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Preparation, Characterisation, and Measurement of the in vitro Cytotoxicity of Mesoporous Silica Nanoparticles Loaded with Cytotoxic Pt(II) Oxadiazoline Complexes

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Abstract : Cytotoxic platinum compounds play a major role in the chemotherapy of a large number of human cancers. However, due to the severe side effects for the patient and other problems associated with their use, there is a need for the development of more efficient drugs and new methods for their selective delivery to the tumours. One way to achieve the latter could be in the use of nanoparticular substrates that can adsorb or chemically bind the drug. In the cell, the drug is supposed to be slowly released, either by physical desorption or by dissolution of the particle framework. Ideally, the cytotoxic properties of the platinum drug unfold only then, in the cancer cell and over a longer period of time due to the gradual release. In this paper, we report on our first steps in this direction. The binding properties of a series of cytotoxic Pt(II) oxadiazoline compounds to mesoporous silica particles has been studied by NMR and UV/vis spectroscopy. High loadings were achieved when the Pt(II) compound was relatively polar, and has been dissolved in a relatively nonpolar solvent before the silica was added. Typically, 6-10 hours were required for complete equilibration, suggesting the adsorption did not only occur to the outer surface but also to the interior of the pores. The untreated and Pt(II) loaded particles were characterised by C, H, N combustion analysis, BET/BJH nitrogen sorption, electron microscopy (REM and TEM) and EDX. With the latter methods we were able to demonstrate the homogenous distribution of the Pt(II) compound on and in the silica particles, and no Pt(II) bulk precipitate had formed. The in vitro cytotoxicity in a human cancer cell line (HeLa) has been determined for one of the new platinum compounds adsorbed to mesoporous silica particles of different size, and compared with the corresponding compound in solution. The IC50 data are similar in all cases, suggesting that the release of the Pt(II) compound was relatively fast and possibly occurred before the particles reached the cells. Overall, the platinum drug is chemically stable on silica and retained its activity upon prolonged storage.

Keywords : cytotoxicity, mesoporous silica, nanoparticles, platinum compounds
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