Antiproliferative activity of a new quinone-copper(II) complex and a related naphthoquinone derivative.

Nathália Florencia B. Azeredo[*1,2], Christiane Fernandes[1], Adolfo Horn Jr[1], Pio Colepicolo[2], Ana Maria da C. Ferreira[2], Jackson A. L. Resende[3], e Chaquip Daher Netto[4].

[1]LCQUI / UENF, Campos dos Goytacazes, Brazil; [2]IQ / USP, São Paulo, Brazil. [3]UFF, Niterói, Brazil; [4]UFRJ, Macaé, Brazil;

*e-mail: nflorencia@usp.br

Naturally occurring quinones and their synthetic analogs are an important source of antineoplasic products, and some of these compounds have been used in clinic as chemotherapeutic agents[1]. Lapachol is an example of quinone which occurs in the wood of several species of the *Bignoniaceae* family and it has been commercialized in Brazil as an antitumor drug since the 1970's[2]. In this sense, we describe here the synthesis, characterization and evaluation of antiproliferative activity against two human uterine sarcoma tumor cells (MES-SA and analogous resistant MES-SA/Dx5) of a new copper(II) complex and a related compound, both naphthoquinone derivative. The new copper(II) complex [Cu(HBPA)(L)]Cl **(1), [**where HBPA is (2-hydroxybenzyl-2-pyridylmethyl)amine], was obtained by the reaction between the precursor $Cu(HBPA)Cl_2$[3] and the quinone-stilbene (L)**.** A related *o*-furan compound (Figure 1) was also obtained, through the catalyzed cyclization reaction by $CuCl_2$, and it was characterized by X-rays diffraction and electronic spectroscopy. Complex **(1)** was characterized by IR, UV/Vis spectroscopy, melting point, elemental analysis, X-rays diffraction, condutivimetry, and electrochemical measurements (CV), ESI(+)-MS, and EPR. Results obtained by MTT assays revealed that the copper(II) complex **(1)** is less active against the tested sarcoma cells, however the *o*-furan derivative presents antitumor activity three and ten times higher than the current medicine doxorubicin for MES-SA and MES-SA/Dx5, respectively.

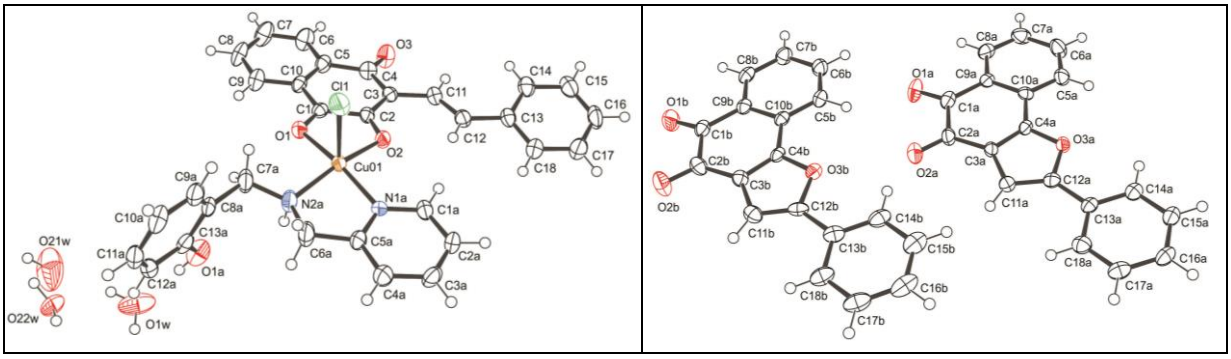

Fig. 1. X-ray structures obtained for the copper(II) complex (left) and for the *o*-furan (right).

1. Almeida, J.C.; Paixao, D.A.; Marzano, I.M.; Ellena, J.; Pivatto, M.; Lopes, N.P.; Ferreira, A.M.D.C. ; Pereira-Maia, E.C.; Guilardi, S.; Guerra, W. Polyhedron, **2015**, 89, p. 1-8.

2. De Moraes, P.; Gaspar, F.; Borges, R.; Netto, C.D.; Leão, R.; Nájera, C.; Costa, P. Synthesis (Stuttgart), **2015**, 47, 3505-3512.

3. Borges, L.J.H.; Bull, E.S.; Fernandes, C.; Horn Jr, A.; Azeredo, N. F. B; Resende, J. A. L.C.; Carvalho, E.C. Q.; Jerdy, H.L.; Kanashiro, M.M. Manuscript accepted by Eur J Med Chem.

FAPERJ, FAPESP, CAPES, CEPID-REDOXOMA