The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022)
01–30 NOVEMBER 2022 | ONLINE

Interactions between heterometallic bridged *cis*-or *trans*-Pt(II)-Zn(II)complexes and calf thymus DNA

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pharmaceuticals MDPI

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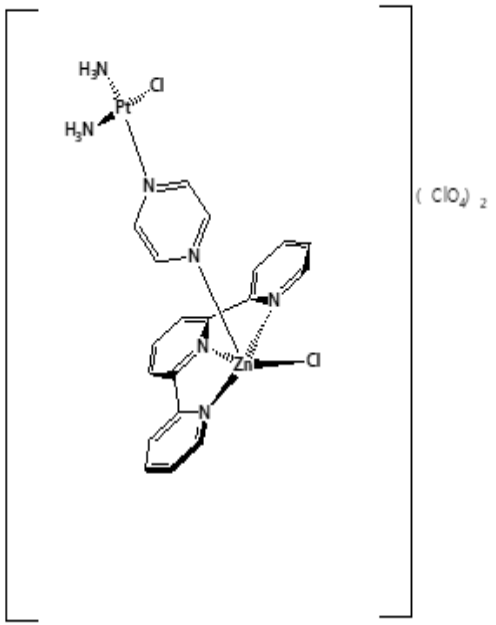

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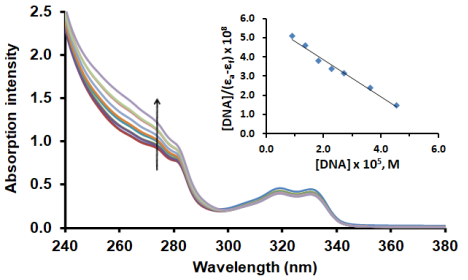

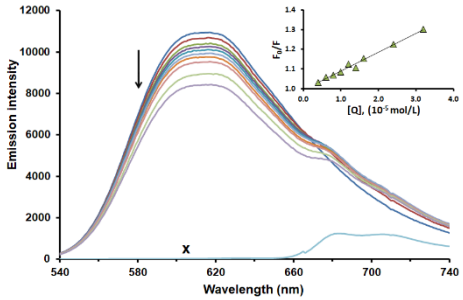

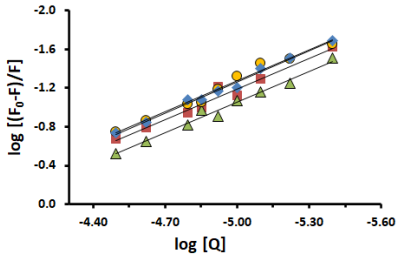

Abstract:

More recently scientific attention is paid on non-platinum based drug especially on bio-essential metal ions. Design of the heterometallic complexes is possible way to overcome limitation of platinum-based drugs. The four novel complexes [{*cis*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$, [{*trans*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$, [{*cis*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ and [{*trans*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ (where terpy = 2,2′:6′,2′′-terpyridine) were synthesized and characterized. The binding of the heterometallic bridged cis-or trans-Pt(II)-Zn(II) complexes to calf thymus DNA (CT-DNA) was studied using UV absorption and fluorescence emission spectroscopy. The results indicate that the complexes bind strongly to DNA (K_b, in the order of 10^4 M^{-1}) through groove binding, hydrogen bonds, and hydrophobic or electrostatic interaction. According to Stern–Volmer quenching constant (K_{SV}) and binding constant *(K*), the [{*cis*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$ complex interacts with CT-DNA-EB more strongly than the rest of the studied complexes.

Keywords: zinc(II); platinum(II); DNA interactions; heterometalic complexes;

Introduction

- *cis*-$[PtCl_2(NH_3)_2]$ or cisplatin[1] and their analogs, such oxaliplatin, carboplatin or nedaplatin, etc., in treatment of various cancer types showed numerous the negative side effects such as resistance, nephrotoxicity, ototoxicity, neurotoxicity, cardiotoxicity, and consequently limit its effectiveness.

