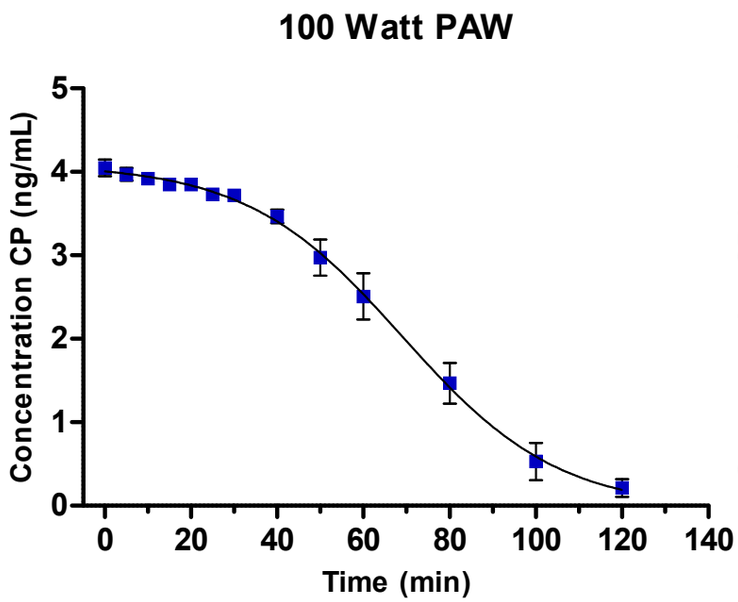


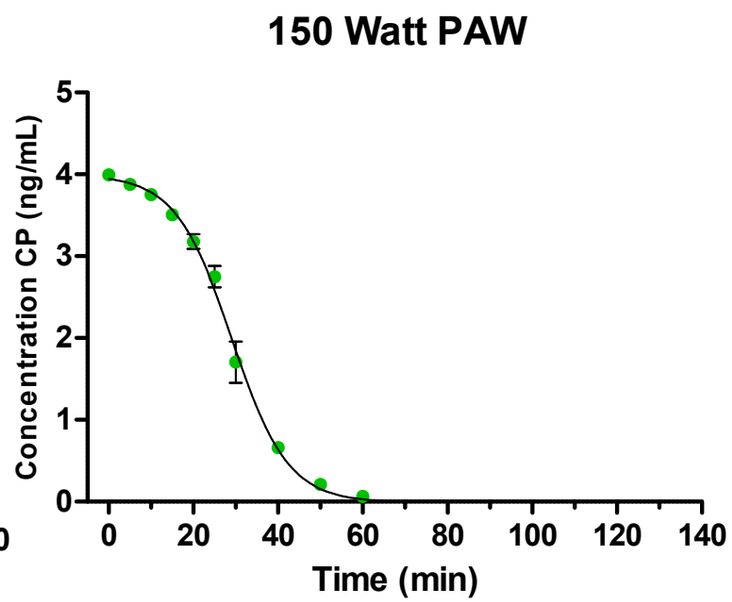


H_2O → PAW

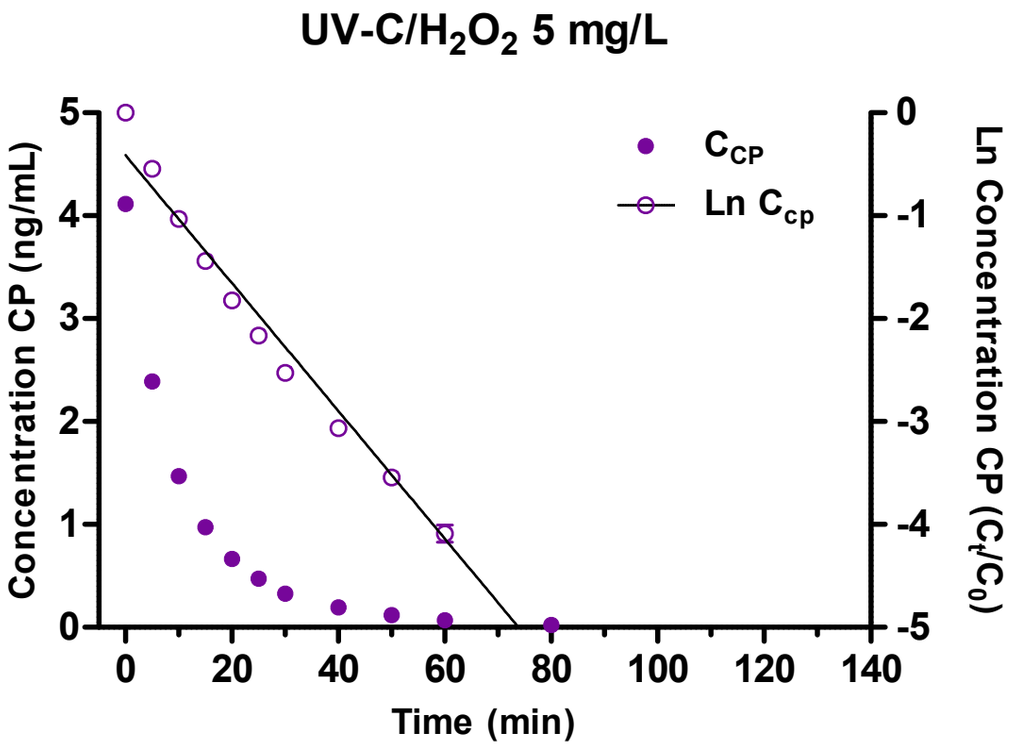
PAW Results: 4 µg/L CP

