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Synthesis and structural studies of transition metal (II) Complexes with β-lactam antibiotic-Amoxicillin

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Abstract
Three neutral transition metal (II) complexes with β-lactam antibiotic ligand amoxicillin have been synthesized. Three metal ions Fe (II), Ni (II) and Cu (II) ions have been taken for complexation. The newly synthesized complexes were characterized on the basis of their elemental analysis, molar conductivities, magnetic properties as well as IR, nmr and UV spectra. On the basis of these analyses, it has been confirmed that the amoxicillin acts as tridentate ligand during the complexation with transition metal (II) ions. The six and four coordinated complex with Fe (II), Ni (II) and Cu (II) ions respectively have been established on account of above mentioned analytical measurements. Solubility of the complexes has been determined by using different solvents. Melting point of the complexes was determined by the open capillary tube and hence is uncorrected.

Keywords: Transition metal(II) complexes, amoxicillin, tridentate ligand, Fe(II), Ni(II), Cu(II), spectroscopic characterization

Introduction
The organometallic and coordination chemistry of transition metals are dominated by the variable valence state [5. 6], according to their position in periodic table. The applications of the divalent transition metal complexes are innumerable, from industrial catalysis [7], to luminescence [8], to biomedical applications [9].
Antibiotics that possess the β-lactam ring structure are predominant class of agents currently used for the *chemotherapy* of bacterial infections [11]. Amoxicillin is a fine, white to off-white, crystalline powder that is sparingly soluble in water [11]. It is chemically 6-[D-(-)-α-amino-p-hydroxyphenylacetamido] penicillanic acid, a semi synthetic penicillin introduced in 1974, is simply the p-hydroxy analogue of ampicillin [12]. Amoxicillin has largely replaced ampicillin for the treatment of certain systemic and urinary tract infections for which oral administration is desirable. Amoxicillin is reportedly less effective than ampicillin in the treatment of bacillary dysentery, presumably because of its greater gastrointestinal absorption [13].
In this present research work complexes of transition metal Fe (II), Ni (II) and Cu (II) ions with antibiotic ligand amoxicillin have been reported.

Complexes of amoxicillin with transition metal (II) ions
All chemicals such as amoxicillin trihydrate, transition metal (II) salts, methyl alcohol, ethyl alcohol, acetone, DMF and DMSO used in this study were of analytical grade. These chemicals purchased from CDH or Merck and used without further purification.

Preparation of solution
A 0.01 M amoxicillin trihydrate solution was prepared by dissolving the 0.21 g of amoxicillin trihydrate ligand in 50 ml distilled water.
A 0.01 M solution of transition metal (II) salts were prepared by dissolving by appropriate amount of metal salts in 50 ml of distilled water.

Preparation of complex
The complex was prepared by the addition of 50 ml of 0.01 M metal salt solution to 50 ml of 0.01 M of ligand amoxicillin solution with continuous stirring at ice cold temperature and at

pH values 8.2 - 8.8 adjusted by solution of 0.1 M Na_2CO_3 using a pH meter. The solution was converted into syrupy liquid which when filtered in suction pump, washed with distilled water, ethanol and acetone several times and dried in a desiccator over calcium chloride, then solid complex was obtained.

Analytical data of transition metal (II) complexes with ligand amoxicillin are given in following table:

Table 1: Analytical data of metal complexes

Complexes	C Cal/ (Found)	H Cal/ (Found)	N Cal/(Found)	M Cal/ (Found)
[Fe(amox)$(H_2O)_2$Cl]	39.04/(38.74)	4.47/(4.39)	8.54/(8.38)	8.54/(8.38)
[Ni(amox)Cl]	41.86/(41.52)	3.92/(3.88)	9.16/(8.98)	12.80/(12.60)
[Cu(amox)Cl]	41.52/(41.28)	3.92/ (3.88)	9.06/(8.91)	13.71/(13.53)

The Physical properties of transition metal (II) complexes with ligand amoxicillin are given in following table:

Complexes	Colour	M.Pt.	Solublity	Conductance (Ω^{-1})	μ_{eff}
[Fe(amox)$(H_2O)_2$Cl]	Brown	>300^{0}c	DMSO and DMF	13.20	Diamagnetic
[Ni(amox)Cl]	Green	>300^{0}c	DMSO and DMF	11.23	Diamagnetic
[Cu(amox)Cl]	Light green	>300^{0}c	DMSO and DMF	10.30	1.73

Result and discussion

Infrared spectra

The infrared spectra of the solid transition metal (II) complexes with ligand amoxicillin are given below.