- Design of the heterometallic complexes is possible way to overcome limitation of platinum-based drugs.

- Metal ion zinc(II) as part of zinc-finger family metalloproteins is involved in:

- control of nucleic acid replication,
- transcription and repair,
- plays important role in tumor growth,
- progression, angiogenesis and metastasis[2,3]

References:

1. a) B. Lippert, *Cisplatin chemistry and biochemistry of leading anticancer drugs*. Wiley- VCH, Zürich, **1999.**

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2. I. Bertini, H.B. Gray, E.I. Stiefel, J.S. Valentine, *Biological inorganic chemistry. Structure and reactivity*, University Science Books. Sausalito, CA, **2007**.

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Introduction

In our previous studied we have synthesized the two heterometallic complexes[4]:

- ✓ [{*cis*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ and
- ✓ [{*cis*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$ and

And by the same procedure we synthesized two new analogs:

- ✓ [{*trans*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ and
- ✓ [{*trans*-PtCl(NH_3)(μ-4,4′-bipyridyl)ZnCl(terpy)}](ClO_4)$_2$

References:

4. T. V. Soldatović, E. Selimović, N. Milivojević, M. Jovanović, B. Šmit , Novel heteronuclear Pt(II)-L-Zn(II) complexes: synthesis, interactions with biomolecules, cytotoxic properties. Two metals give promising antitumor activity?" Appl. Organomet. Chem. 2020, aoc5864, 1-14

Results and discussion

DNA binding experiments

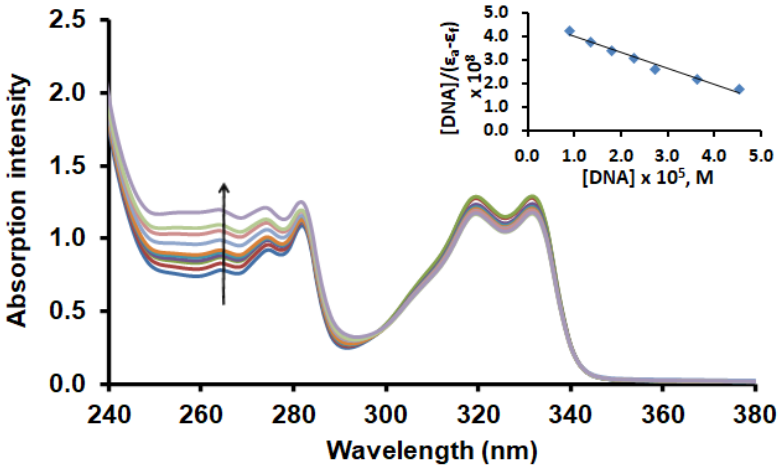

Figure 1. Absorption spectra of complex **[{*cis*-PtCl(NH$_3$)(*μ*-pyrazine)ZnCl(terpy)}](ClO$_4$)$_2$** at room temperature in PBS buffer upon the addition of CT–DNA. [C] = 5.2 × 10^{-5} mol dm^{-3}, [CT–DNA] = 0–6.35×10^{-5} mol dm^{-3}. Inset: plot of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA].

Increasing amounts of CT-DNA

The absorption band of all the complexes at λ_{280} showed hyperchromism

Complexes could bind to CT–DNA *via* groove binding, hydrogen bonds, and hydrophobic or electrostatic interaction[5]

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Results and discussion

Ethidium bromide (EB) displacement studies

The increasing concentration of the complexes decreasing fluorescence intensity of EB bound to CT-DNA at 613 nm.