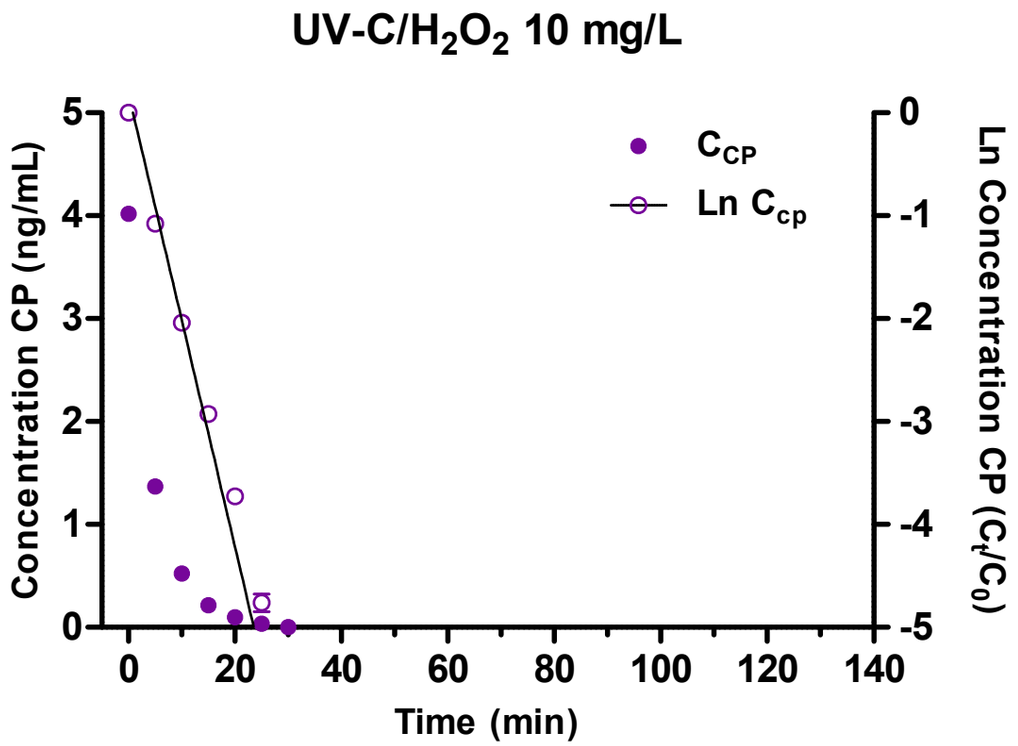




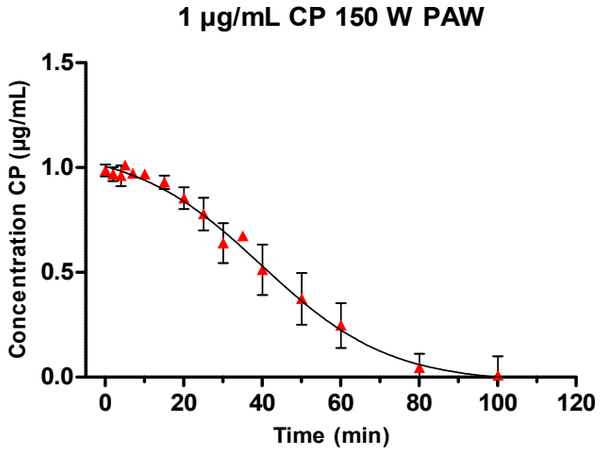


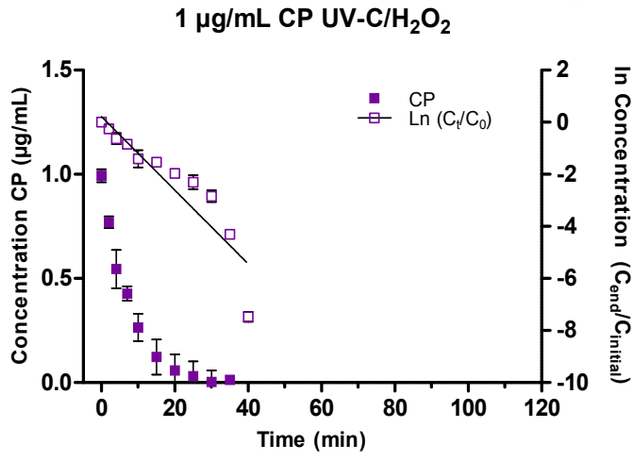
UV-C/H_2O_2 Results: 4 µg/L CP

