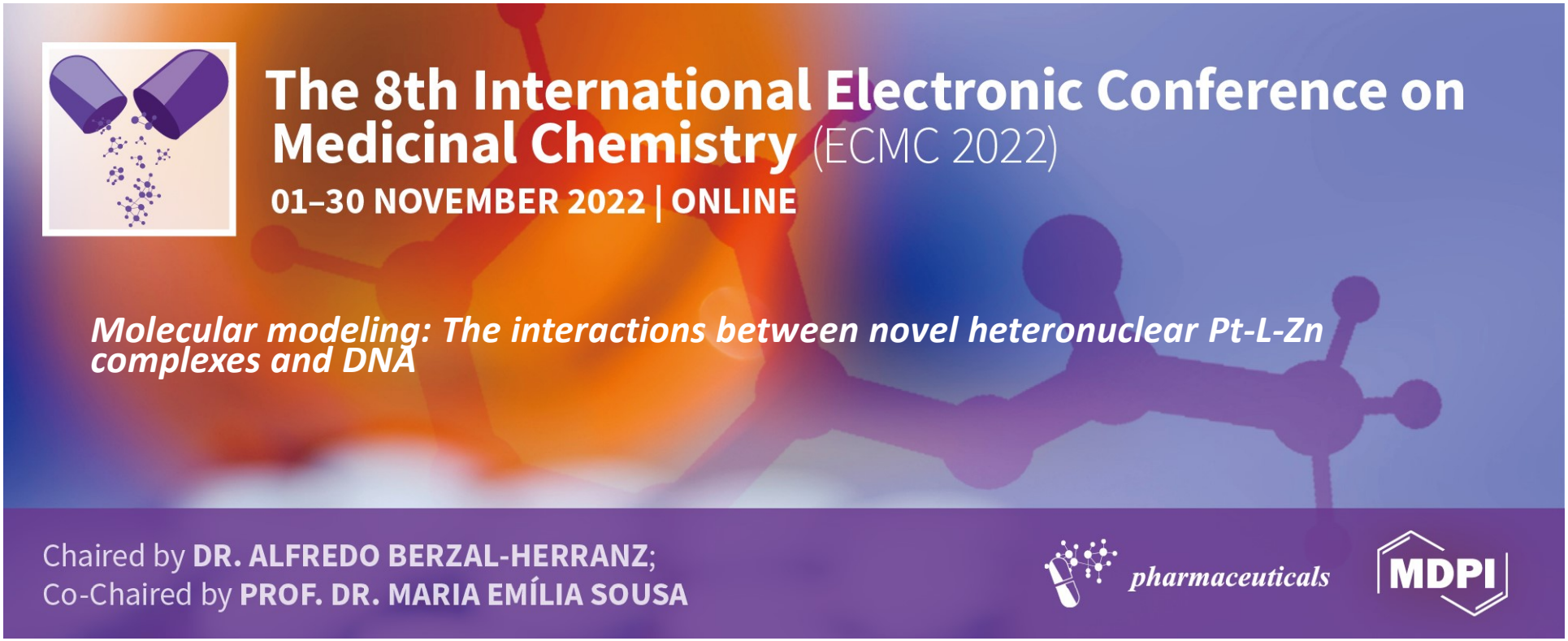

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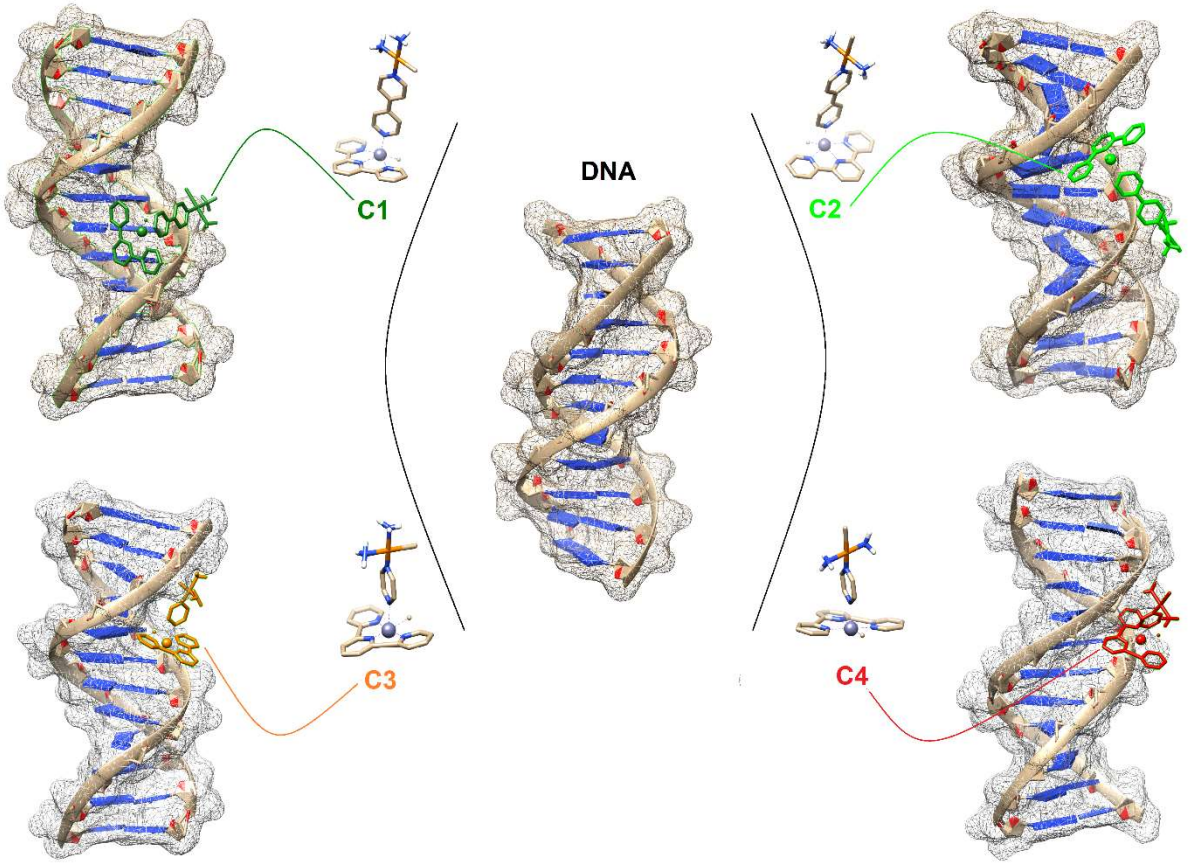
Molecular modeling: The interactions between novel heteronuclear Pt-L-Zn complexes and DNA



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Abstract

The four novel complexes [{*cis*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$ (**C1**), [{*trans*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$ (**C2**), [{*cis*-PtCl(NH3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ (**C3**) and [{*trans*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ (**C4**) (where terpy = 2,2′:6′,2′′-terpyridine) were investigated using molecular docking as a powerful *in silico* method for determination of interaction between hetronuclear complexes and DNA.

The principal attraction between **C1** complex and DNA came from H-bonds (at the sites DT19, DA18 nucleotides), and van der Waals forces. Likewise, connection between **C2** complex and DNA included covalent H-bonds (DA18, DT19, DG4). On the other hand, complex **C3** was bind with DC3, DG2 and DT19 nucleotide basis through conventional H-bonds. The complex **C4** was bind with DG10, DT20 and DT19 through conventional H-bonds. Additionally, the complexes **C1-C4** show that π interactions were also involved in their binding with DNA. The chelating ability of terpy ligands enhances the complex stability, while their planarity promotes intercalative interaction of the complexes with DNA due to π - stacking between the plane of the aromatic rings and DNA base pairs.