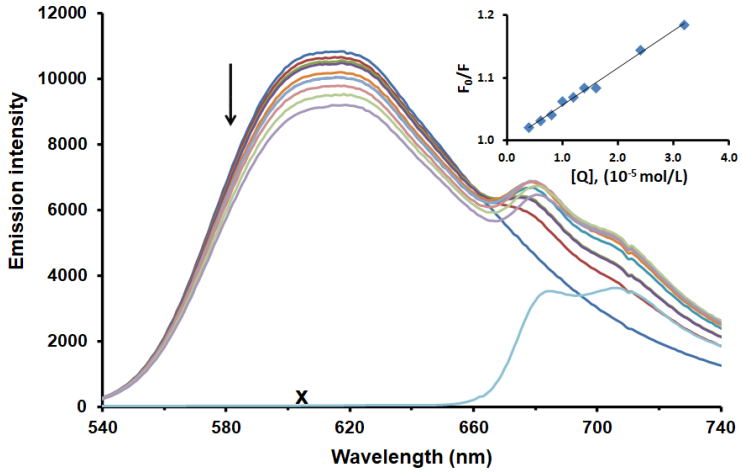

Figure 2. Fluorescence emission spectra of CT–DNA–EB system with various concentrations of complex [{*cis*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$. [EB] = 6.0×10^{-6} mol dm^{-3}; [CT–DNA] = 1.36×10^{-5} mol dm^{-3}; [C] = 0-3.2×10^{-5} mol dm^{-3}. T = 298 K. Inset: Stern-Volmer plot for quenching of CT–DNA–EB complex with [{*cis*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ complex . The arrow shows the emission intensity changes upon increasing [{*cis*-PtCl(NH_3)(μ-pyrazine)ZnCl(terpy)}](ClO_4)$_2$ concentration. **x** represents 3.6×10^{-5} mol dm^{-3} complex only.

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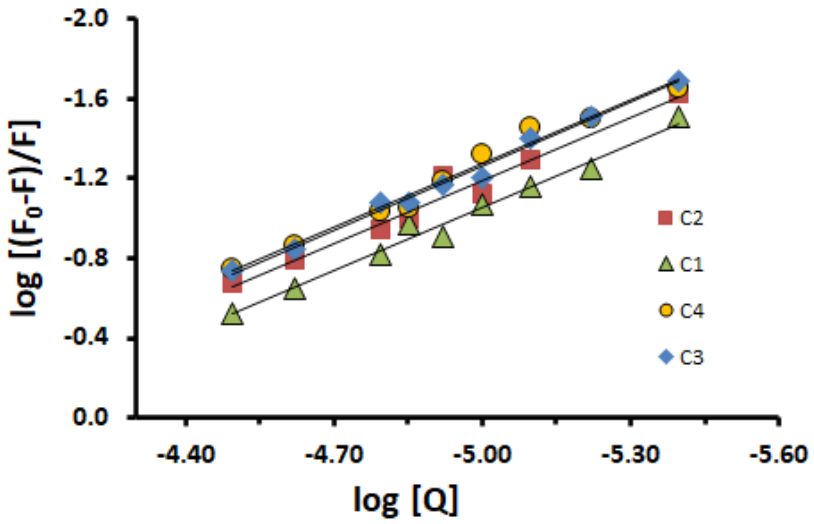

Figure 3. The plots of log((F_0 − F)/F) vs. log([Q]) at 298 K.

Table 1. Binding parameters of studied complexes (C1-C4) with CT-DNA-EB system.

Complex	K × 10^{-4} (M^{-1})	R^{2a}	n
[{*cis*-$PtCl(NH_3)(\mu$-pyrazine)$ZnCl(terpy)$}]$(ClO_4)_2$	1.24	0.9909	1.07

[a] R is the correlation coefficient

Conclusions

The DNA interaction binding properties of the new complexes were evaluated by:

- ✓ Absorption spectroscopy
- ✓ Fuorescence spectroscopy

The studied complexes bind well to CT-DNA through groove binding or electrostatic interactions. Also. it can be useful in the development of their potential pharmaceutical, biological and physiological implications in the future.

Acknowledgments