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FT-Raman Spectroscopy of Heavy Metal-Nucleotide Complexes

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FT-Raman spectroscopic study was made on an interaction between deoxyguanosine 5'-monophosphate (dGMP) and Cd^{2+} and Cu^{2+} in an aqueous solution with various metal ion concentrations. The spectrum reveals that both the ions bind to the phosphate groups. The spectral changes observed for the vibrations of deoxy ribose moiety near 844 cm^{-1} in Cd-dGMP complexes shows that the C2'-endo/anti conformation is completely eliminated at higher concentration (r = 1) whereas in Cu-dGMP complex the glygosyl bond shows more flexibility. Spectral changes are also observed for the guanine base vibration and the mode of interaction is discussed in detail.

Key Words: Interaction, FT-Raman spectrum, DNA, Metal ions.

INTRODUCTION

The binding of metals by nucleosides and nucleotides has been investigated for a number of years[1-4]. Because of recent observations that some metal ions cause chromosome damage and consequently is mutagenic, there is renewed interest in the binding of heavy metals to polynucleotides[3,4]. In this work, the interaction of Cu^{2+} and Cd^{2+} with deoxyguanosine 5'-monophosphate (dGMP) in aqueous solution are studied using FT-Raman spectroscopy to obtain information on the binding of the heavy metal ions to dGMP, which can serve as model systems to study the action of such substances on the DNA structure[1].

EXPERIMENTAL

Deoxyguanosine monophosphate (dGMP) was purchased from the Sigma Chemicals Co. and used as supplied. Chloride salts of the metal cations were obtained from Aldrich Chemical and used without further purification.

Sample preparation: A solution of dGMP (0.1 M) was prepared and kept at 4 ºC for 24 h to ensure the formation of a homogeneous solution. This solution was then mixed with a solution of the corresponding metal salt to give mixture with the desired metal: dGMP ratio (1:5 and 1:1). An aliquot of 50 µL was sealed in glass capillary tubes for Raman analysis[1].

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FT-Raman spectra of the dGMP samples presented in the present work were measured with an IFS FT-IR Spectrometer coupled to a FRA 106 FT-Raman accessory (Bruker). Raman scattering was excited by a 1.06 μm continuous-wave Nd:YAG laser using approximately 180 mW of radiant power at the sample. The FT-Raman accessory, used with a near-IR beam splitter, collected stokes data over a range of 1750-600 cm^{-1}. Data collection and processing were carried out with data system CS-42 (Bruker).

RESULTS AND DISCUSSION

Cu(II)-dGMP binding: The FT-Raman spectrum of aqueous dGMP and that in the presence of Cu(II) at 1:5 and 1:1 metal:dGMP ratios are given in Figs. 1-3, respectively. Confirmationally sensitive Raman bands are discussed and the results are summarized in Table-1 along with the assignments. A comparison of the spectra indicates that Cu^{2+} ions have a pronounced effect on the structure of dGMP. The 676.5 cm^{-1} band observed in the free dGMP is assigned to a breathing motion of the guanine coupled through C1'-N9 glycoside bond to deoxyribose and also characterizes the C2'-*endo/anti*-conformation of B-DNA in aqueous solution[5].

TABLE-1
FT-RAMAN SPECTROSCOPIC DATA OF Cu^{2+} AND Cd^{2+}-NUCLEOTIDE COMPLEXES

Frequency (Intensity) cm^{-1}					
dGMP	Cu^{2+}/dGMP (r = 1/5)	Cu^{2+}/dGMP (r = 1)	Cd^{2+}/dGMP (r = 1/5)	Cd^{2+}/dGMP (r = 1)	Assignments
676.5 (5.5)	688.2 (5.7)	688.2 (9.8)	682.3 (8)	–	ν(C1'-N9)
844.1 (3.6)	821.3 (5.8)	829.4 (8.2)	850.8 (4.3)	–	B-backbone
886.3 (10)	887.6 (10)	893.0 (10)	887.6 (10)	884.0 (10)	Sugar phosphate
1091.5 (6.0)	1094.1 (7.0)	1089.6 (8.2)	1090.8 (8.4)	1095.7 (8.7)	ν_s (PO_2^-)
1333.7 (2.4)	–	1335.3 (3.4)	1329.4 (3.7)	1339.6 (3.4)	dG (ring stretching)
1370.5 (2.0)	1359.0 (3.8)	1359.3 (3.8)	1069.7 (3.7)	1380.0 (1.7)	dG imidazole ring
1495.0 (4.9)	1490.1 (5.5)	1476.5 (6.4)	1498.3 (6.4)	1496.7 (4.3)	dG ν(N7-C8)
1578.3 (4.0)	1587.4 (4.5)	1588.2 (5.5)	1588.2 (4.7)	1590.0 (3.4)	dG(N1-H, $N2H_2$)
1605.8 (3.2)	1650.4 (5.0)	1600.0 (9.0)	1626.6 (5.2)	1620.0 (6.3)	δ(N1-H)
1633.8 (4.4)	–	1605.0 (9.9)	1635.9 (6.5)	1648.0 (5.5)	dG [δ(N1-H) δ($N2H_2$) ν_s (C6=O)]
1647.0 (4.1)	1635.0 (4.7)	1636.0 (9.0)	1658.8 (4.8)	1660.1 (7.0)	δ($N2H_2$)
1680.2 (3.5)	1672.0 (4.0)	1677.6 (9.2)	1674.0 (5.1)	1680.0 (5.6)	dG [δ(N1-H, $N2H_2$) ν_s (C6=O)]

