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Research Article

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Synthesis, Characterization (I.R, Elemental analysis, Molar Conductivity), and Antibacterial Investigation of Complex produced by the reaction between Co (II) ion with mixed ligands of (Amoxicillin and Salen)

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Abstract

The complex of cobalt (II) was prepared with the mixed ligand (amoxicillin and salen), and the formed complex was characterized using infrared (I.R.) spectroscopy, elemental analysis of (C%, H%, N%, and M%), molar conductivity methods, and melting point to characterize the complex. The results indicated that the complex is relatively insoluble in aqueous solutions and has significant antibiotic activity against colon bacteria. They also showed that the mixed complex formed has an octahedral structure and has a good electrolytic nature.

Keywords: Amoxicillin- Salen, Co complex, Infrared spectra, antibiotic.

INTRODUCTION

Metal complexes of drugs have changed many of the toxicological, pharmacological, physical, and chemical properties of those drugs (Wu et al., 2003). Dosage forms and drug distribution are strongly tied to a medication's physicochemical properties, and these properties are influenced by the complex formation mechanism in one way or another, which may be beneficial or maybe the opposite. These properties include the complex's solubility, energy absorption, stability, and chemical reaction mechanics (Nogueira Silva et al., 2008; Eze et al., 2014). Some studies have shown that the dissolution of some compounds is faster and the bioavailability is greater than that of the physical mixture, and it has been found that the processing properties such as physical state, flow ability, stability, etc. for complexes are better than those of free drugs (Marcolino et al., 2011).

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Numerous metallic drug complexes were created to increase their potency, and after they had undergone a few successful clinical trials, they were analyzed and evaluated. (Mustapha et al.,2014) Amoxicillin is a β-lactam antibiotic that inhibits carboxypeptidase and transpeptidase enzymes, preventing the synthesis of peptidoglycan. Amoxicillin's bio-functional activity, like that of other penicillin, is based on the β-lactam ring (Hrioua et al., 2021). Blocking the activity of beta-lactamases, which are produced by certain bacteria, is currently the most advanced approach. These enzymes make the bacteria resistant to beta-lactam antibiotics. Metallic particles have gained a lot of attention due to their high surface-area-to-volume ratio and usefulness in biological applications. (Khatoon et al., 2017; Khatoon et al., 2018). Amoxicillin is a drug with a molecular weight of 419.45 gm.mole^{-1} and the chemical formula $C_{16}H_{19}N_3O_5S.3H_2O$. It is a crystalline powder that is an almost white or off-white powder that is only moderately soluble in alcohols like methanol ethanol and water (Martindale, 2009). Its UV maximum wavelength (λ_{max}) is 229,272 nm in 0.1N HCl and 230,274 nm in ethanol (O'Neil & Budavari, 2006). Amoxicillin complexes were synthesized with Ni (II), Cu (II), Zn (II), and Ag (I) ions and analyzed using C, H, and N elemental analysis as well as IR spectroscopy. The complexes exhibited enhanced biological activity for the drug (Imran et al., 2006).

