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Gentamicin sulfate based metal complexes: Synthesis, characterization and antimicrobial activity

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The growing resistance of microorganisms to conventional antibiotics necessitates the development of novel therapeutic strategies. Metal complexation has emerged as a promising approach to enhance the efficacy of existing drugs. This study aims to synthesize and characterize novel metal complexes derived from gentamicin sulfate and evaluate their potential for improved antimicrobial activity. Gentamicin sulfate has been reacted with various metal salts to form novel complexes. The synthesized compounds have been characterized using Fourier-transform infrared (FTIR) spectroscopy, melting point determination, and solubility tests. Their antimicrobial efficacy has been assessed *in vitro* against a panel of nine pathogenic bacterial and four fungal strains. Several complexes have demonstrated significantly enhanced antibacterial and antifungal activity compared to standard gentamicin. The strontium and cobalt complexes exhibit superior antibacterial activity against *Staphylococcus aureus* and *Salmonella abony*, respectively. The nickel, zinc, iron, and magnesium complexes show increased antifungal efficacy against *Aspergillus fumigatus*, while the zinc, iron, and magnesium complexes are also more potent against *Aspergillus niger*. The findings confirm that coordination with metal ions can significantly potentiate the antimicrobial spectrum and effectiveness of gentamicin sulfate. These gentamicin-metal complexes represent a highly promising avenue for combating resistant microorganisms and warrant further investigation as alternative antimicrobial agents.

Keywords: Gentamicin sulfate, Metal complexes, Synthesis, Antimicrobial activity, Differential scanning calorimetery (DSC)

Like many other organisms, bacteria and fungi exhibit a complex relationship with metals that is marked by a dual nature of attraction and aversion. Although a particular metal might be necessary for their survival, in some situations and at high concentrations, it can also become toxic. The antimicrobial properties of metal ions have long been recognized, and with the growing concern about antimicrobial resistance, there has been a greater emphasis on them. Consequently, metal ions, nanoparticles, and metal complexes that demonstrate antimicrobial efficacy have been included in the search for novel antimicrobial agents, commonly referred to as metalloantibiotics[1]. The integration of innovative medications with cutting-edge technology presents a significant advantage, creating opportunities for novel approaches to treat infectious disease. Development of antimicrobial drugs marks a substantial achievement in this area and serves as a remarkable enhancement to public health. As they not only lessen suffering but also herald a new era in health and wellness, the ground-breaking discoveries and advancements demonstrate the important collaboration between modern science and our pursuit of a healthier, thriving society[2]. Antimicrobials, including antibiotics, antivirals, antifungals, antiseptics, as well as antiparasitic are medicinal substances used to treat or prevent infections. In contrast, disinfectants are antimicrobial substances specifically used on non-living surfaces. These agents focus on essential cellular metabolic processes, potentially resulting in the eradication or suppression the growth of microorganisms. This could involve altering the activity of cellular enzymes, influencing cellular structures like the cell wall and membranes, or interfering with the synthesis of biological macromolecules[3,4,5].

The implication of ions of metals in biological systems has been recognized for quite some time. Their unique properties, such as redox activity, the

List of Abbreviations: DNA: Deoxyribonucleic acid; RNA: Ribonucleic Acid; FTIR: Fourier Transform Infrared Spectroscopy; DSC: Differential Scanning Calorimetry.

presence of coordination sites, and their reactivity with organic compounds, distinguish them from other elements. The development of cancer is one of the many health issues that have been linked to increased metal ion concentrations. Because of their special qualities, coordination metal complexes are especially fascinating and alluring as possible therapeutic candidates in the field of medicinal chemistry[6,7].

Our goal is to enhance the discovery process by creating metal complexes from common antibiotics, effectively converting them into promising new antibiotics. Metals are recognized for their ability to boost drug efficacy, serving as effective chelating agents, stabilizing compounds, and interacting with biomolecules like DNA, RNA, proteins, receptors, and lipids[8]. The objective of this research was to synthesize metal-gentamicin complexes using gentamicin sulfate (Fig. 1) with various metal salts, followed by detailed characterization and evaluation of their antimicrobial activities.