In Cu-dGMP complex, the intensity of the 676.5 cm^{-1} band increases enormously from 5.5 units to 9.8 units (Table-1) at 1:1 metal-dGMP ratio. This result indicates that the glycoside bond becomes more flexible in the presence of Cu^{2+} ions[6-8]. The band observed at 844.1 cm^{-1} in free dGMP is due to antisymmetrical phosphodiester vibration and also characteristic of B-conformation of DNA. In the presence of Cu^{2+} ions at r = 1/5 and r = 1, the above band shifts, respectively to 821.3 and 829.4 cm^{-1} indicating that the C2'-*endo/anti*-conformation of guanine nucleoside is not affected in Cu-dGMP complex[5,9-11].

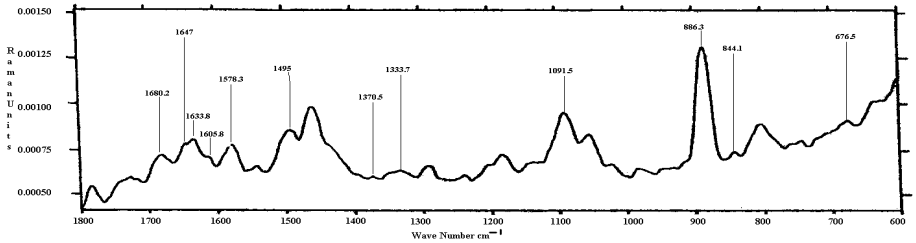

Fig. 1. FT-Raman spectrum of free dGMP

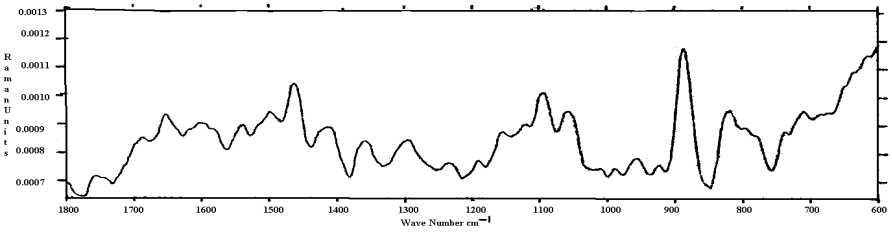

Fig. 2. FT-Raman spectrum of Cu/dGMP (r = 1/5)

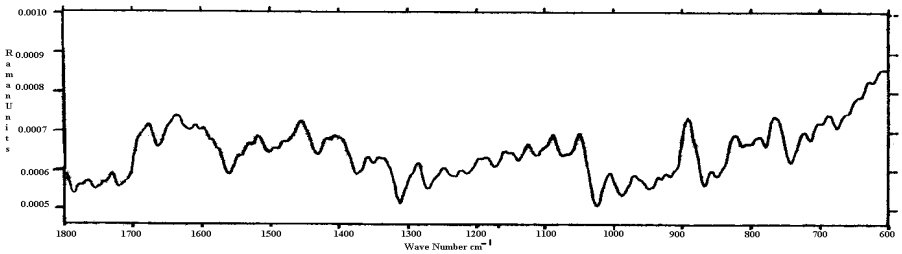

Fig. 3. FT-Raman spectra of Cu/dGMP (r = 1)

The band at 1091.5 cm^{-1} in metal free dGMP is assigned to symmetrical vibrations of PO_2^- groups[9-11]. In the presence of Cu^{2+} ions at r = 1/5 and r = 1, the above band is shifted to 1094.1 and 1089.6 cm^{-1} and shows enhanced intensity. This indicates that the Cu^{2+} ions are involved in the formation of water-separated ion pairs with the phosphate groups. This interpretation is consistent with previous assessments based on Raman studies of phosphate-metal interactions[12,13].

There are several indications that the Cu^{2+} ions interact also with the guanine base of dGMP. The most convincing proof comes from the spectral changes observed for the in-plane ring stretching vibrations at 1333.7, 1370.5,1495 and 1578.3 cm^{-1}. In Cu-dGMP complex all the above bands gradually exhibit lower frequency shift with substantial intensity increase (Table-1) as the metal ion concentration increases. These effects are interpreted as resulting from metal ion binding at N7 position of guanine through water molecule. The effect of the metal ion in this metal(II)-O(H)-H -N7 type of aggregate is to increase the strength of the hydrogen bonds between the N7 of guanine and hydrogen of water, causing a decrease in stretching frequency of the C8 = N7 bond[10-13].

