Structure-Activitity Study of Pt(II) and Pd(II) Spermidine Complexes

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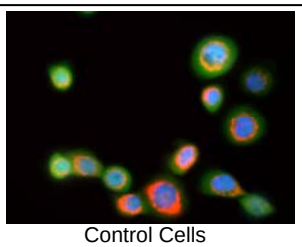
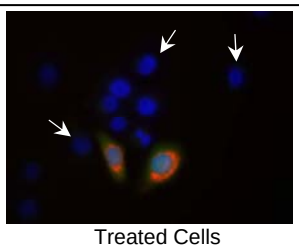
The widely used anticancer drug cisplatin ($PtCl_2(NH_3)_2$, *c*DDP) presents several and severe drawbacks. Therefore, the search for alternative antitumour agents has been a particularly active area of research in the last decade. Some of these third-generation drugs are multinuclear complexes containing two or more *c*DDP-like centers, linked by polyamine bridging units of variable length.

We describe the study of such chelates - synthesized as in Navarro-Ranninger *et al.* - which are under investigation as to their conformational preferences through spectroscopic methods and *ab initio* molecular orbital calculations. The biological effect of the compounds was evaluated by using end-points for cell viability and density, with Alamar Blue and sulphorhodamine-B, respectively. We also used epifluorescence microscopy with the mitochondrial probe TMRM, the nuclear probe Hoescht 33342 and calcein-AM, a probe for plasma-membrane integrity (Fig.1). Expectantly the conjugation of these different techniques would gather information on the *structure-activity relationships* ruling their biological activity.



Control Cells



Treated Cells

Figure 1 – Squamous cell carcinoma cells (HSC-3) subcultured six times in the presence of Pd -spermidine complex at 7μM. Images were taken using a 63x oil objective.

White arrows point dead adherent cells.
Blue stands for Hoescht 33342, red for TMRM and green for calcein-AM.

1. Navarro-Ranninger *et al., J. Inorg. Biochem, **53**,* 177-190 (1994).

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