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(Me₂phen)(acy)₂][NO₃]₂ (1) and [Pt(phen)(acy)₂][NO₃]₂ (2) containing the bidentate 1,10-phenanthroline (phen) or 2,9-dimethyl-1,10-phenanthroline (Me₂phen, neocuproine) and the antiviral agent acyclovir (acy). The above mentioned complexes showed different in vitro toxicity, the Me₂phen 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 Me₂phen 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.

Acknowledgments: The authors thank the University of Bari, the Italian “Ministero dell’Istruzione, Università e Ricerca (MIUR)” (PRIN 2004 n. 2004032118_003), and the EC (COST Chemistry projects D20/0001/2000 and D20/0003/01) for support.