Structural Properties of Pt-based Anti-cancer Drugs; Computational Studies

Sofia S. M. C. Godinho[a,b], Leif A. Eriksson[a], [a]*Department of Natural Sciences and Örebro Life Science Center University of Örebro, 701 82 Örebro, Sweden.* [b]*Grupo de Física Matemática, Universidade de Lisboa, Lisboa, Portugal.* E-mail: sofia.godinho@nat.oru.se

It is generally accepted that *cis*-$[PtCl_2Pyr_2]$ is cytotoxic while *trans*-$[PtCl_2Pyr_2]$ is not. Although original empirical structural-activity studies indicated *trans* Pt complexes as being inactive as anti-cancer drugs, it has subsequently been found that *trans*-$[PtCl_2Pyr_2]$ is in fact active, both *in vitro* and *in vivo*, and that for the latter the compound is even more active than the corresponding *cis* form. A more likely explanation for the lack of antitumour activity is instead that the *trans* isomer is kinetically more reactive and more susceptible to deactivation than the corresponding *cis* form [1].

We have in the current work investigated both isomers and their corresponding step-wise activation (aquation) processes in order to provide more detailed insights into their mechanisms. The results are also compared to corresponding data for the parent compounds *cis* and *trans*-platin $[PtCl_2(NH_3)_2]$. Implicit as well as explicit solvent effects have previously been shown to be important for these types of reactions [2,3], and thus included in the study.

[1] Wong E., Giandomenico M., *Chem. Rev.*, 1999, **99**, 2451. [2] Raber J., Zhu C., Eriksson L.A., *Mol. Phys.*, 2004, **102**, 2537. [3] Zhu C., Raber J., Eriksson L.A., *J. Phys. Chem. B,* 2005, *in press*.

Keywords: anticancer compounds, DFT, platinum antitumour agents