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DNA interaction studies of oxovanadium, manganese, copper and nickel complexes

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DNA is a molecule that carries most of the genetic instructions and interaction between small molecules and DNA often causes DNA damage in cancer cells, blocking the division, resulting in cell death. Towards the same, DNA interaction studies of transition metal complexes have been explored extensively. Further, the geometry of complexes can be tuned by the choosing the appropriate ligand bringing about perfect synergism to achieve greater therapeutic efficacy. In this context, we have synthesized and characterized V^{IV}, Mn^{II}, Cu^{II} and Ni^{II} complexes using 4-(2-amino-phenylimino)-2-methyl-4*H*-pyran-3-ol ligand. UV absorption titration and gel electrophoretic study brings about the comparative DNA binding and cleaving ability of synthesized complexes. Based on the results, the efficacy towards anticancer potential can be ascertained.

Keywords: Metal complexes, Schiff base, DNA interaction, binding constants.

Introduction

Schiff base-metal complexes containing O, N donor atoms including vanadium, copper, nickel and manganese have attracted much attention and their chemical and biological activities have been widely investigated including anticancer activity[1–6]. Among these, vanadium and copper are the most promising anticancer drug apart from their other medicinal uses[7]. This may be attributed to disruption of cellular metabolism through the generation of reactive oxygen species. Its compounds act as possible alternatives to platinum-based metal complexes[8a,9]. DNA is an important target for cytotoxic drugs. Thus, several reports state that transition metal complexes interact non-covalently through intercalation, groove binding or electrostatic binding[10]. Herein, we have synthesized copper, nickel, manganese and vanadium complexes based 4-(2-amino-phenylimino)-2-methyl-4*H*-pyran-3-ol ligand and studied their DNA interaction abilities.

Experimental

Materials and methods:

All the reagents and solvents used in the reaction were purchased commercially. They were used without any further treatments like purification.

UV spectrophotometry electronic spectral titration experiments was performed in 50 mM Tris-HCl buffer at 7.2. DNA cleavage activity by agarose gel electrophoresis using pBR322 plasmid with 25 μL DNA concentration of 1 mg/ml was incubated with varying concentration of complex (20–100 μL) at 37°C for 2 h. The gel was run in 10X TBE (Trisborate EDTA) buffer (pH 7.4) at 50 V for 2 h.

Synthesis of ligand [HL]:

0.126 g (1 mmol) of 3-hydroxy-2-methyl-4-pyran and 0.108 g (1 mmol) of *o*-phenylenediamine were dissolved in ethanol and mixed together and kept for stirring with reflux for 5 h at 60–70°C. The brown colour solid was obtained. Ligand: UV-Visible: 218 (π-π*) and 276 nm (n-π*); FTIR: 3361 (N-H), 1614 (C=N), 1369 (C-O), 3246 cm^{-1} (O-H); Mass 216.23.

Synthesis of metal complexes: 1 mmol of metal salts [0.163 g ($VOSO_4.H_2O$); 0.269 g ($MnSO_4.H_2O$); 0.272 g ($NiCl_2.6H_2O$); 0.134 g ($CuCl_2.2H_2O$)] was dissolved in 10 ml water. 0.126 g (1 mmol) of ligand [HL] dissolved in 10 ml

ethanol was added drop-wise to metal salt solution and kept stirring at room temperature until the colour changes to reddish brown. Finally, 0.1 ml triethylamine was added and continued stirring for about 1 h, filtered and evaporated to obtain the solid product (Scheme 1). Complex: UV-Visible[1,11]: V: 217 nm, 269 nm, 342 nm and 418 nm; Cu: 215 nm, 273 nm, 342 nm and 427 nm; Mn: 214 nm, 268 nm and 446 nm; Ni: 225 nm, 266 nm and 433 nm; FTIR[1,12]: 3188–3226 (N-H), 1498–1600 (C=N), 1274–1348 (C-O), 964 cm^{-1} (V=O); Mass: Cu: 277.75; Mn: 269.15; Ni: 272.90; V: 281.12.

