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Inhibition of proteosynthesis as a new mode of action of half-sandwich ruthenium(II)complexes

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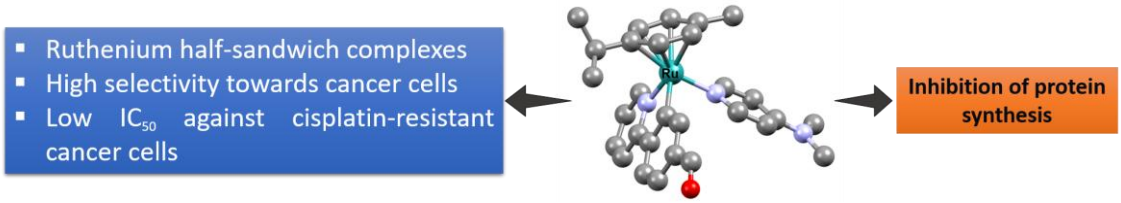
Topic: Old Elements, New Technologies: how to improve the quality of life

Abstract:
Ruthenium was discovered in 1840 by Karl Karlovich Klaus.The name comes from the Latin form of the word Russia, Ruthenia. Since its discovery, the main use of this element has been hardening alloys with other noble metals, such as palladium and platinum,that are mainly used in jewelry.[1] One of its most recent uses is the application of compounds based on this element aspotential anticancer drugs.This is the case of the ruthenium drugs NAMI-A and NKP1339, that are currently in phase I of clinical trials.[2]In this work we have synthetized six new half-sandwich ruthenium(II) complexes of the type $[(\eta^6\text{-}p\text{-cymene})Ru(C\text{^}N)(X)]^{0/+}$ where X= Cl, py or 4-NMe_2-py and the cyclometallated ligand are deprotonated 4-(2-pyridyl)-benzaldehyde and 4-(1H-pyrazol-1-y)-benzaldehyde.[3]All the synthesized complexes were characterized by ^1H and ^{13}C nuclear magnetic resonance spectroscopy and by high resolution liquid chromatography coupled to mass spectrometry (HPLC-MS).The interaction study of these compounds with human serum albumin was also determined by determining the association constants by fluorescence spectroscopy.The cytotoxicity of the six complexes was evaluated in several human cancer cell lines. All compounds shows low values of IC_{50}, where the complexes with 4-dimethylaminopyridine are the more cytotoxic against tumoral cells whereas they are inactive towards healthy cell lines. The study of the mechanism of action of the most active complexes reveals that they inhibit the proteosynthesis, which is a new mode of action for half-sandwich metal complexes



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