Methodology

Chemical and reagents

Gentamicin sulfate (Potency 99.11%) was collected as a kind gift of Eskayef Pharmaceuticals Ltd., Dhaka, Bangladesh. Manganese(II) sulfate ($MnSO_4.H_2O$), strontium chloride hexahydrate ($SrCl_2.6H_2O$), cobalt(II) nitrate hexahydrate $Co(NO_3)_2.6H_2O$, calcium carbonate ($CaCO_3$), nickel(II) sulfate ($NiSO_4.6H_2O$), magnesium carbonate ($MgCO_3$), barium sulfate ($BaSO_4$), copper(II) sulfate ($CuSO_4.5H_2O$), zinc sulfate monohydrate ($ZnSO_4.H_2O$), iron(II) sulfate ($FeSO_4.7H_2O$), magnesium sulfate ($MgSO_4.7H_2O$), lead (II) nitrate $Pb(NO_3)_2$, DMSO were of analytical grade and procured from Merck, Germany. The analytical solutions were prepared using double-distilled water.

Instruments

Melting point apparatus (Model: Melting point B-545, Buchi, Germany), Fume hood (BFSD-201, Biolab Scientific, India), FT-IR (IRTracer-100 type 8400S spectrometer, Shimadzu, Japan), Automatic Digital Autoclave (Model-LS-50HD, Manufacture in China & Origin Taisite, USA), Laminar Air Flow bench (Wincom Company Ltd., China), Heat control stirring water bath (Model- Unitronic OR, JP Selecta Company Spain), Hand round automatic autoclave steam sterilizer (LS-50HD, NANBEI Instrument ltd, China) were used in the study.

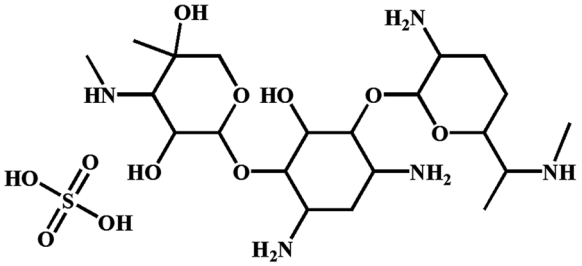

Fig. 1 — Structure of gentamicin sulfate

Drug-metal interactions

Gentamicin sulfate and twelve different metal solutions were prepared at the concentration of 1 mMol in a mixture of methanol (90%) and water (10%). Gentamicin sulfate was prepared by dissolving 162.75 mg of gentamicin sulfate API powder in 500 mL of methanol (90%) and water (10%) to get the solution of 1 mMol, and 1 mMol 25 mL of salt solution was prepared by using 4.225 mg, 6.6655 mg, 7.27575 mg, 2.4 mg, 6.57125 mg, 2.108 mg, 5.8345 mg, 6.24225 mg, 4.48625 mg and 6.95025 mg of manganese(II) sulfate ($MnSO_4.H_2O$), strontium chloride hexahydrate ($SrCl_2.6H_2O$), cobalt(II) nitrate hexahydrate $Co(NO_3)_2.6H_2O$, calcium carbonate ($CaCO_3$), nickel(II) sulfate ($NiSO_4.6H_2O$), magnesium carbonate ($MgCO_3$), barium sulfate ($BaSO_4$), copper(II) sulfate ($CuSO_4.5H_2O$), zinc sulfate monohydrate ($ZnSO_4.H_2O$), iron(II) sulfate ($FeSO_4.7H_2O$), magnesium sulfate ($MgSO_4.7H_2O$) and lead (II) nitrate $Pb(NO_3)_2$ respectively. Drug solution and each salt solution was mixed individually at the molar ratio of 1:1 *i.e.*, 25 mL of drug solution and 25 mL of each salt solution was mixed separately[9]. All the mixture solutions prepared were filtered by using 0.45 μm membrane filter. After that, the filtrates were heated for 6.5 hours at the temperature between 70 and 75°C in a water bath while being stirred periodically. Then the mixtures were kept overnight in an oven at 100°C for drying to get the complexes[10,11].

