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A speciation investigation of new Ruthenium/DMSO/quinolone metallodrug candidates

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The use of coordination compounds as biologically active agents against several pathogens and tumors is firmly established within the scientific community. Among bioactive coordination compounds, ruthenium-based complexes are notable metallodrug cadidates[1,2] and those structures that bear DMSO as ligands demonstrate interesting anticancer properties[1]. Making use of drug repositioning, and in light of recent discoveries of the antibacterial class of quinolones as inhibitors of human topoisomerase[3], we report the synthesis, characterization and biomolecule interactions of four new ruthenium(II)-dmso complexes with quinolone antibacterials oxolinic **(1)** and nalidixic acid **(2)** as ligands. The complexes follow the general formula *fac*-[RuCl(dmso-S)$_3$(*O-O*)] (A) and *cis*-[RuCl(dmso-S)$_2$(*O-O*)(PPh$_3$) (B) and were characterized via spectroscopic and physical methods and single crystal x-ray diffraction. The quinolones act as bidentate ligands through the ketone/carboxylato oxygen atoms and a chlorido ligand balances out the positive charge on the metal center. Stability of the complexes in water was conducted and monitored via ^{1}H and ^{31}P NMR (dmso-d$_6$, dmso-d$_6$/D$_2$O (5%) and D$_2$O) and the results showed that the compounds are stable in water for at least 3 days. The speciation of labile chloride by water was investigated: for B1 and B2, it occurs almost immediately after solubilization, nonetheless the quinolones stay bonded in all complexes. The stable labilization and availability of one coordination site of the compounds is being used to explore their interactions with target biomolecules such as DNA, HSA, glutathione and 5-GMP. *In vitro* cytotoxic essays against tumor cell lines to establish the compounds' IC$_{50}$ values and discussion will be shown.

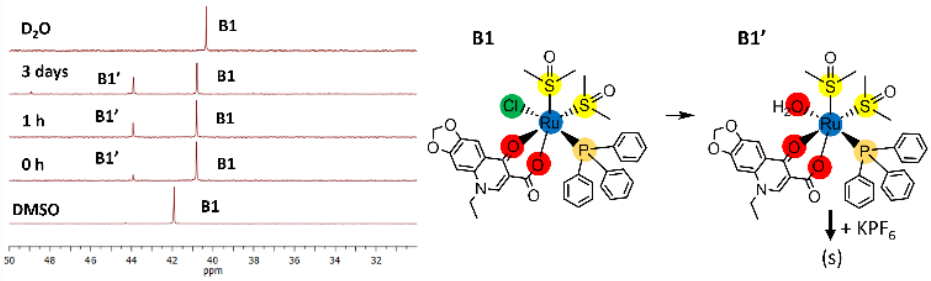

Figure 1. Structures of B1 and its acquo species B1' and speciation monitored via ^{31}P{^{1}H} NMR.

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