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Oxorhenium(V) complexes in the drug combination study

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Rhenium complexes merit particular attention in the area of metallodrug design due to rhenium's broad spectrum of oxidation states and consequently, the possibility to design compounds of a great structural diversity. Thus, the synthesis, chemical characterization and antitumor activity in vitro of the three Re(V) complexes is described. Novel compounds were obtained via reaction of [ReOCl₃(PPh₃)₂] with corresponding ligands (pyridine-2-carboxylic acid, 3-methylpyridine-2-carboxylic acid and 6-methylpyridine-2-carboxylic acid) in acetonitrile at 78 °C for 3h. The complexes were fully characterized using NMR, IR, MS and elemental analysis. Their octahedral geometry with bidentate NO ligand was confirmed by X-ray diffraction analysis. Antiproliferative effect was determined by MTT assay and only the complex with pyridine-2-carboxylic acid (1) showed dose-dependent cytotoxic potential, particularly toward triple-negative breast adenocarcinoma cells MDA-MB-231 with IC₅₀ $68.90 \pm 1.73 \mu M$ and pancreatic adenocarcinoma cells PANC-1 with IC₅₀ 69.8 ± 2.3 µM. Drug combination studies in PANC-1 cells with 1 and Verapamil hydrochloride (VRP) showed slight arrest of cell cycle in the S phase and also it increase its antiproliferative potential to IC_{50} 51.4 ± 2.8 μM. Part of the research included a depletion of the glutathione (GSH) level by Lbuthionine-sulfoximine (L-BSO) at sub-toxic concentrations (100 µM) in PANC-1 cells which caused an increase of activity of 1 to the IC₅₀ 57.67 \pm 6.51 μ M.

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