Characterization

The formed complexes were characterized by studying the melting point, Fourier Transform Infrared (FT-IR) spectra and DSC thermograms. For FT-IR analysis disc were prepared by using potassium bromide in conjunction with a metal-antibiotic complex in a 1:1 ratio.

Antimicrobial susceptibility test

Culture used: Antimicrobial testing was conducted with culture at the laboratory of the Department of Pharmacy of the International Islamic University in

Chittagong, Bangladesh. The bacterial strains *Staphylococcus aureus, Bacillus subtilis, Bacillus tropicus, Bacillus cereus, Pseudomonas aeruginosa, Salmonella typhi, Salmonella abony, E. coli and Klebsiella pneumonia, and fungal species Penicillium species, Candida albicans, Aspergillus fumigatus,* and *Aspergillus niger* were used in the study.

The antimicrobial effectiveness of the drug-metal complexes was evaluated using the disc diffusion method[12-14]. After preparing the nutrient agar and potato dextrose agar (PDA) media, they were autoclaved for 21 minutes at 121°C at 1 atmospheric pressure, and then cooled to 45°C. The media were then transferred into sterile petri dishes and allowed to solidify the media. A sterile swab was used to inoculate on the solidified media of each plate with the appropriate microbial suspension. A control disc and discs with the corresponding complexes were placed on the solidified media followed by incubation at 35°C for 24 h. The diameters of the zones of inhibition surrounding the discs were measured and recorded in millimeters after the incubation period. The incubation period for antibacterial susceptibility testing (AST) ranged from 18 to 24 hours for most bacterial species, while the typical duration for antifungal susceptibility testing was between 5 and 7 days.

Results and Discussion

The synthesized complexes were analyzed through melting point determination, FT-IR spectrophotometry and DSC[15]. The physical properties along with the percentage yield and melting point (MP) of different salts, gentamicin sulfate (precursor drug) and its metal complexes are shown in Table 1 and Table 2. The melting point (MP) of the ligand (gentamicin sulfate) was found to be different from those of the corresponding complexes, indicating the formation of a new complex molecule.

Characterization of the complexes by FT-IR

Gentamicin sulfate and its corresponding complexes were found to have FT-IR spectra that ranges between 4000 cm^{-1} and 400 cm^{-1}. A comparison with the spectra

Table 1 — Physical characteristics of gentamicin sulfate and different metal salts

Sample	MW	Appearance/color	Solubility	Melting point (°C)
Gentamicin sulfate	477.6	White to buff colored, odorless, and hygroscopic powder.	Soluble in water DMSO and ethanol	220
Manganese (II) sulfate monohydrate- $MnSO_4.H_2O$	169	Pale pink	Water	710
Strontium chloride hexahydrate- $SrCl_2.6H_2O$	266.62	White crystals	Water and alcohol	115
Cobalt (II) nitrate hexahydrate, $Co(NO_3)_2.6H_2O$	291.03	Red crystalline (hexahydrate)	Water and alcohol	55
Calcium carbonate- $CaCO_3$	100	White powder	Methanol	825
Nickel (II) sulfate hexahydrate- $NiSO_4.6H_2O$	262.85	Green solid	Water	53
Magnesium carbonate- $MgCO_3$	84.32	White powder	Water	990
Barium sulfate -$BaSO_4$	233.38	white, odorless, and small crystalline solid	Water	1580
Copper (II) sulfate pentahydrate- $CuSO_4.5H_2O$	249.69	blue, crystalline solid	Water	330
Zinc sulfate monohydrate- $ZnSO_4.H_2O$	179.45	White powder	Water	238
Iron (II) sulfate heptahydrate- $FeSO_4.7H_2O$	278.01	Green crystals	Water	64
Magnesium sulfate heptahydrate - $MgSO_4.7H_2O$	246.48	Colorless to white with pale shades of pink and green crystals	Water	1124
Lead (II) nitrate-$Pb(NO_3)_2$	331.2	Colorless to white powder	Water	470