Keywords: molecular docking; DNA interactions; heteronuclear complexes

Introduction

Medicinal inorganic chemistry has become the most important new area of chemistry thanks to discovery of the anticancer properties of *cis*-$[PtCl_2(NH_3)_2]$ or cisplatin [1]. Despite of the success of cisplatin and their analogs, in treatment of various cancer types, the negative side effects limit its efficacy. The toxicity of these compounds is result of the interactions between Pt(II) and other biomolecules [1-6]. Synthesis of new complexes is possible way to overcome side effects of these drugs. Here, we synthesized four new complexes [{*cis*-$PtCl(NH_3)(\mu$-4,4'-bipyridyl)$ZnCl(terpy)\}](ClO_4)_2$ (**C1**), [{*trans*-$PtCl(NH_3)(\mu$-4,4'-bipyridyl)$ZnCl(terpy)\}](ClO_4)_2$ (**C2**), [{*cis*-$PtCl(NH_3)(\mu$-pyrazine)$ZnCl(terpy)\}](ClO_4)_2$ (**C3**) and [{*trans*-$PtCl(NH_3)(\mu$-pyrazine)$ZnCl(terpy)\}](ClO_4)_2$ (**C4**) and investigate binding with CT–DNA using Docking simulation to provide insight into possible mode of action of studied complexes toward DNA.

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Results and discussion

The types of interactions of all tested complexes with DNA investigated by molecular docking simulations. The docking results are displayed in table 1 (with obtained Δ*G* and K_i values) and in figures 1-3.

Table 1. Docking results of studied complexes (C1-C4) toward DNA.