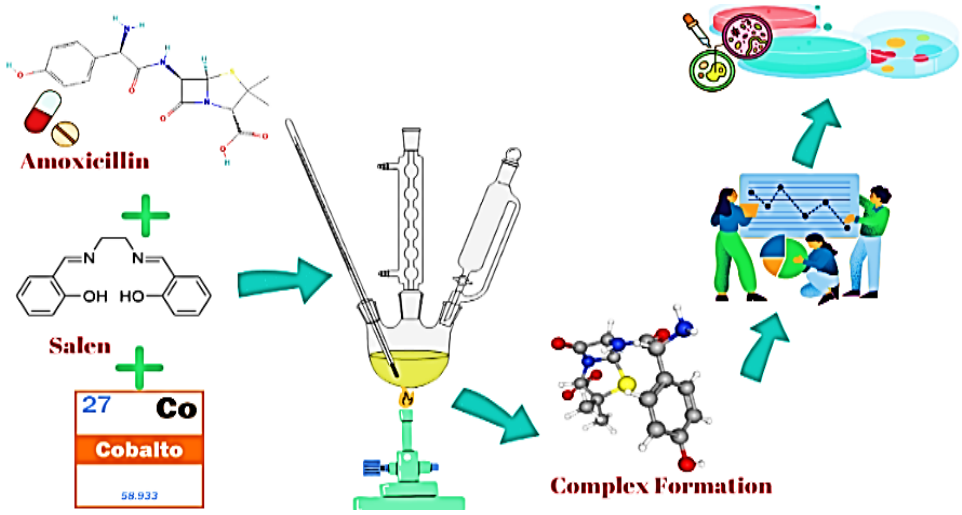

Fig (1). Graphical Abstract

In many kinds of literature, the efficacy of amoxicillin metallic complexes has been discussed (Abou-Hussein & Linert, 2014; Chohan et al., 2004). Studies conducted on the metal complexes of amoxicillin showed that it has great physiological and pharmacological importance, as the drug complexes are stronger than the drugs themselves (Anacona et al., 2002). The stability of complexes in aqueous and non-aqueous solutions has been investigated using a variety of physical and chemical approaches, such as spectroscopic methods (Ravichandran et al., 2014), potentiometric methods (Sonkamble, 2014), and methods of measuring conductivity (Rezayi et al,. 2011). In a previous study, researchers synthesized several complexes of amoxicillin with some transition metals. These complexes were analyzed using elemental analysis, IR, and mass spectra. The stability constant (K_f) of these chelates fell within the range of 10-7 to 10-14, and the molar ratio of the complexes was found to be Metal: Drug = 1:1, 1:2. (Zayed & Abdallah, 2005), In a recent study, mixed complexes of the β-lactam antibiotics ampicillin, amoxicillin, and cephalexin were prepared using solutions containing Co (II) and glycine anions (Gly). These complexes, named [Co Gly Ampicillin, Co Gly Amoxicillin, and Co Gly Cephalexin], were analyzed by pH-metric titration at 20 °C in an alkaline medium. (Alekseev & Samuilova, 2008). Salen is very important as a ligand as it easily binds to metal ions, forming complexes of various geometries due to the N_2 and O_2 donor

sites it contains. (Clarke & Storr, 2014; Atwood & Harvey, 2001). This study was aimed to synthesis, characterization (I.R, Elemental analysis, Molar Conductivity), and antibacterial investigation of complex produced by the reaction between Co (II) ion with mixed ligands of (Amoxicillin and Salen).

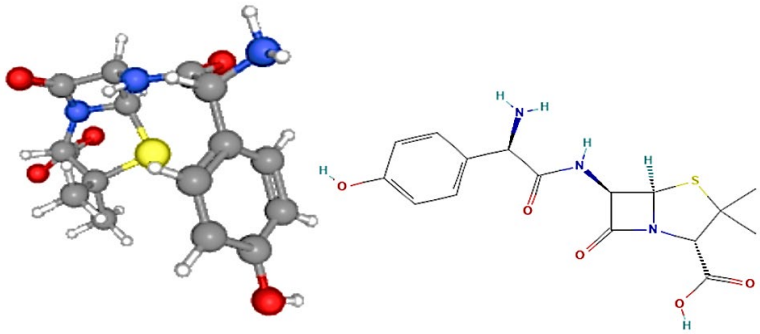

Fig 2: Chemical structure of amoxicillin (AMX)

MATERIALS AND METHODS

Amoxicillin-containing antibiotics were bought from commercial sources. 500 mg of amoxicillin capsules. Other chemicals used in this study are analytical-grade reagents and high purity from Fluka company. All buffer solutions from Sigma–Aldrich.

Synthesis of Salen ligand

To prepare Salen, 0.601 g (0.01 mol) of ethylene diamine and 2.44 g (0.02 mol) of salicylaldehyde were mixed in 50 ml of ethanol. The resulting mixture was re-condensed for 60 minutes. The red crystals formed were isolated by filtration. The crystals were then washed with ethanol and dried at room temperature in a dark place (Tsumaki, 1938).

Synthesis of the Metal-AMX Complexes

A solution of 25 ml methanol was used to dissolve 3 mmol of amoxicillin, followed by adding a solution containing 1 mmol of Co (II) metal chloride in 25 ml of methanol. The ligand was added in a 1:1:1 mole ratio, and the pH was adjusted to 8–9 by adding 1 M methanolic ammonia solution. The mixture was heated at 60–70 ºC with constant stirring for about 2 hours. It was then left overnight, filtered, and washed with residual anhydrous calcium chloride and methanol. The collected yield was 62.7% (Refat et al., 2014; Bufarwa & Abdel-Latif, 2022).

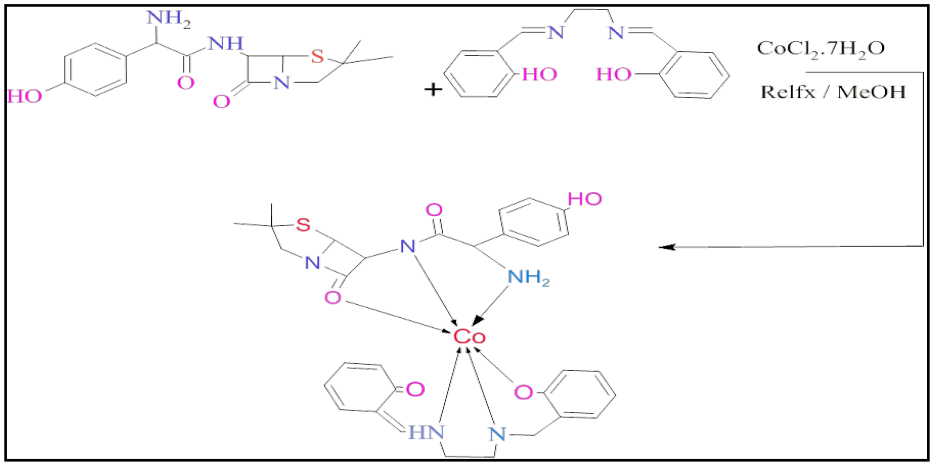

Fig 3: Preparation of [Co (AMX)(S)]

Molar Conductance

The conductivity of a 10^{-3} M complex solution in DMF was measured on a model HACH meter to determine its molar conductance.