Table 2 — Physical characteristics of metal complexes of gentamicin sulfate with different salts

Sample	Appearance/ colour	Solubility	Yield (%)	Melting point (°C)
Manganese- gentamicin complex	Pale pink	Water	75	50.2
Strontium- gentamicin complex	Brown	Water and methanol	81	204.3
Cobalt- gentamicin complex	Reddish	Water and methanol	80	394.5
Calcium - gentamicin complex	Whitish powder	Methanol	76	222.6
Nickel- gentamicin complex	Green solid	Methanol	85	246.2
Magnesium-gentamicin complex	White powder	Methanol	82	*
Barium-gentamicin complex	yellowish powder	Methanol and DMSO	85	*
Copper (II) - gentamicin complex	Blue powder	Water	78	*
Zinc - gentamicin complex	White powder	Water	82	*
Iron (II) - gentamicin complex	Green powder	Water	80	199.5
Magnesium - gentamicin complex	Black	Water and methanol	85	*
Lead - gentamicin complex	White powder	Water	90	*

* >400°C

of the parent compound, gentamicin sulfate, is described. The antibiotic's and its metal complexes' overlaid FT-IR spectra are shown in Fig. 2. The following descriptions indicate the key bands, especially those that are influenced by coordination bonding. Gentamicin sulfate showed 2879.72 cm^{-1} (alkane group), 2079.26 cm^{-1} (week alkyne group), at fingerprint region a prominent peak at 1031.92 cm^{-1} (amine**)** with others (Fig. 2A).

Mn-gentamicin complex showed 2885.1 (alkane group), at fingerprint region 2 prominent peak 1745.58 cm^{-1} (ester group), 169.46 cm^{-1} with others. Co-gentamicin complex showed 2879.72 cm^{-1} (alkane group), at fingerprint region two prominent peaks at 1365.60 cm^{-1} and 1037.70 cm^{-1} (alcohol, ether, ester, carboxylic acid, anhydride groups) with others. Gentamicin complex showed many prominent peaks at fingerprint region at 1714.72 cm^{-1} (carboxylic acid group), 1577.77 cm^{-1}, 1665.60 cm^{-1} (amide group) with others. Ni-gentamicin complex displayed 2978.09 cm^{-1} (alkane group) and at fingerprint region three prominent peak at 1741.51 cm^{-1} (ester group), 1373.32 cm^{-1} (anhydride group), 1072.42 cm^{-1} (alcohol, ether, ester, carboxylic acid, anhydride groups) among others (Fig. 2B).

Mg-gentamicin complex showed peaks at 2357.01 cm^{-1}, 2316.51 cm^{-1}, at fingerprint region two prominent peaks at 1743.65 cm^{-1} (ester group), 1371.39 cm^{-1} (nitro group) among others. Ba-gentamicin complex yielded peaks at 3001.24 cm^{-1} (alkene group), 2929.87 cm^{-1}, 2853.51 cm^{-1} (alkane groups), at fingerprint region three prominent peaks at 1712.79 cm^{-1} (ketone group), 1361.74 cm^{-1}, 1220.94 cm^{-1} (amine group) among others. Cu-gentamicin complex produced peaks at 2879.72 cm^{-1} (alkane group), at fingerprint region two prominent peaks at 1749.44 cm^{-1}, 1371.39 cm^{-1} (ester group) among others. Zn-gentamicin complex gave peaks at 3257.77 cm^{-1} (alkene group), 3024.38 cm^{-1}, 2821.86 cm^{-1} (alkane group), 2310.72 cm^{-1}, at fingerprint region two prominent peaks at 1741.72 cm^{-1} (ester group), 1373.32 cm^{-1} among others (Fig. 2C). Fe-gentamicin complex showed peaks at fingerprint region at 1757.15 cm^{-1} (anhydride group), 1271.09 cm^{-1} among others. Mg-gentamicin complex showed peaks at

