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TITLE: Trithiolato-Bridged Dinuclear *p*-Cymene Ruthenium Complexes:
A Study of their High *in vitro* Anticancer Activity

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CURRENT CATEGORY: Bioinspired Coordination and Organometallic Chemistry

ABSTRACT BODY:

Abstract Body: Since 1980, ruthenium complexes have attracted a large attention as promising anticancer drugs offering less side effects and toxicity compared to platinum derivatives [1-2]. However their mechanism of action is still unclear; in particular, only in very few cases, DNA or proteins could be unambiguously established as the main target responsible of their cytotoxicities.

We recently synthesized three series of thiophenolato-bridged dinuclear *p*-cymene ruthenium complexes of general formula $[(\eta^6\text{-}p\text{-}MeC_6H_4Pr^i)_2Ru_2(SR)_3]^+$, which proved to be highly cytotoxic against human ovarian cancer cells A2780 and their cisplatin resistant mutant A2780cisR, the IC_{50} values being in the nanomolar range [3-4]. We have investigated their possible mechanism of action by NMR measurements, in which we have incubated some complexes with nucleotides and aminoacids. Surprisingly, these complexes are substitutionnally inert and we have found that they were actually highly efficient catalysts for the oxidation reaction GSH -> GSSG.) [4-5]. Furthermore a correlation between cytotoxicity, lipophilicity and Hammett's constants of the corresponding thiol ligand was possible [4-5].

Here, we present our results obtained using NMR and CD spectroscopy showing the possible interactions between some of these ruthenium complexes with four proteins implicated in relevant biological process: albumin, transferrin, myoglobin and ubiquitin.

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