Label		ΔG[a]	K_i[b]
C1	[{*cis*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$	-8.18	1.01
C2	[{*trans*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$	-8.07	1.22
C3	[{*cis*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$	-6.47	18.05
C4	[{*trans*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$	-6.53	16.30

[a] kcal mol^{-1}; [b] uM

Results and discussion

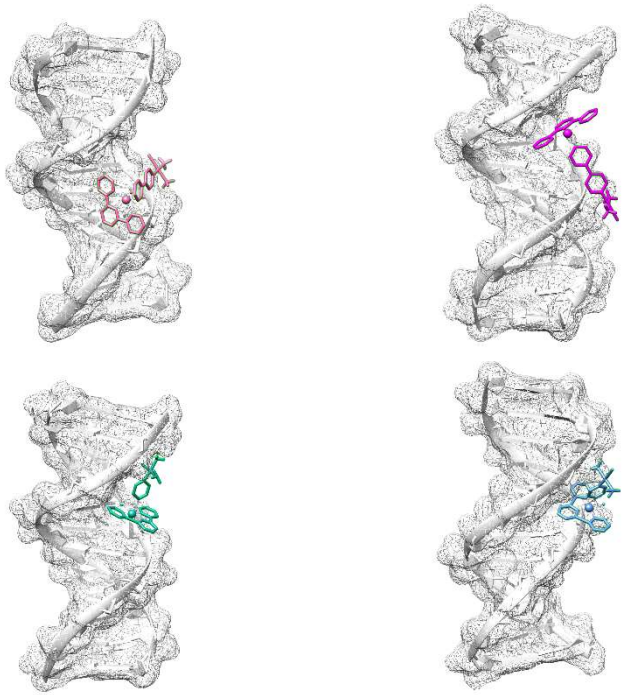

Figure 1. Major groove binding of the complexes with DNA: up left (**C1**), up right (**C2**), down left (**C3**) and down right (**C4**).