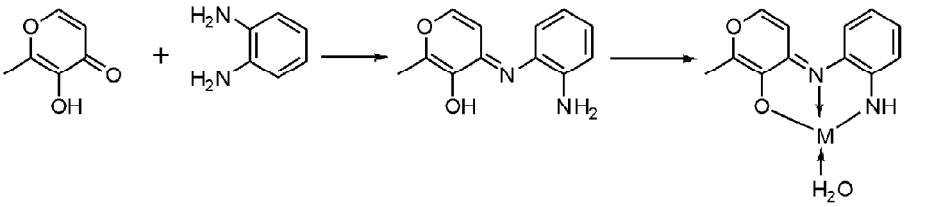
Results and discussion

DNA binding and cleavage studies:

V and Cu complexes show hypochromism indicating the probable intercalative binding mode. This is exhibited due to coupling of π* orbital of the intercalated ligand and π orbital of DNA base pair, which reduces transition energy resulting in bathochromism. Mn and Ni complexes show hyperchromism indicating groove binding mode (Fig. 1). The binding constants of the Cu^{II}, V^{IV}, Mn^{II}, Ni^{II} complexes are 3.97 + 0.092×10^4 M^{-1}, 4.20 + 0.07×10^4 M^{-1}, 2.035 + 0.07×10^4 M^{-1}, 1.52 + 0.06×10^4 M^{-1} respectively.

Gel electrophoresis:

The cleavage of the pBR322 with the complexes were observed with the transition from supercoiled form (Form I - move fastest) to nicked circular form (Form II - moves less faster than supercoiled form) and linear forms (Form III - moves in between supercoiled and nicked). The gel pictures are shown in Fig. 2a, b, c and d. In Fig. 2(a), lane 1-5 has shown supercoiled form favoring hydrolytic binding of DNA with copper complex. In Fig. 2(b), lane 1-4 has shown the cleavage of DNA with manganese complex with both supercoiled and nicked circular form. Lane 5 has shown no cleavage activity of DNA. Fig. 2(c) 1-5 lanes has shown good DNA binding activity with Ni complex and thereby exhibiting the supercoiled form. Lastly, in Fig. 2(d) lane 1-5 has shown both supercoiled and nicked circular form with oxovanadium complex. On the basis of the above mentioned observation and results, it can be concluded that the complexes have DNA binding and cleaving ability[8b].



Scheme 1

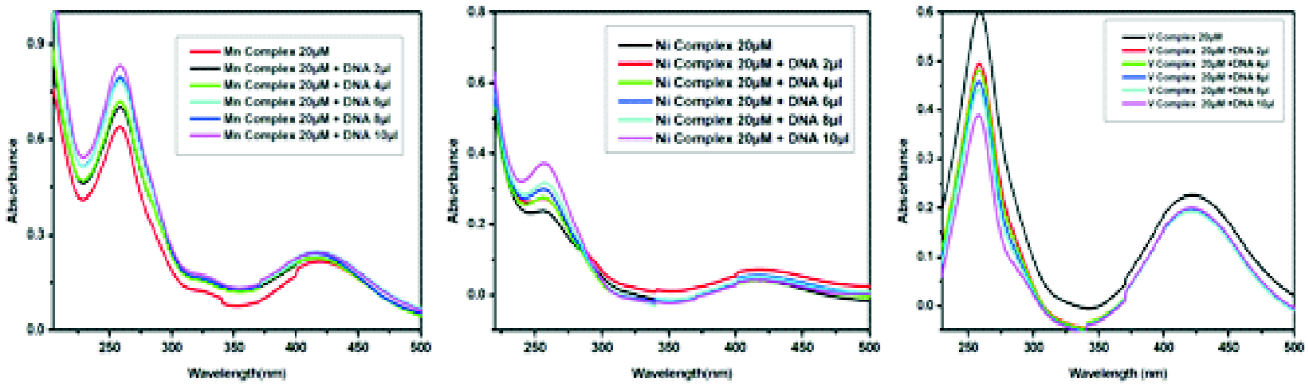


Fig. 1. Absorption spectral titration of complexes with DNA.

