SELF-SORTING OF PLATINUM(II) COMPLEXES INSIDE CUCURBIT[8]URIL

Shib Shankar PAUL,[1,2] Pia JURČEK,[1,2] Jan NOVOTNÝ[1,2], Radek MAREK[1,2]

Introduction of cisplatin as a chemotherapeutic agent significantly improved the survival rate for many cancer patients. Following the discovery of cisplatin, numerous cisplatin-like compounds have been introduced worldwide but only two compounds, oxaliplatin and carboplatin have been approved by FDA. Despite the great success of cisplatin and its analogous bifunctional compounds, these compounds have several side effects due to low selectivity toward cancer cells and binding to the off-target biological nucleophiles.[1] To overcome the challenges several thousand drug candidates have been reported in the past few decades but they are not void of similar drawbacks. The concept of supramolecular prodrug can be used to make the drug protected and more selective towards tumor cells. In this approach, the drug is entrapped into a carrier molecule thereby achieving temporary deactivation and extending its lifetime in the extracellular environment, enabling the anti-tumor warhead to reach its target efficiently.[2]

In this contribution, we will demonstrate new supramolecular drug-carrier systems based on monofunctional Platinum(II) complexes and cucurbit[8]uril (CB8). We designed new monofunctional Pt(II) compounds with aromatic anchors and characterized their binding to CB8. Due to the larger size of CB8 cavity, it can encapsulate two of the Pt(II) guests. We synthesized two types of ternary assemblies, i) homo-ternary assembly (two same Pt(II) complex), ii) hetero-ternary assembly (two different Pt(II) complex) inside CB8. Time-dependent ^{1}H-NMR reveals the presence of several kinetically stable forms depending on the orientation of the two Pt(II) guests and hydrolyzed state of the Pt(II) center, but after several days those converge to one thermodynamically stable form. 2D-ROESY spectra and mass spectrometry revealed a very unusual head-head orientation of two highly charged Pt(II) centers (**Fig 1**).

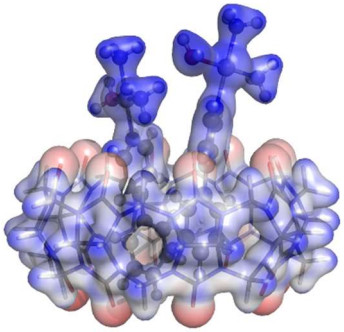

Fig 1: ESP map of homo-ternary assembly

References:

1. Johnstone T. C. *et. al.*, *Chem. Rev.,* **2016**, 116, 3436-3486
2. Geng. W *et.al.*, *Chem. Soc. Rev.*, **2020**, 8, 2303-2315