Towards enhanced antitumoral activity of ferrocene derivatives by formation of inclusion complexes with β-cyclodextrin

Laura Morel[a], Leyth Saglio[a]
Supervisor: Namita Raju John[b]

[a] Département de Chimie, École normale supérieure, PSL University, 75005 Paris, France
[b] Laboratoire des BioMolécules (UMR 7203), École normale supérieure, PSL University, 75005 Paris, France

Introduction

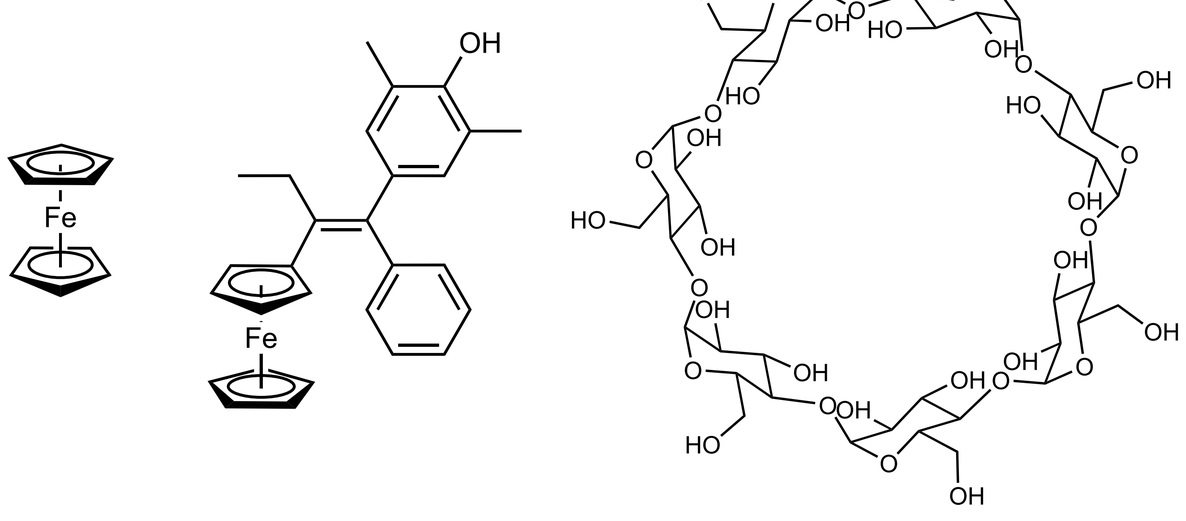
- Investigating antitumoral activity of ferrocene derivatives, especially in breast cancer
- Challenge: Low water solubility limits bioavailability of these complexes
- Proposed solution: Use β-cyclodextrin to enhance water solubility and stability
- Objective: Form an inclusion complex (ferrocifen:β-cyclodextrin) to improve delivery into cancer cells
- Goal: Increase antitumoral activity of ferrocene derivatives

Strategy

- Develop two inclusion complexes:
  - ferrocene:β-cyclodextrin (Fc:β-CD)
  - ferrocifen:β-cyclodextrin (Ffn:β-CD)
- Evaluate their redox properties as well as cytotoxicity
- Compare these properties with those of non-complexed ferrocene and ferrocifen

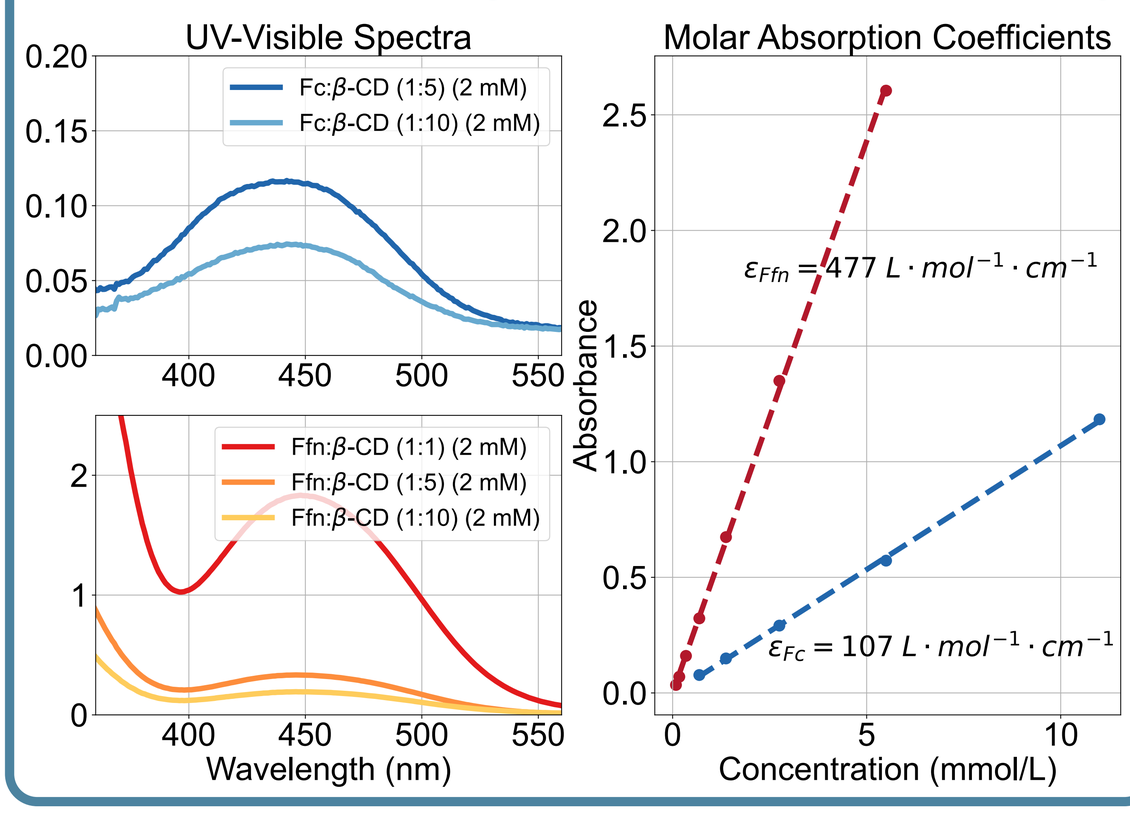
Synthesis of Fc/Ffn:β-CD inclusion complexes

