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Water soluble platinum (II) complexes: GLUT mediated cytotoxic properties and selective tumor targeting**Ran Liu**

Tianjin University, P R China

A series of sugar-conjugated malonato-platinum (II) complexes were designed and synthesized to evaluate the influence of different substitutions and different carbon chain lengths of the leaving group on water solubility and cytotoxicity against 6 human carcinoma cell lines. The complex Glu-F-Pt exhibited a higher water solubility by almost 150 times and processed up to 10 fold more active in cytotoxicity against HT-29 cell lines in comparison to the most commonly used platinum anticancer drug oxaliplatin. The therapeutic index (LD50/IC50) was measured on BALB/c nude mice and the result showed that Glu-F-Pt expanded anticancer therapeutic window, indicating the potency in enhancing drug safety. In addition, the maximum tolerated dose finding experiments of Glu-F-Pt was performed on DBA/2 mice in order to evaluate their toxicity profiles. The mean life span of Glu-F-Pt was compared with that of oxaliplatin under an equitoxic dose regimen and the result was of % ILS>191.4 for Glu-Pt, and 148.0 for oxaliplatin, respectively. Cytotoxicity assay of Glu-F-Pt with and without phlorizin, an established inhibitor of mammalian glucose transporter, was performed to verify our hypothesis that the anti-tumor activity of sugar conjugated platinum complex is due to the active uptake by glucose transporters (GLUTs). This result suggested that the uptake of the 2C-Glu was regulated via the glucose transporters, whereas the cell-killing potency of oxaliplatin was not affected under the same circumstances, which confirmed our speculation that the sugar conjugated platinum (II) complex is transported by cancer cell through glucose transporter and achieves selective tumor targeting. Based on these arguments, the fluoro-substituted sugar conjugate further supported (pre)clinical development for it to become a new class of Pt (II) antitumor agents for targeted therapy drugs.

Biography

Ran Liu is a Doctoral Candidate at School of Pharmaceutical Science and Technology, Tianjin University. Her major is Medicinal Chemistry and now she mainly focuses on the biological evaluation of anti-tumour compounds. She has published more than 6 papers in reputed journals.

liurantj@tju.edu.cn**Notes:**