Zn(II) complexes with pyridyl-based 1,3-selen/thiazolyl-hydrazones: A comparative study

Abstract

The Zn(II) complexes $[Zn(HLSe^2)_2](NO_3)_2{\cdot}CH_3OH$ (**2-NO_3-Se**) and $[Zn(HLSe^3)_2](NO_3)_2{\cdot}DMF$ (**3-NO_3-Se**) with selenazolyl-hydrazone ligands 4-(4-methoxyphenyl)-2-(2-(pyridin-2-ylmethylene)hydrazinyl)-1,3-selenazole ($HLSe^2$) and 4-(4-methylphenyl)-2-(2-(pyridin-2-ylmethylene)hydrazinyl)-1,3-selenazole ($HLSe^3$) have been synthesized and characterized using singe crystal X-ray diffraction analysis. Antiproliferative activities of **2-NO_3-Se** and **3-NO_3-Se**, the corresponding ligands and sulphur isosteres of the complexes and the ligands were determined on non-malignant HTR-8/SVneo extravillous trophoblast cell line and malignant JEG-3 and JAr choriocarcinoma cell lines. All Zn complexes exhibited cytotoxic effect, comparable to that of a reference metal-based drug, cisplatin. The antioxidant activity of all compounds was determined in three antioxidant assays: ORAC (Oxygen Radical Absorbance Capacity), ABTS [(2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt] and CERAC [Ce(IV)-based reducing capacity]. As a result of synergy between Zn(II) and selenazolyl-hydrazone ligands, the complexes **2-NO_3-Se** and **3-NO_3-Se** appeared to be more active than Trolox, which is not the case for their sulfur counterparts. *In-silico* calculations of ADME properties pointed that the compounds possess some of desirable Lipinski rule principles. Applied algorithms did not report the compounds as potential PAINS or covalent inhibitors, although due to high molecular weight none of the compounds represent a potential lead compound. Toxicity prediction of the compounds is performed using machine learning models. The complexation of the ligands most likely reduces their toxicity or reduces their negative metabolic effects.