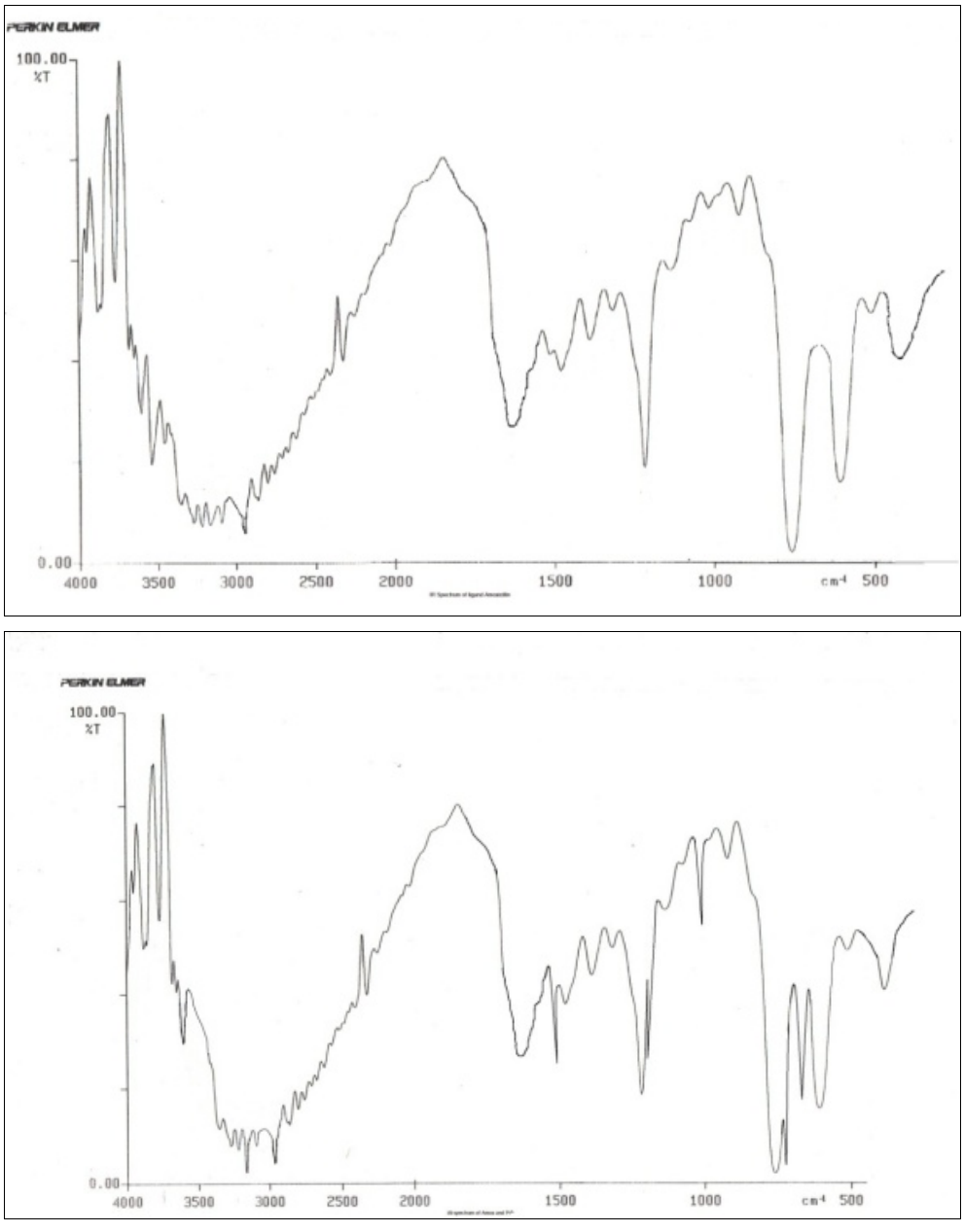


Fig 1: IR spectrum of ligand Amoxicillin Fig. IR Spectrum of complex Fe^{2+} with ligand Amoxicillin