Various bonds in the 1750-1600 cm^{-1} region of free dGMP assigned to stretching vibrations of C6=O[14] and in-plane deformation of N1-H and N2-H_2 groups[15,16] exhibit increase intensity and lower frequency shift in Cu-dGMP complex. Among the most informative of these is the band at 1680.2 cm^{-1}, which shifts to lower frequency and increase in intensity with metal concentration (Table-1). These results indicate that the strength of the carbonyl bond decreases while that of N-H bond increases upon metal complexation[17,18].

Cd(II)-binding: The FT-Raman spectrum of aqueous dGMP in the presence of Cd(II) at 1:5 and 1:1 metal:dGMP ratios are given in Figs. 4 and 5, respectively. Confirmationally sensitive Raman bands are discussed and the results are summarized in Table-1 along with the assignments. The Raman spectra indicate that the mode of binding of Cd^{2+} ions by dGMP is quite different from that of Cu^{2+} ions. The perturbation observed for the C2'-*endo/anti*-confirmative marker of guanine nucleoside (676.5 cm^{-1}) in Cd-dGMP is similar to that observed in Cu-dGMP complex. On the other hand the B-form confirmation marker (844.1 cm^{-1}) is eliminated in Cd-dGMP. The phosphodioxy vibration of free dGMP at 1091.5 cm^{-1}, which exhibits lower frequency shift in the presence of Cu^{2+} ions, is shifted to higher frequency in Cd-dGMP complex. This result is due to partial disruption of the hydrogen bond network with water molecules in the neighbourhood of the phosphate groups, which is known to displace the symmetric stretching vibration of PO_2^- groups to higher value[19,20].

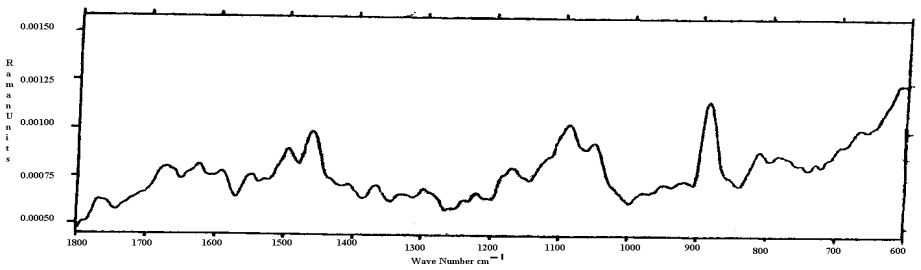

Fig. 4. FT-Raman spectrum of Cd/dGMP (r = 1/5)

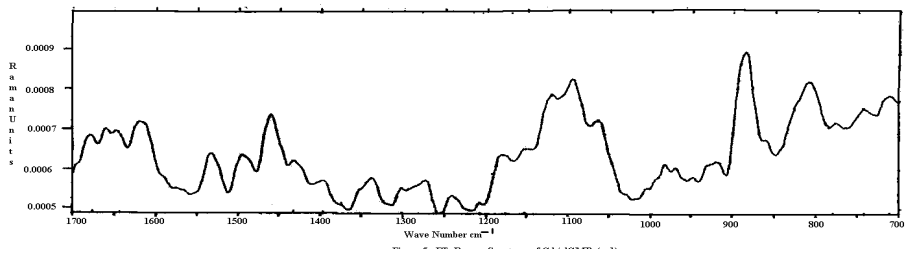

Fig. 5. FT-Raman spectrum of Cd/dGMP (r = 1)

Raman bands of the base observed at 1333.7, 1370.5, 1495, 1578.3 cm^{-1} in free dGMP are shifted to higher frequencies in Cd-dGMP whereas all the above bands exhibit lower frequency shifts in the presence of Cu^{2+} ions. The spectral changes observed are consistent with metal binding at N7 and N1 atom of guanine[17].

The perturbations observed for the vibrations in the "double-bond region" in Cd-dGMP are also different from that observed in Cu-dGMP. The vibration due to N1-H bending mode of free dGMP at 1605.8 and 1633.8 cm^{-1} shift, respectively to 1626.6 and 1635.9 cm^{-1} at r = 1/5 and to 1620 and 1648 cm^{-1} at r = 1 in Cd-dGMP complex. These results clearly indicate Cd^{2+} ion binding at N1 of guanine. The carbonyl vibration on the other hand is not much affected in Cd-dGMP complex[17,19-21].

Conclusion

The following conclusions are derived from the present study of the FT- Raman spectra of the solutions of dGMP in the presence of Cu(II) and Cd(II) ions.
(i) Interaction with the phosphate group is observed for both the ions. (ii) The C2-*endo/anti* conformation of guanine nucleoside is conserved in both the metal complexes. (iii) The B-conformation of the backbone is not much affected in Cu-dGMP, whereas it is completely eliminated in Cd-dGMP complex. (iv) Both Cu(II) and Cd(II) have strong affinity for N7 atom of guanine, which makes the rotation about the glycosyl bond more flexible. Additionally, Cd(II) ions have strong affinity for N1 atom. (v) The strength of hydrogen bond associated with carbonyl groups increases in Cu-dGMP whereas it is not much affected in Cd-dGMP.

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