IN VITRO STUDY OF A NOVEL SYNTHETIC NAPHTHOQUINONE (PIC20) AGAINST LUNG CANCER

1,2Diandra Z. dos Santos, 1,3Paulo CM Lyra-Júnior, 1,3Isabella S. Guimarães, 4Maicon Delarmelina, 4João F. Allochio Filho, 1,3Nayara G. Tessarollo, 1Roger C. Zampier, 1Laura F. R. L. Oliveira, 1Krislayne V. Siqueira, 4Sandro J. Greco, 1,2,3Leticia BA Rangel, 3,5Ian V. Silva

1 Laboratory of Cellular and Molecular Biology of Human Cancer, Department of Pharmaceutical Sciences; 2Biochemistry and Pharmacology Program; 3Biotechnology Program/RENOBIO; 4Laboratory of Medicinal and Organic Synthesis, Department of Chemistry; 5Department of Morphology, Universidade Federal do Espírito Santo, Vitória, ES, Brazil

Lung cancer (LC) is a highly lethal malignancy, which is characterized by metastatic and chemoresistant phenotypes. Therefore, there is an urge for novel therapeutic strategies against the disease. In this context, synthetic naphthoquinones have emerged as promising molecules. Although the precise anticancer mechanisms of naphthoquinones are still under investigation, there is a strong body of evidences pointing to the involvement of reactive oxygen species (ROS) that, in turn, modulate a plethora of biological effects such as cellular proliferation, differentiation, and apoptosis. Interestingly, there is an intricate cross-talk between ROS and the phosphoinositide 3-kinase (PI3K)/AKT pathway, a key cancer-related signaling mechanism. The present work aimed to investigate the cytotoxic activity of a novel synthetic naphthoquinone (PIC20) in human large cell LC lineage (H460).

In silico docking analysis has revealed the putative interaction between PIC20 and PI3K (-8.9 vs. -9.5 and -8.8 Kcal/mol for PIC20, LY294002 and Wortmannin, respectively) or topoisomerase 2 (-5.3 vs. -5.6 and -5.7 Kcal/mol for PIC20, doxorubicin and etoposide, respectively). PIC20 decreased H460 cellular metabolic viability (CMV; MTT assay) in a dose-dependent manner, being the maximum effect observed with PIC20 10^{-4} M (- 70%; p<0.0001). On the other hand, superoxide dismutase (SOD) modulated PIC20 effect; whereas SOD improved the effect of PIC20 10^{-7} - 10^{-5} M, it partially reversed the anticancer effect of PIC20 10^{-4} M (p<0.05) in H460 cells. Altogether, our data suggest that the production of ROS in cancer microenvironment, thus the occurrence of oxidative DNA damage, likely plays an important role in the effect of PIC20 against LC. Ongoing experiments seek to elucidate the correlation of ROS, PI3K, and topoisomerase 2 in PIC20-treated H460 LC cells. In any event, our study opens a new avenue in the fight against LC, possibly introducing a low cost substance obtained through a simple synthetic chemical route in the portfolio of anticancer drugs.

Key words: lung, cancer, naphthoquinones
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