Results and discussion

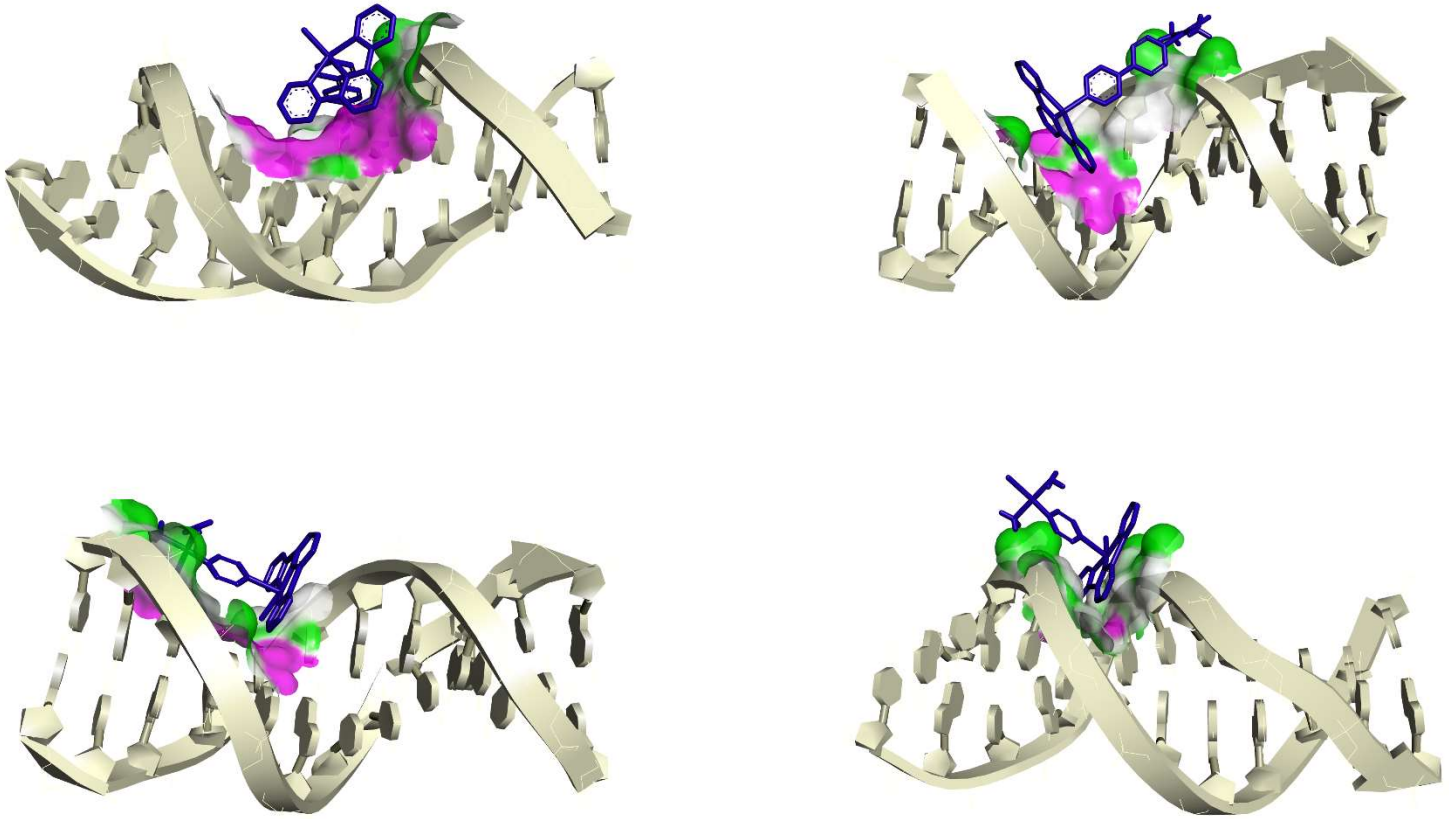

Figure 2. The best docking poses of the complexes with DNA: up left (**C1**), up right (**C2**), down left (**C3**) and down right (**C4**).

Results and discussion

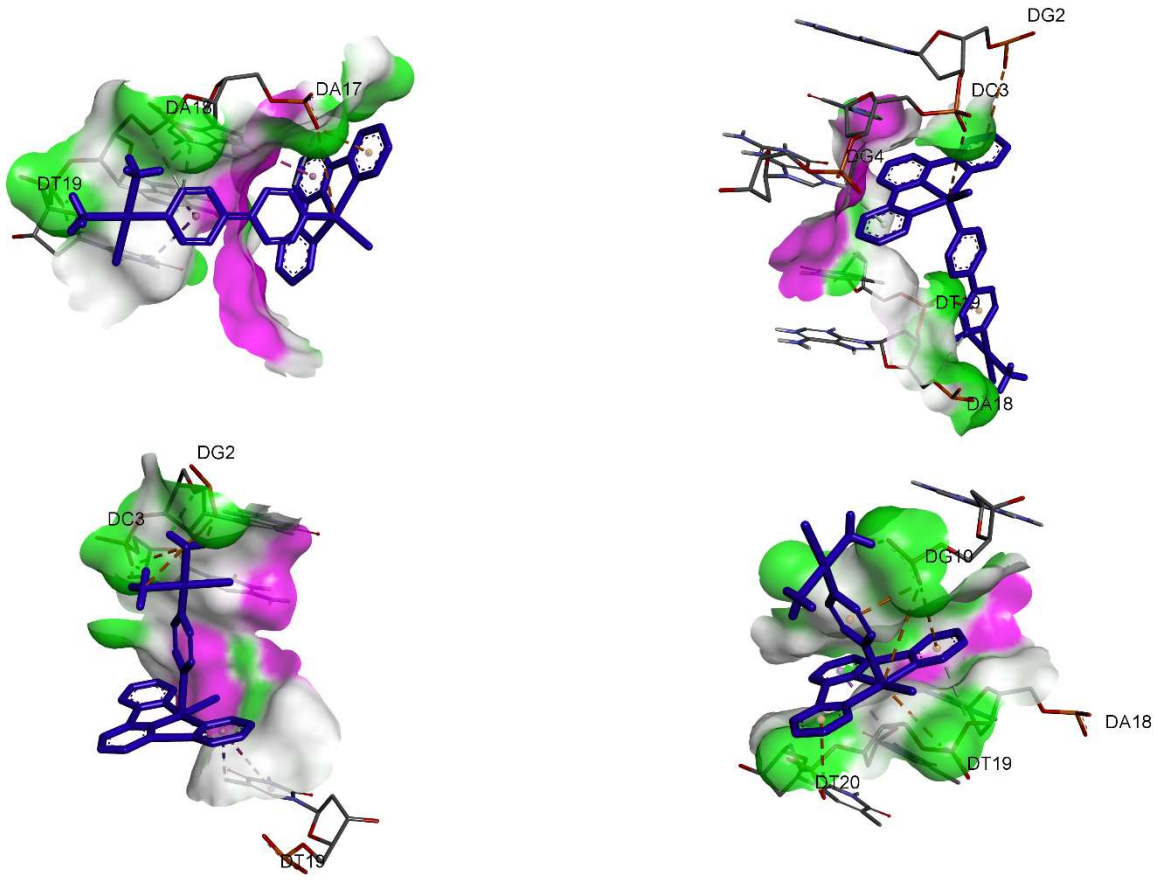

Figure 3. H-bond contributions in interaction of **C1-C4** complexes with DNA: up left (**C1**), up right (**C2**), down left (**C3**), down right (**C4**).

Conclusions

- Docking results are in good agreement with obtained experimental results.
- The nature of interactions between explored complexes and DNA are mostly coming from H-bonds connections.
- Those discoveries are important since hydrogen bonds play important role in transportation of medications in the organism.

Acknowledgments

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