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New analogues of cisplatin with anticancer activities: syntheses, vibrational spectra and calculations by the DFT methods

Abstract

Due to an increasing number of cancer diseases, the search for new compounds with antiproliferative properties is extremely important. The platinum(II) complexes constitute a significant group of drugs used in the anticancer therapy. The discovery by Rosenberg of the antitumor properties of cisplatin has prompted the development of studies on other platinum complexes.

The main goal of this PhD Thesis was the synthesis and investigation of the structural, spectroscopic and anticancer properties of new analogues of cisplatin, with a general formula *cis*-[PtL1L2], where L1- labile (leaving) ligand and L2- transporting ligand.

In Introduction, the biological properties of cisplatin and several new generation drugs (including picoplatin) were described. The mechanism of action of the platinum drugs was discussed taking cisplatin as an example (from a transport to the formation of adducts with DNA). A need of new drugs with a higher selectivity of action and a lower toxicity with respect to the normal cells was substantiated.

In the theoretical part, the optimal level of calculations has been determined. The optimal level means the density functional method combined with the basis sets which reproduces the best the molecular geometry and vibrational spectra of the investigated platinum complexes.

In the experimental part, the syntheses of 8 cisplatin analogues were described. Among these analogues were: picoplatin, two orotate derivatives of picoplatin and five imidazole derivatives of cisplatin. Five of these complexes have been synthesized for the first time. For two of them, the crystal and molecular structures were determined by a single crystal X-ray diffraction analysis. The theoretical molecular structures and vibrational spectra were calculated for eight synthesized platinum complexes by using the DFT methods. Detailed vibrational assignment of the experimental IR and Raman spectra was obtained on the basis of the normal coordinate analysis (the calculations of the potential energy distribution, PED).

In the last part of this thesis, the anticancer activities of all the obtained platinum complexes were evaluated against several human cancer cell lines of different etiology.