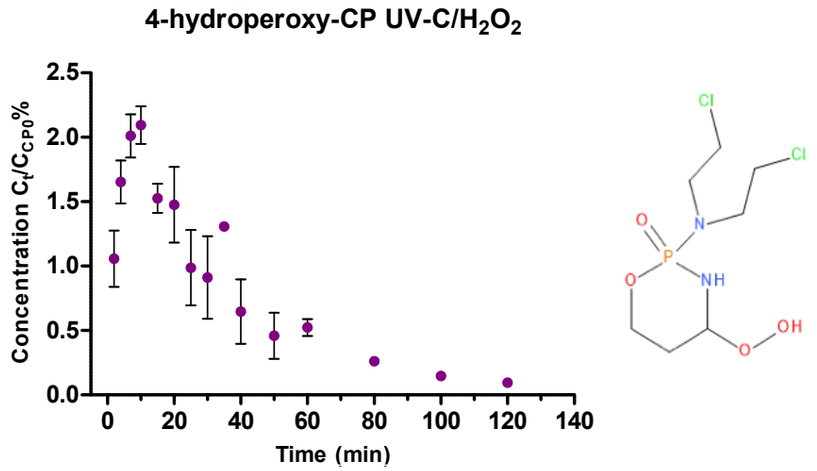


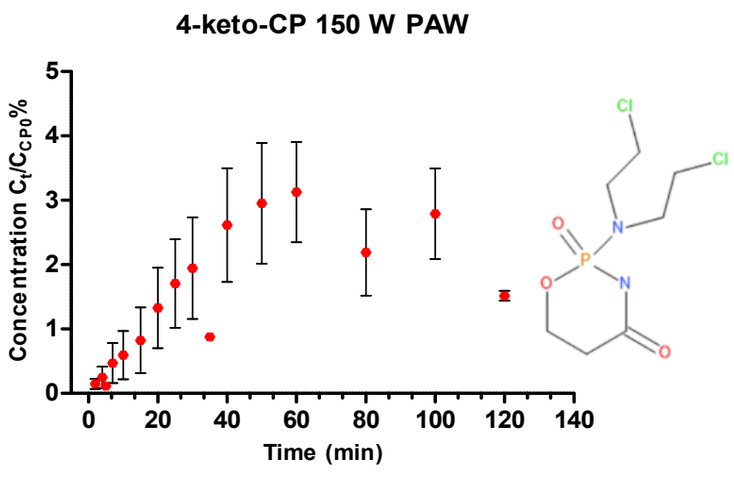


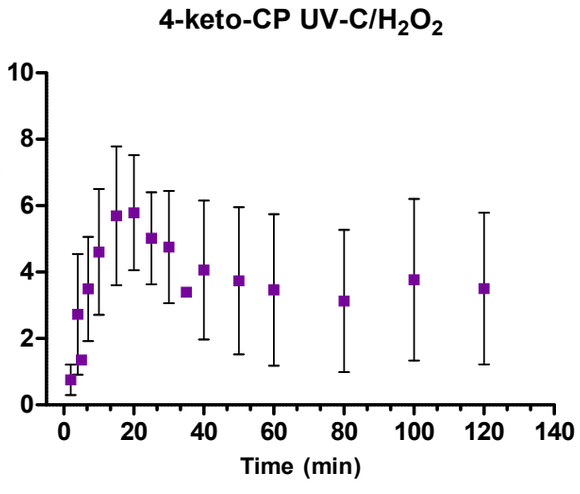
Reaction intermediates after ‘High’ CP degradation