Melting point measurements

To determine the melting points of the complex, we used the Stuart Scientific electrothermal melting point apparatus with glass capillary tubes in Celsius degrees.

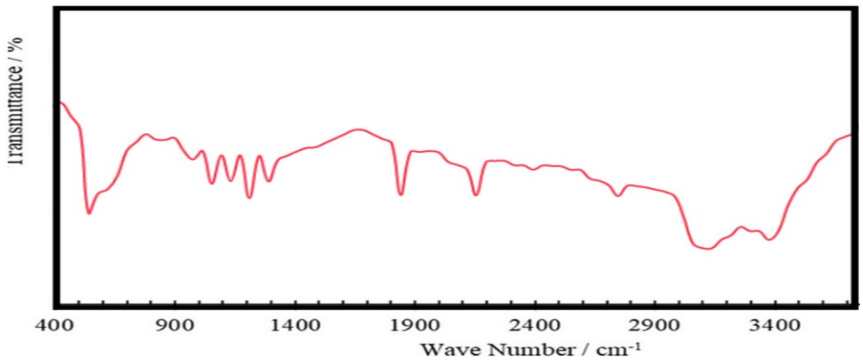

Fig 4: FT-IR of [Co(AMX)(S)]

RESULTS AND DISCUSSION

Elemental analysis of the solid complex was conducted to compare the calculated and found values for carbon, hydrogen, and nitrogen. Table 1 shows the obtained elemental analysis values. Conductivity measurement of the prepared complex also revealed that chloride ions are present outside the coordination sphere.

Table 1: The proposed formula, color, melting point, conductivity, and elemental analysis of the complex

Compound	M. wt. (g/mol)	Yield %	Color	Conductivity µS	M.P	Anal. Calc. (Found)%			
						N	H	C	Co
[Co (AMX)(S)] $C_{31}H_{37}CoN_5O_5S$	650.65	62.7	Red	121	248	54.75 (57.22)	5.38 (5.73)	9.88 (10.76)	8.52 (9.06)

FT-IR spectra: Studying the infrared spectrum is very important to determine the status of the chelation process as well as the location of coordination. Figure 3 shows the FT-IR spectra of the mixed complex of amoxicillin (AMX) and salen (S) with the cobalt (II) ion. At 1400cm^{-1}, the benzene ring's stretching vibration band v(C=C) is exhibited (Hrioua *et al*., 2021). While the bands of the hydroxyl and ammonium groups still appear unchanged, as they have not undergone any displacement because they did not enter as ligands in the formation of the complex (Gasheva *et al*., 1984). The stretching and vibration bands between metal ions and oxygen of the carbonyl group are responsible for the occurrence of bands at 500-600 cm^{-1}. Similarly, the vibration bands between amino groups and metal ions are classified as v(M-N) stretching bands between 400 and 500 cm^{-1} (Reiss *et al*., 2015). The distinctive band at about 3300 cm-1 indicates the presence of water molecules outside the coordination sphere in AMX complexes.

Antibacterial activity

The disk diffusion method has been used to examine the antibacterial effectiveness of the cobalt complexes (AMX.S) against ***E. coli*** (Bonev *et al*., 2008). The type of the metal ion and the chelate stability are likely to be blamed for the antibacterial action of AMX-salen complexes (Hrioua *et al*., 2021). Antibiotics made of metal complexes are very effective against resistant strains. Due to their potential to affect drug-induced metallo-enzyme inhibition, cobalt ions remain an area of interest in bioinorganic research for their impact on pathogens, influenza, cancers, and inflammation (Saleh *et al*., 2023).

Table 2: Inhibitor zone of antibacterial by different concentrations of complex

Concentration µg/L	Inhibitor zone diameter (in mm)	
	AMX	[Co(AMX)(S)]
10	-	10.76
25	-	15.68
50	12.4	19.43

CONCLUSION

The mixed amoxicillin ligands were studied in the form of capsules and the salen ligand with the cobalt binary ion, and some properties were studied to confirm the formation of a complex of mixed ligands of this type. The results showed that the complex formed has an octahedral form, and is an electrolyte in nature because the two chloride atoms are outside the coordination sphere of the complex, and are stable under normal conditions. It was observed that as the concentration of the complex increased, its effectiveness against E. coli bacteria increased.

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Author contributions: Contribution is equal between authors.

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