Effect of glutathione upon *in vitro* cell growth inhibition of platinum(II) complexes with antitumoral and antiviral aromatic heterocycles.

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This investigation concerns the interaction with glutathione (γ-glutamyl-cysteinyl-glycine, GSH) of platinum(II) compounds $[Pt(Me_2phen)(acy)_2](NO_3)_2$ (**1**) and $[Pt(phen)(acy)_2](NO_3)_2$ (**2**) containing the bidentate 1,10-phenanthroline (phen) or 2,9-dimethyl-1,10-phenanthroline (Me_2phen, neocuproine) and the antiviral agent acyclovir (acy). The above mentioned complexes showed different *in vitro* toxicity, the Me_2phen complexes being appreciably more toxic than the phen complexes. In order to explain the different behavior, we investigated the reaction of complexes (**1**) and (**2**) with an ubiquitous biological substrate, glutathione, a peptide believed to play an important role in driving the cellular effects of platinum antitumoral drugs.[1] The reaction led to different products. While the phen complexes formed a stable binuclear μ-thiol bridged species (Figure 1) still containing the phenanthroline, the Me_2phen complexes released the neocuproine ligand and formed an insoluble material. *In vitro* tests confirmed that the greater cell toxicity of complex (**1**) is due to the displacement of the neocuproine ligand by GSH.[2] The results also highlight the great dependence of the platinum reactivity upon relatively small changes in its coordination sphere.

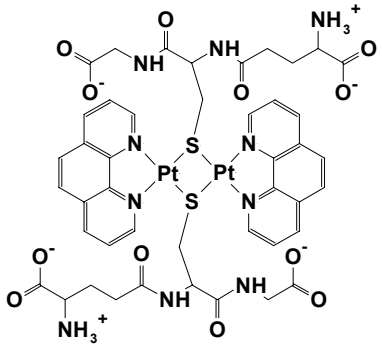

Figure 1

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