- Mixture of aqueous β-CD solution with Fc or Ffn in EtOH stirred 1 h at 65°C
- Crystallization 24h at room temperature

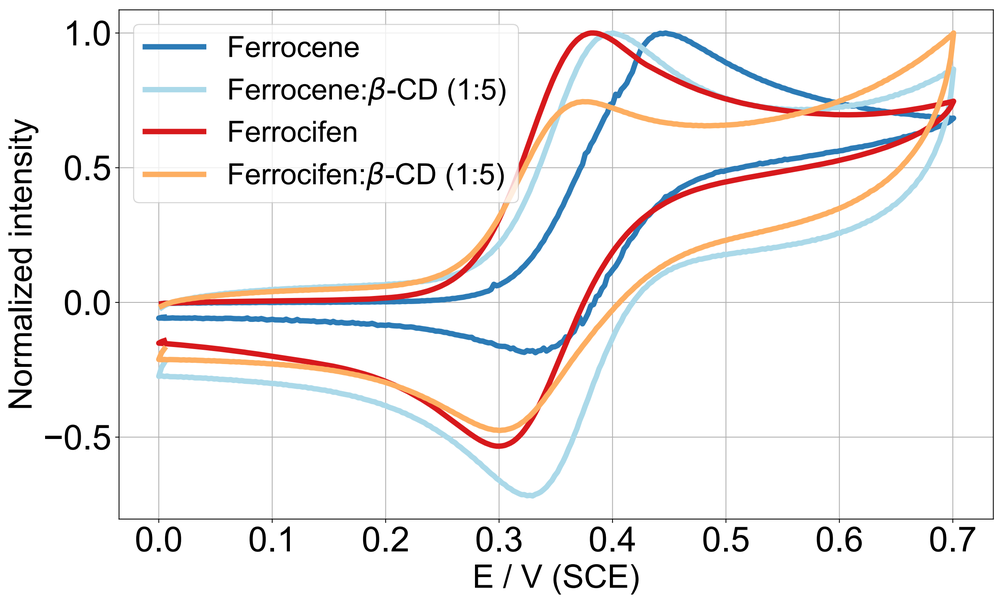


Ferrocene | Ferrocifen | β-cyclodextrin

Characterization by UV-Visible spectrometry



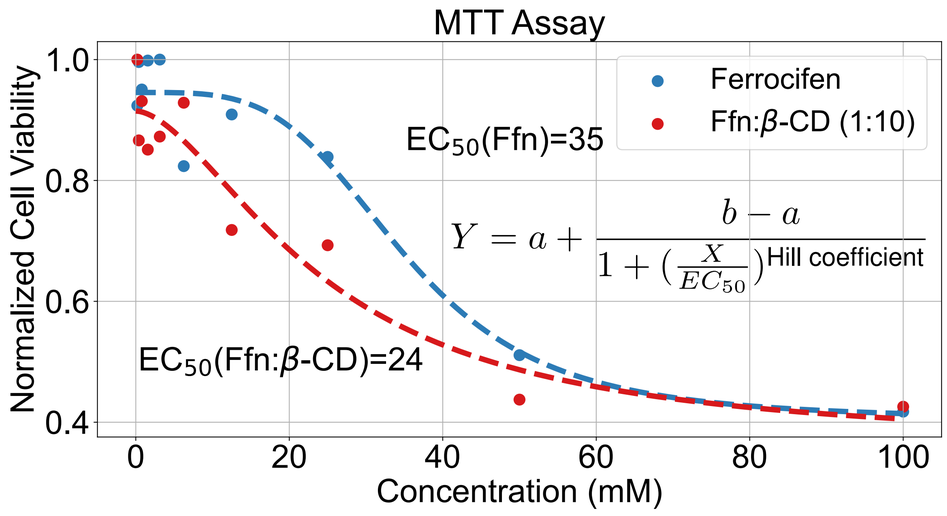
Analysis of Redox properties



Cyclic voltammetry in MeOH/$TBABF_4$ (0.1 M) recorded at glassy carbon (3 mm ø) with a scan rate of 50 mV/s.

	Fc/Fc:β-CD	Ffn/Ffn:β-CD
Observations	• abnormal irreversible Fc signal • a shift in lower potential for the inclusion complex test	• reversible signals • no shift in potential for the inclusion complex
Hypothesis	• misinterpretation due to abnormal Fc signal • weak complexation • very weak complexation constant	• solubility issue • weak complexation

Cytotoxicity analysis by MTT Assay



MTT assay of murine colorectal carcinoma cells (CT26) carried out after 24h incubation with the Ffn complexes.

Conclusion & Perspectives

- Synthesis and characterization of different inclusion complexes of ferrocene and dimethyl-hydroxy-ferrocifen with varying concentrations of β-CD
- Preliminary cellular studies are promising
- Further investigation on the complexes formation can be carried out by NMR spectroscopy
- Antitumoral activity on breast cancer cells may be studied

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