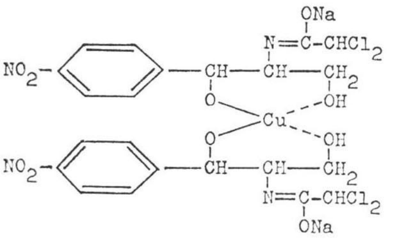
GREEN AND PURPLE COPPER (II)-CHLORAMPHENICOL COMPLEXES IN METHANOL: EVIDENCE FOR THE COORDINATION OF DEPROTONATED AMIDE NITROGEN

Sir:

Chloramphenicol having the possible three metal-binding sites, an amide and two hydroxy groups, is a well known antibiotic, but its reaction schemes with metal ions were not fully established, although the importance of metal interactions with antibiotics in relation to their subsequent actions has been discussed[1]. Medvedovskii *et al* proposed the structure **I** in Fig. 1 to the purple complex in reaction of Cu (II) with chloramphenicol in alkaline aqueous solution[2]. On the other hand, a green Cu (II)-chloramphenicol complex was isolated from methanol by Fazakerley *et al*[3], who were unable to characterize the coordination mode in this complex. In a recent communication, Jeremic *et al* concluded that the amide group was not involved in coordination in the purple complex suggesting the structure **II** in Fig. 1[4].

In this paper we propose structures for the two kinds of complexes colored green and purple, which were formed in the reaction of Cu (II) and chloramphenicol under different pH conditions. A characterization of these complexes in methanol demonstrates that Cu (II) is bound to the nitrogen atom of deprotonated amide groups.

Fig. 1. Proposed structures for Cu (II)-chloramphenicol complexes[2,4].

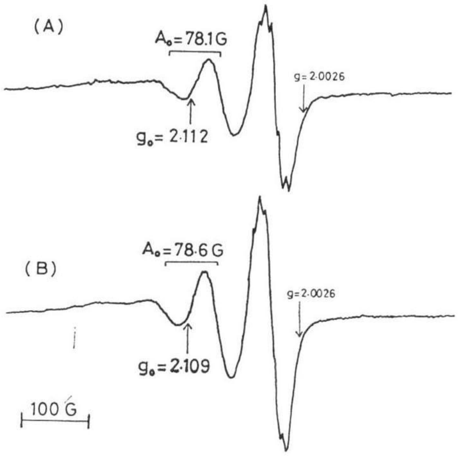


(I)

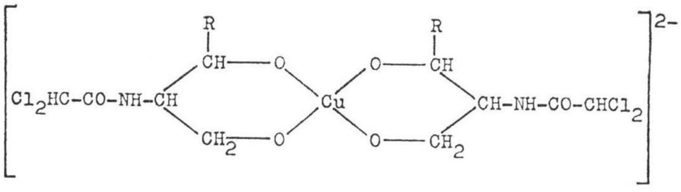
Fig. 2. ESR spectra of green (A) and purple (B) Cu (II)-chloramphenicol complexes in methanol at room temperature.

chloramphenicol - KOH - Cu (II)=2: 4: 1 (A),
2: 6: 1 (B)

[chloramphenicol]=2×10^{-2} M



Chloramphenicol, D (−) - *threo* - 2 - dichloroacetamido - 1 - *p* - nitrophenyl - 1, 3 - propenediol, was obtained from Sigma Chemical Company. The methanol solution which contained 2: 1 chloramphenicol and Cu (II) was titrated with methanolic KOH solution. As moles of KOH added per mole of chloramphenicol were two and three, the very stable green and purple colors were developed exhibiting the absorption maxima at 600 nm ($\varepsilon=59$) and 545 nm ($\varepsilon=58$), respectively. This shows clearly the presence of three coordination sites in chloramphenicol and also that in the green and purple complexes the metal-binding sites are two and three, respectively. Further, these titration and optical data suggested the presence of the coordination to Cu (II) from the deprotonated amide nitrogen in chloramphenicol[5]. The compositions of the two complexes were found to be 2: 1 in the ratio of ligand



(II)

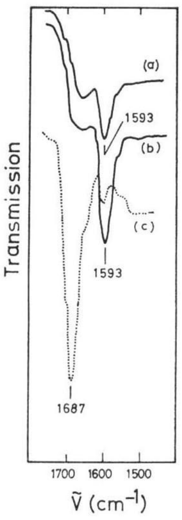


Fig. 3. Infrared spectra of purple (a), green (b) Cu (II)-chloramphenicol complexes and chloramphenicol (c) in methanol.

Chloramphenicol - KOH - Cu (II) = (a) 2: 6: 1, [chlorampnenicol]$=6\times10^{-2}$M; (b) 2: 4: 1, [chloramphenicol]$=6.7\times10^{-2}$ M; (c) [chloramphenicol]$=10^{-1}$ M

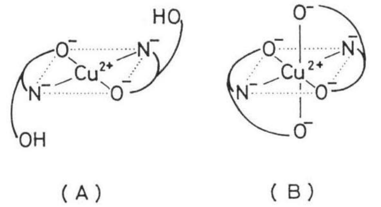
to Cu (II) by the molar ratio method, corresponding well with the result of JEREMIC *et al*[4]. The two complexes showed unique and almost the same CD spectra with each other with the sign (−+−) above 400 nm and the purple complex gave a larger magnitude than the green one.

Involvement of the two nitrogen atoms as the metal-binding sites in the green and purple 1: 2 Cu (II)-chloramphenicol was unequivocally demonstrated by ESR detection of the ligand hyperfine splittings (5 lines) due to the equivalent nitrogen atoms (^{14}N, I=1) (Fig. 2). The presence of the deprotonated amide nitrogen bound to Cu (II) in both complexes was further corroborated by monitoring the frequencies of carbonyl groups with the IR spectra measured in methanol (Fig. 3). The band at 1593 cm^{-1} in both complexes is assigned to the carbonyl group of the amides which involve deprotonated amide nitrogens bound to Cu (II)[5,6].

From these data, we propose that Cu (II)-chloramphenicol green complex has two coordination sites with Cu (II), the deprotonated amide nitrogen and oxygen attached to C1 or C3 forming a tetracoordinated square planar configuration. The purple one has three sites, the deprotonated amide nitrogen and two oxygen attached to C1 and C3 forming a hexacoordinated octahedral configuration (Fig. 4). At present we can not answer which oxygen atom attached to C1 or C3 is used to form the chelation in the green complex.

Further investigations are under way to establish this point.

Fig. 4. Possible coordination modes of green (A) and purple (B) Cu (II)-chloramphenicol complexes in methanol.



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HIROMU SAKURAI
SHIGERU SHIMOMURA
*KAZUHIKO ISHIZU

Faculty of Pharmaceutical Sciences,
University of Tokushima,
Scho-machi 1, Tokushima 770,
Japan
*Faculty of Sciences,
Ehime University,
Matsuyama, Ehime 790,
Japan

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