Poster

In vitro evaluation of the efficacy of gold metallophosphazenes as antitumor compounds

Batanero Mantero, Ana(1), Gil López, Ana(1), Llana Ruiz-Cabello, María(1), Maisanaba Hernández, Sara(1), Jiménez Villar, Josefina(2), Repetto Kuhn, Guillermo(1)

(1)Department of Molecular Biology and Biochemical Engineering. Toxicology Area. Pablo de Olavide University, 41013 Seville, Spain.

(2)Department of Inorganic Chemistry. Faculty of Sciences, Institute of Chemical Synthesis and Homogeneous Catalysis. University of Zaragoza-CSIC, 50009 Zaragoza, Spain.

Tutor académico: Repetto Kuhn, Guillermo; Maisanaba Hernández, Sara

Keywords: cancer; gold metallophosphazenes; in vitro toxicity assays

ABSTRACT

Motivation: The presence of side effects due to therapeutic cancer strategies is a constant driver in the development of new alternatives [1]. One of them is the use of metallic compounds like gold metallophosphazenes. The purpose of this study was the evaluation in vitro of the cytotoxic capacity of two metallophosphazenes (1 and 2), with different gold content, in two tumor cell lines: MCF-7 and HepG2.

Methods: The cytotoxicity of both metallophosphazenes was evaluated by in vitro toxicity assays. On the one hand, the Neutral Red Uptake assay (NRU), based on the inhibition of lysosomal uptake of the NR dye. Only living cells, take it and show absorbance variations measured in the spectrophotometer [2]. On the other hand, the Alamar Blue assay (AB). It allows to determine the proliferation of a cell culture, based on the properties of resazurin, a redox indicator with color changes by chemical reduction and production of fluorescence [3]. Cells were exposed during 48h from 0 µM to 8 µM. Median efective concentration (EC50) was calculated and statistical distribution of the data was evaluated with the GraphPad program using Dunnet's test, considering significant values those with $p<0.05$.

Results: Both metallophosphazenes had EC50 values lower than 2,5 µM. In relation to compound 1, the MCF-7 cell line showed statistical significant differences with respect to the negative control from concentrations 1 µM and 2 µM, with EC50 values of 1.572 µM for the biomarker NR and 2.340 µM for AB, respectively. In the HepG2 cell line, results showed significant differences from concentrations 2 µM and 0.5 µM, with EC50 values of 2.471 µM for NR and 2.378 µM for AB, respectively. With respect to compound 2, both cell lines were more sensitive. In the MCF-7 cell line, results showed significant differences with respect to negative control from concentration 0.5 µM, with EC50 values of 1.262 µM for NR and 1.378 µM for AB. In the HepG2 cell line, results showed significant differences from concentrations 0.5 µM and 0.125 µM, with EC50 values of 1.557 µM for NR and 1.693 µM for AB, respectively.

Conclusions: Compound 2 was more potent to both cells lines. The reason could be the extra gold atom of compound 2. The greater the number of gold atoms, the greater the antitumor activity. The uptake of NR was more sensitive than AB and MCF-7 was more sensitive than HepG2 cell line. In order to confirm the findings, other studies are necessary to determine mechanisms of action.

REFERENCES

[1] Chopra, D., Rehan, H.S., Sharma, V., Mishra, R., 2016. Chemotherapy-induced adverse drug reactions in oncology patients: A prospective observational survey. Indian J Med Paediatr Oncol. 37(1), 42-46. https://doi.org/10.4103/0971-5851.177015.

[2] Repetto, G., del Peso, A., Zurita, JL., 2008. Neutral red uptake assay for the estimation of cell viability/cytotoxicity. Nat Protoc. 3(7), 1125-1131. https://doi.org/10.1038/nprot.2008.75.

[3] Rampersad, S.N., 2012. Multiple applications of Alamar Blue as an indicator of metabolic function and cellular health in cell viability bioassays. Sensors (Basel). 12(9):12347-60. https://doi.org/10.3390/s120912347.