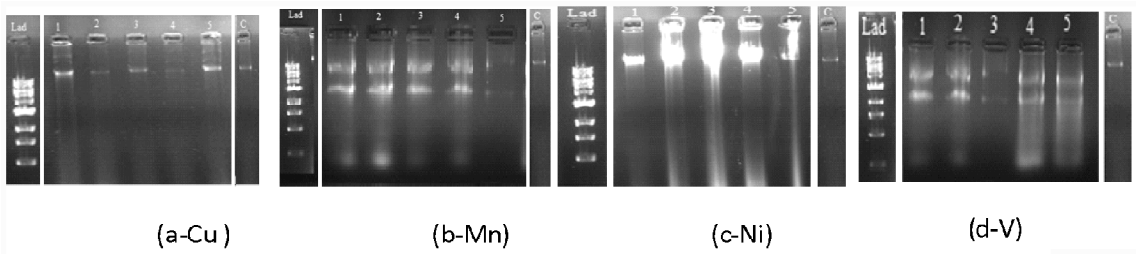


Fig. 2. Gel electrophoretic pattern of metal complexes.

Conclusion

The synthesized complexes possess good DNA binding ability with both intercalative and groove binding modes. The binding constant values prove their comparative binding efficiency. Further, by gel electrophoretic study, the complexes have shown significant bands corresponding to supercoiled and nicked forms of DNA favoring their cleaving ability. Further investigations are required to prove their anticancer potential, which is underway.

References

1. Z. Kazemi, H. Amiri Rudbari, V. Mirkhani, M. Sahihi, M. Moghadam, S. Tangestaninejad, I. Mohammadpoor-Baltork, A. Abbasi Kajani and G. Azimi, *Eur. J. Med. Chem.*, 2017, **135**, 230.
2. N. Lotfi, I. Sheikhshoaei, S. Y. Ebrahimipour and H. Krautscheid, *J. Mol. Struct.*, 2017, **1149**, 432.
3. S.-P. Zhang, Z. Feng, B. Wu, J.-J. Jiang, D.-R. Zhu and B. He, *J. Coord. Chem.*, 2018, **71**, 46.
4. J.-A. Zhang, Y. Li, Y.-Z. Fan, X.-Z. Zou, Y.-J. Liu, L.-J. Zhang and S.-R. Zheng, *Inorg. Chem. Commun.*, 2014, **49**, 136.
5. S. Jagadeesan, V. Balasubramanian, P. Baumann, M. Neuburger, D. Haussinger and C. G. Palivan, *J. Inorg. Chem.*, 2013, **52**, 12535.
6. X. Feng and J. Liu, *J. Inorg. Biochem.*, 2018, **178**, 1.
7. S. A. Elsayed, A. M. Noufal and A. M. El-Hendawy, *J. Mol. Struct*., 2017, **1144**, 120.
8. (a) P. R. Inamdar and A. Sheela, *Int. J. Biol. Macromol.*, 2015, **1**, 269; (b) P. R. Inamdar, R. Chauhan, J. Abraham and A. Sheela, *Inorg. Chem. Commun.*, 2016, **67**, 67.
9. S. K. Mal, T. Chattopadhyay, A. Fathima, C. S. Purohit, M. S. Kiran, B. U. Nair and R. Ghosh, *Polyhedron*, 2017, **126**, 23.
10. C. P. Chinthala and A. Sheela, *Appl. Organomet. Chem.*, 2017, **31**, 3700.
11. D. Moreno, V. Daier, C. Palopoli, J. P. Tuchagues and S. Signorella, *J. Inorg. Biochem.*, 2010, **104**, 496.
12. C. M. Da Silva, D. L. da Silva, L. V. Modolo, R. B. Alves, M. A. de Resende, C. V. Martins and A. de Fatima, *J. Adv. Res.*, 2011, **2**, 1.