# Nitric oxide-releasing TEOS nanoparticles antitumoral action on melan-a cells

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**INTRODUCTION:** Although a variety of small molecule NO donors have been reported effective against different tumor types including pancreatic, colon, ovarian and skin cancers[1], they have also suffered from highly toxic side effects of the drug by product and poor cellular permeability and retention[2]. The development of novel delivery systems for NO donors that may overcome these limitations is of crucial importance to advance the feasibility of NO-based therapies. The use of tetra-ethyl-ortho-silicate (TEOS) nanoparticles (NP) has been considered as one approach to overcome these limitations[2]. In this work, we tested the ability of this drug delivery system to entrap ruthenium nytrosyl complex (*trans*-$[Ru(NO)(NH_3)_4py](BF_4)_3$ (**I**), *trans*-$[Ru(NO)Cl(cyclam)](PF_6)_2$ (**II**), and [Ru(NO)(Hedta)] (**III**)) and their cytotoxic effect on melan-a cells.

**METHODS:**

The nitrosyl complexes were immobilized in TEOS nanoparticles using the sol-gel process[3]. These particles were evaluated in relation to size using dynamic light scattering (DLS), zeta potential, drug encapsulation efficiency, release profile, and external morphology using scanning electron (SEM) and atomic force (AFM) microscopies. Cell toxicity was evaluated using a cell viability measurement (MTT)[4].

**RESULTS:**

The NO donors were loaded into TEOS nanoparticles, with an entrapment efficiency of 92 ± 4%. SEM, AFM and DLS revealed that the particles are spherical in shape, have a diameter between 180 and 260 nm, and show low tendency to aggregate, confirmed by zeta potential of 16.7 ± 3.5 mV, 1.3 ± 0.9 mV, and 2.3 ± 0.2 mV for **I**, **II**, and **III**, respectively. Cell toxicity showed that in the absence of light irradiation, the nitrosyl complexes in solution are non toxic at concentrations lower than $1x10^{-4}$ M, and when entrapped in TEOS nanoparticles they are non toxic for melan-a cells. In addition, upon light irradiation, the encapsulated complexes are able to release NO that can diffuse out of the matrix, reaching the adjacent cell membranes, and promoting the tumor cell death of 52.1% for *trans*-$[Ru(NO)(NH_3)_4py](BF_4)_3$, 39.7% for *trans*-$[Ru(NO)Cl(cyclam)](PF_6)_2$, and 33.9% for [Ru(NO)(Hedta)], in relation to the control.

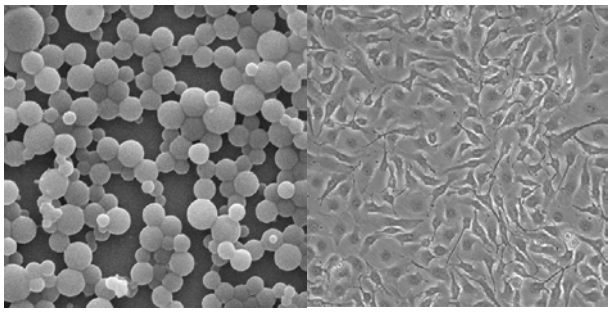

Figure 1 – (A) Surface morphology of TEOS nanoparticles and (B) melan-a cells (Magnification 20,000 and 400x respectively).

**CONCLUSIONS:** These results can be associated to higher entrapment efficiency, mainly compared to *trans*-$[Ru(NO)(NH_3)_4py](BF_4)_3$ entrapped in PLGA microparticle that lead to 12% of cell death[4].The phototoxicity strongly suggests that cell death is due to NO released from the complex entrapped in the TEOS nanoparticles, which can release NO locally at the tumor cell by irradiation with light

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