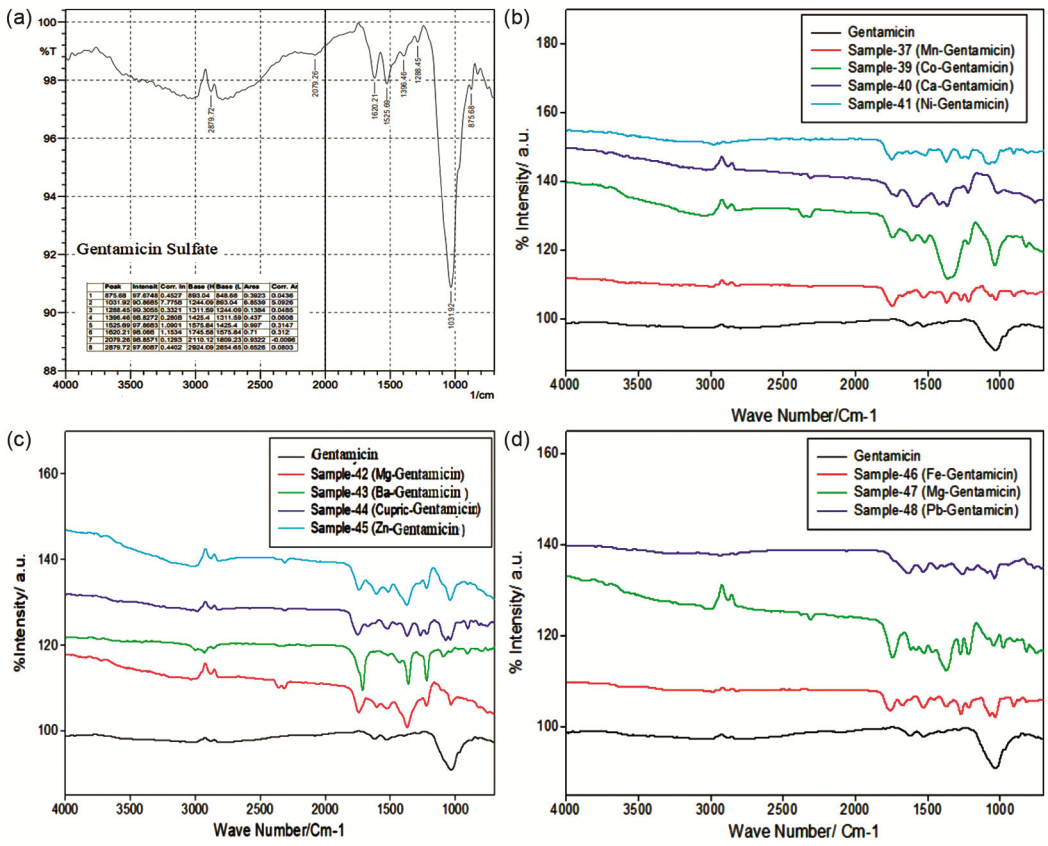

Fig. 2 — (A) FT-IR spectra of gentamicin sulfate and overlaying FT-IR spectra of gentamicin sulfate and complexes, (B) Gentamicin sulfate and complexes of Mn, Co, Ca and Ni metals, (C) Gentamicin sulfate and complexes of Mg, Ba, Cu (II) and Zn metals, (D) Gentamicin sulfate and complexes of Fe (II), Mg and Pb metals

