Conjugates of bile acid platinum complexes with gold nanoparticles

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Abstract

The bisursodeoxycholate(ethylenediamine)platinum(II), [Pt(UDC)$_2$(en)], PtU2 compound was synthesized according to the procedure of Criado et al.[1-3]

The conjugates of PtU2 with gold nanoparticles (PtU2-AuNP) were prepared by mixing the solid PtU2 compound directly in the colloidal solution of the nanoparticles. All the solutions were vortexed for at least twenty minutes and then stored at 4℃ until use in cell cultures. The conjugates were characterized by UV-visible spectroscopy, fluorescence emission spectroscopy, transmission electron microscopy (TEM) and scanning electron microscopy (SEM) (Figures 1 and 2).

The PtU2-AuNP complex exerted an important cytotoxic activity against MG63 osteosarcoma cells which was already clearly detectable after 48 h of culture (Figure 3) [4]. The precise mechanisms by which the presence of AuNPs increases the cytotoxic activity of the drug remain elusive and require further investigations.

References

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[2] Criado, J J; Rodríguez, E; Manzano J L; Alonso, A; Barrena, S; Medarde, M; Pelaez, R; Tabernero, M D; Orfao, A. Bioconjugate Chem. **16** (2005) 275-282.

[3] Pérez-Andrés, M.; Benito, J. J.; Rodríguez-Fernández, E.; Manzano, J. L.; Barrena, S.; Orfao, A.; Criado, J. J. Letters in Drug Desing and Discovery, **4** (2007) 341-345.

[4] Pending of publication.

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Figures

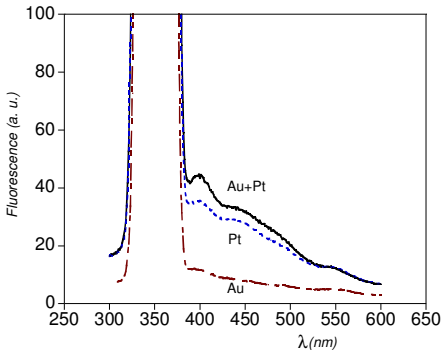
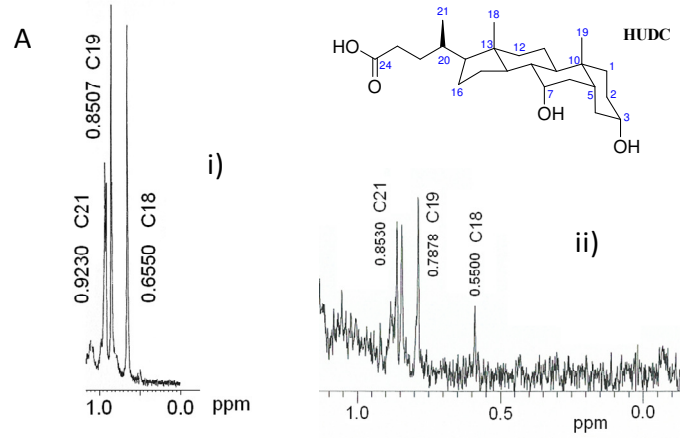


Figure 1. Fluorescence of PtU2 and it adduct with AuNp.
AuNp20 (c = $7 \cdot 10^{11}$ Np/mL) (Au)
PtU2 (c = $4{,}5 \cdot 10^{-4}$ M) (Pt)
Adduct 1:1 (Au+Pt)



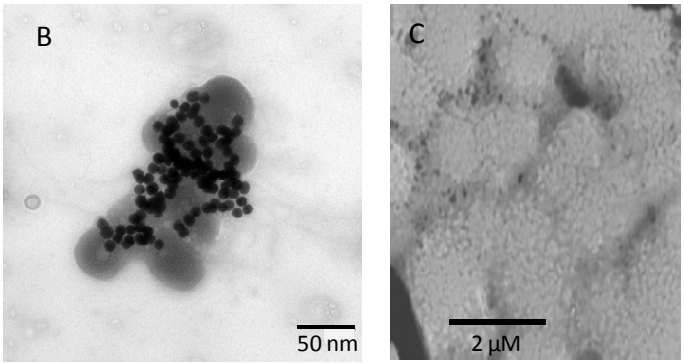


Figure 2. (A) ^{1}H-NMR spectra of the platinum compound (i) and its incubation adduct with gold nanoparticles (ii). HUDC = ursodeoxycholic acid. TEM (B) and SEM (C) images of the PtU2-AuNPs conjugate drug complex in water. After adducts formation, the corresponding ^{1}H-NMR signals (methyl groups C18, C19 and C21), slightly shifted to 0.55 ppm, 0.79 ppm and 0.85 ppm, respectively.

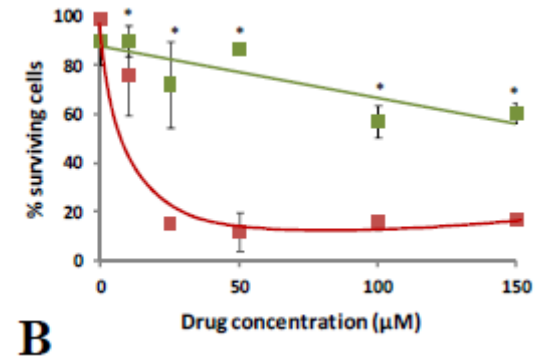


Figure 3
Cytotoxic activity of the PtU2 compound (straight line) and the newly-synthesized PtU2-AuNP complex (curved line) against MG63 (osteosarcoma) cells.
Cytotoxic activity against MG63 osteosarcoma cells which was already clearly detectable after 48 h of culture. Cytotoxic activity is specific for the PtU2-AuNPs complex, since no cytotoxic activity was detected when the cells were incubated with the AuNPs alone.