



**Synthesis and characterization of platinum complexes with ethylenediamine and diethylenetriamine sulphonamide ligands towards biological applications**

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Diethylenetriamine and ethylenediamine are renowned tridentate and bidentate chelating ligands, and have been utilized to synthesize sulfonamide derivatized platinum complexes. The sulphonamide ligands were synthesized with the use of sulfonyl chlorides and the relevant amine in dioxane, while the platinum complexes were formulated by treating  $\text{cis-[Pt(DMSO)}_2\text{Cl}_2]$  with the synthesized ligand. Synthesis of novel platinum-ethylenediamine sulphonamide complexes ( $\text{C1}=[\text{PtCl}_2(\text{N}(\text{SO}_2 \text{ biphenyl})\text{ethylenediamine})]$ ,  $\text{C2}=[\text{PtCl}_2(\text{N}(\text{SO}_2 \text{ azobenzene})\text{ethylenediamine})]$ ) was accomplished using synthesized ethylenediamine sulphonamide ligands, ( $\text{L1}=\text{N}(\text{SO}_2 \text{ biphenyl})\text{ethylenediamine}$ ,  $\text{L2}=\text{N}(\text{SO}_2 \text{ azobenzene})\text{ethylenediamine}$ ) while that of novel platinum-diethylenetriamine sulphonamide complexes ( $\text{C3}=[\text{PtCl}_2(\text{N}(\text{SO}_2 \text{ a z o b e n z e n e})\text{diethylenetriamine})]$ ,  $\text{C4}=[\text{PtCl}_2(\text{N}(\text{SO}_2 \text{ quinoline})\text{diethylenetriamine})]$ ) was carried out with the use of synthesized diethylenetriamine sulphonamide ligands ( $\text{L3}=\text{N}(\text{SO}_2 \text{ azobenzene})\text{diethylenetriamine}$ ,  $\text{L4}=\text{N}(\text{SO}_2 \text{ quinoline})\text{diethylenetriamine}$ ). In this study, amphiphilic ligand systems were considered as an ideal approach to enhance uptake of coordination complexes by target cells. This was executed by employing the hydrophilicity of ethylenediamine and diethylenetriamine and the lipophilicity of the aromatic bulky sulphonamide fragment bound to its terminal amine group. The ligands and complexes were synthesized in good yield (66%-96%) and characterization of these synthesized compounds was conducted using UV-Visible spectroscopy, FTIR spectroscopy and NMR spectroscopy. UV-Visible spectra of the ligands indicate clear changes from starting material along with the presence of intra-ligand  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions, giving rise to absorption peaks around 200-600 nm. Shifts of these peaks can be observed in the UV-Visible spectra of the complexes. The strong S-N band signifying the formation of the sulphonamide bond, was detected in the FTIR spectra of the ligand and was found to shift to higher wavenumbers in the ethylenediamine complexes as well as in the diethylenetriamine complexes. The shift could possibly be due to the donation of the nitrogen lone pair to form the platinum coordination complex. The peaks relevant to stretching vibration frequency of  $-\text{NH}_2$  were found in the 3300-3500  $\text{cm}^{-1}$  region of the FTIR spectra of the ethylenediamine ligands and could be seen shifting to lower wavenumbers in the complex due to coordination with platinum.  $^1\text{H}$  NMR spectra were acquired for

the ligands and complexes, where the noteworthy regions include the aromatic protons found in the range of 6.76-9.00 ppm and the methylene protons of the amine group in the ethylenediamine and diethylenetriamine backbone of the ligands, appearing at 2.80-3.00 ppm. Complexes display slightly higher fluorescence intensities in comparison to that of the ligands. Structural data was obtained from single crystal X-ray diffraction of L2 and C1 which validated the formation of the ligand and complex and provided distinct evidence of the deprotonation of the amine group in ethylenediamine upon coordination to metal in complex C1. Results of the in silico analysis of physicochemical and pharmacokinetic parameters as well as druglikeness of the ethylenediamine sulphonamide ligands show that they obey Lipinski's rule of five along with having lead-likeness. Swiss TargetPrediction was used to identify several probable biological targets, suggesting that the novel compounds may act as lead compounds for novel anti-cancer drugs.

Keywords: p l a t i n u m , e t h y l e n e d i a m i n e , diethylenetriamine