Water-soluble 8-hydroxyquinoline-amino acid hybrids and their interaction with various metal ions: relationship between solution chemistry and cytotoxicity


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Drug resistance in chemotherapy is one of the major problems; moreover, the development of compounds to overcome resistance is a rather challenging task. Among 8-hydroxyquinolines we can find derivatives which are able to target multidrug resistant (MDR) cancer cells, although these compounds are usually fairly lipophilic. Herein, the development and characterization of a series of water-soluble 8-hydroxyquinoline-(homo)proline hybrids are presented in addition to their half-sandwich organometallic Rh(η⁵-C₅Me₅) and Ru(η⁶-p-cymene) complexes.

8-Hydroxyquinolines are efficient metal binders, and the standalone MDR-selective toxicity of certain Mannich-base derivatives is reported to be related to their interaction with endogenous metal ions. Based on this finding, the solution chemical behavior of the novel 8-hydroxyquinoline-(homo)proline hybrids was investigated in detail including the characterization of their acid-base properties, lipophilicity, complex formation equilibria with essential metal ions such as iron(II/III), copper(II) and zinc(II) in addition to the structure and redox properties of the formed metal complexes. The cytotoxicity of these ligands and their organometallic complexes was monitored on chemosensitive and drug-resistant human cancer cell pairs and in one non-tumoral human lung fibroblast cell line to reveal relationship between the solution chemical properties and the anticancer activity.

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