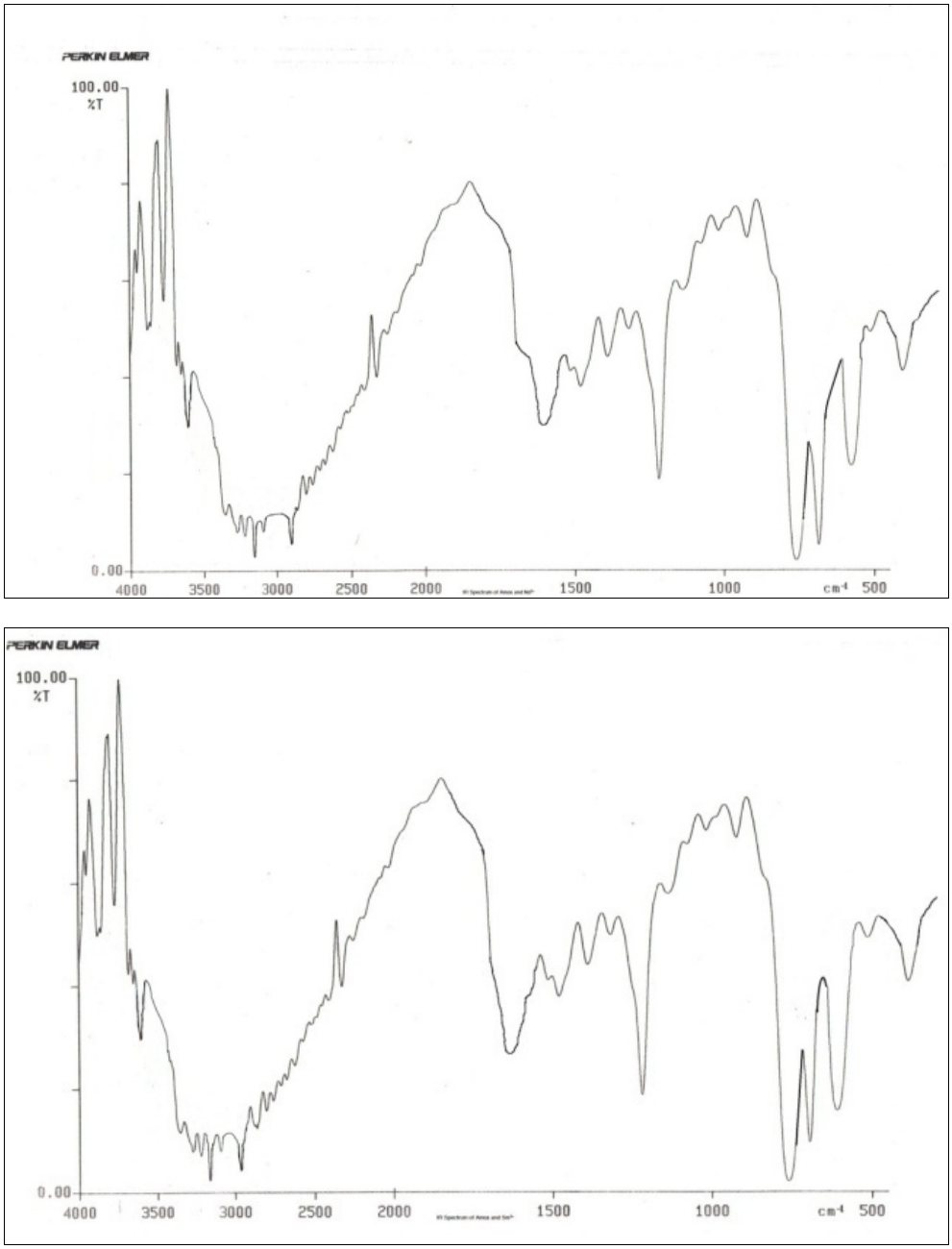


Fig 2: IR spectrum of complex Co^{2+} with ligand Amoxicillin

Fig. IR spectrum of complex Ni^{2+} with ligand Amoxicillin

The IR spectral data and the assignment of the ligand and its transition metal (II) complexes are given in following table.

Compound	$\nu_{(CN)}$ cyclic	$\nu_{(NH2)}$	$\nu_{(CO)}$ β- lact.	$\nu_{(NH)}$ amide	$\nu_{(COO-)}$	$\nu_{(MO)}$	$\nu_{(NO2)}$ $\Delta\nu$	$\nu_{(MN)}$	$\nu_{(enol)}$
Amoxicillin	1379	3200	1774	2968	1582	…….	…….	…….	…….
$[Fe(amox)(H_2O)_2Cl]$	1375	3250	…….	2934	1580	445	208	610	1580
[Ni(amox)Cl]	1378	3260	…….	2927	1595	435	……	555	1600
[Cu(amox)Cl]	1374	3276	…….	2922	1585	420	……	530	1550