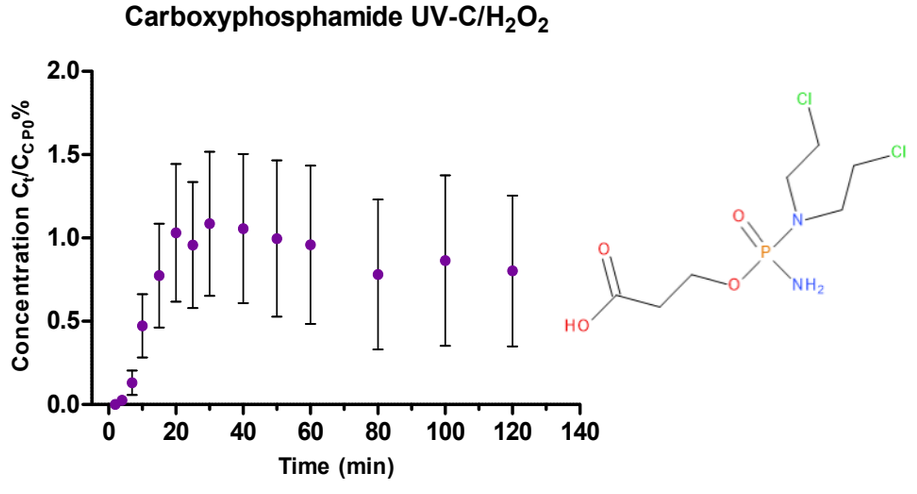






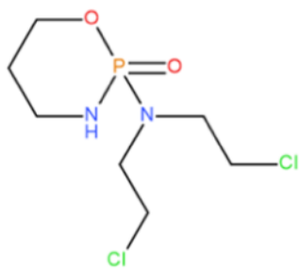


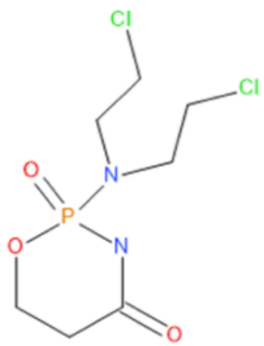




Characterisation and Identification

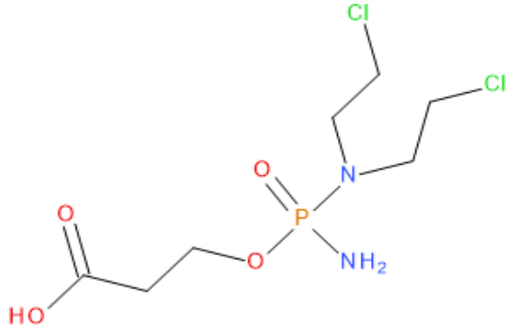
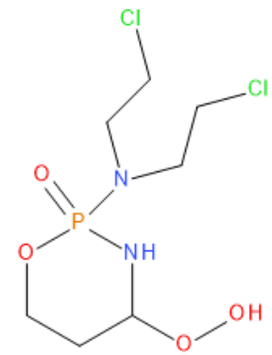
- Oxidation of CP:





- ·mediates PAW vs UV/H_2O_2

- ***Hypothetical mineralisation:***

$$C_7H_{15}Cl_2N_2O_3P_{(aq)} + 47\ \bullet OH_{(aq)} \longrightarrow 7\ CO_{2(g)} + 26\ H_2O_{(L)} + 2\ HCL_{(aq)} + 2\ NH_4NO_{3(aq)} + PO_{4(aq)}$$

Research perspectives

- **Oxidative treatment started for:**
  - Metformin, Carbamazepine, Diclofenac, Iopamadiol
    - Antibiotics

- **The introduction of a more complex matrix:**
  - Urine, mixture, sewage water

- **Testing the toxicity:**
  - Oxidative stress, DNA damage and protein damage

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