The infrared spectra of complexes of amoxicillin with transition metal (II) ions and the ligand amoxicillin were recorded in the range of 400-4000 cm^{-1}. The highest frequency of the bands of the ligand at ~3200 cm^{-1} can be assigned to the asymmetric ν_{NH} vibration of the amino group. The other band at 3000 cm^{-1} may be due to the vibration of the imino group. These two bands are shifted from 3200cm^{-1} to ~3130 cm^{-1} and from 3000 cm^{-1} to ~2924 cm^{-1} on complexations indicating the involvement of both NH_2 and NH groups in complex formation. The shift of ν_{NH} to lower frequency on complexation suggests coordination through the NH_2 and NH of the amide group. The absence of a C=O (β-lactam) ligand band at 1774 cm^{-1} and the appearance of the band at 1603-1523 cm^{-1} in all complexes, suggest that 6, 7-enolization takes place before coordination with metal ions. The occurrence of bands at 625-520 cm^{-1} (M-N) and 420-455 cm^{-1} (M-O) prove the bonding of nitrogen and oxygen to the metal ions. The spectra of the complexes exhibited a lack of broad band about 3600-3440 cm^{-1} indicating the absence of water molecules in the complexes.

^{1}H Nuclear Magnetic Resonance

The triplet peak at δ = 4.70 ppm of β-lactam ring of carbon-6position of amoxicillin is disappeared in all complexes of transition metal (II) ions with ligand amoxicillin. It may be due to the enolization of the carbonyl group before the complexation.

Electronic spectra

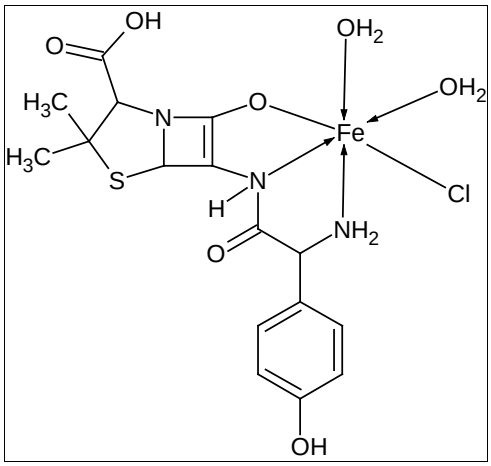
The spectral data for the solution of transition metal (II) ion complexes with ligand amoxicillin investigated in acetonitrile are recorded in CDRI, Lucknow and presented in the following table.

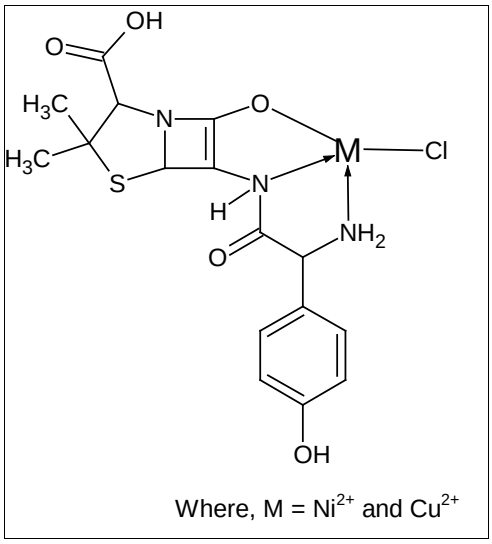
Table 2: Electronic spectral data of amox with transition metal (II) ions in cm^{-1}

Transition metal (II) complexes	Spectral bands	Transitions
[Fe(amox)(H_2O)$_2$Cl]	18500, 22700, 24875, 24900, 25000, 27900, 29500, and 32400.	$\rightarrow {}^6A_{1g}$ $^4T_{1g}$, $^4T_{2g}$ (G), ^4E_g, $^4A_{1g}$, $^4T_{2g}$ (D)
[Ni(amox)Cl]	548, 515, 475.	$\rightarrow {}^3B_{1g}$ ^3E_g, $^3B_{2g}$, $^3A_{2g}$.
[Cu(amox)Cl]	12000.	$\rightarrow {}^2E_g$ $^2T_{2g}$

Conclusion

On the basis of IR analysis it is clear that the ligand amoxicillin acts a tridentate ligand coordinating through β-lactam C=O group, -NH group at C-7 and C=O group at 8-position. Elemental analysis shows that the complex of Fe (II) ion with ligand amoxicillin has one chloride and two water molecules in addition to one amoxicillin ligand. Hence the structure of complex is six coordinated. On the other hand, complexes of Ni (II) and Cu (II) with amoxicillin have one chloride and one amoxicillin. So, structures of complexes are four coordinated as below:





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