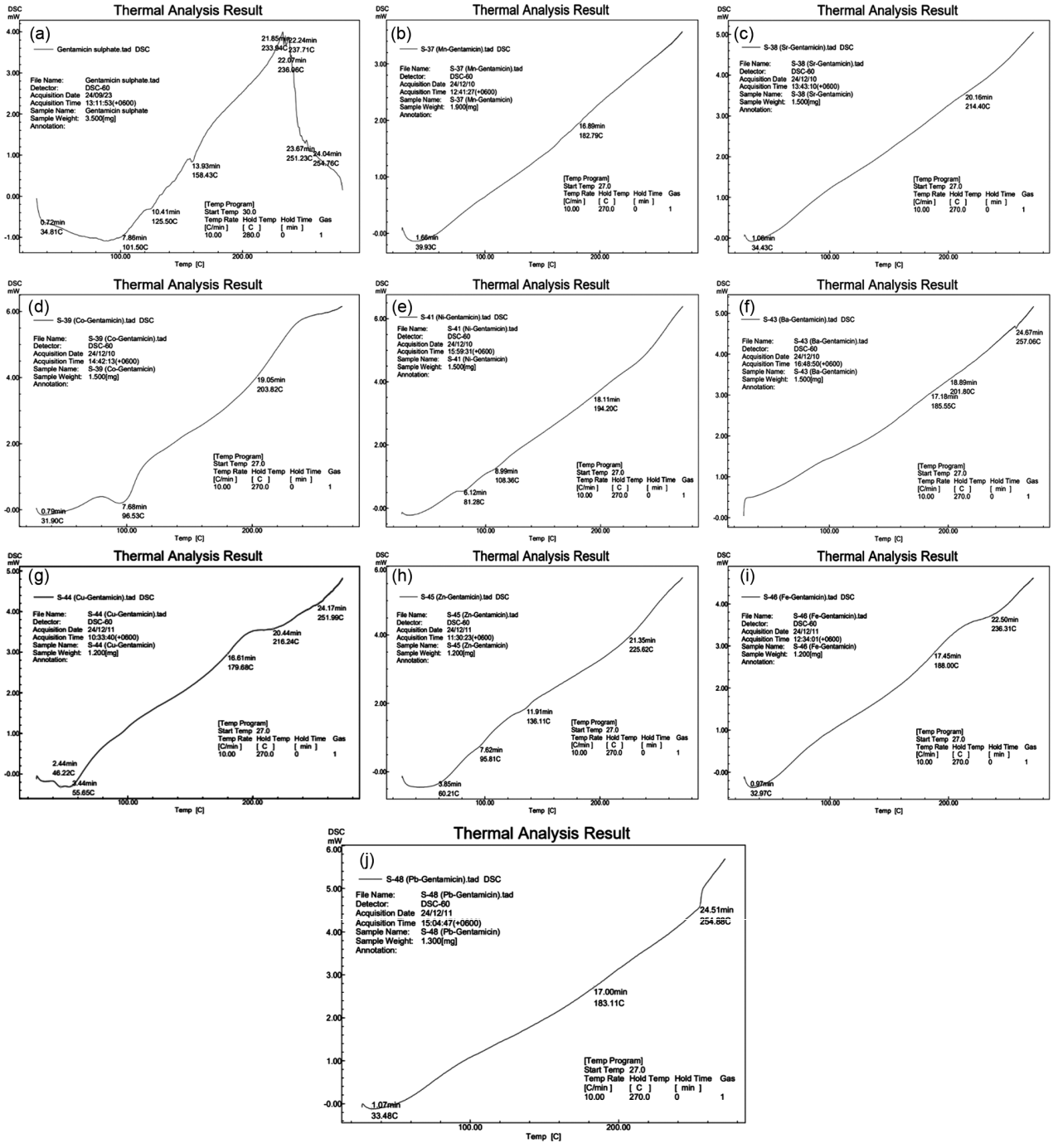

Fig. 3 — DSC thermograms of gentamicin sulfate and its complexes: (A) pure gentamicin sulfate, (B) Mn-gentamicin complex, (C) Sr-gentamicin complex, (D) Co-gentamicin complex, (E) Ni-gentamicin complex, (F) Ba-gentamicin complex, (G) Cu-gentamicin complex, (H) Zn-gentamicin complex, (I) Fe-gentamicin complex, (J) Mg-gentamicin complex, (K) Pb-gentamicin complex

2310.72 cm^{-1}, at fingerprint region at 1743.65 cm^{-1} (ester group) and 1373.32 cm^{-1} (nitro group) among others. Pb-gentamicin complex showed peaks at 2937.59 cm^{-1}, at fingerprint region at 1635.64 cm^{-1} (amide group), 1529.55 cm^{-1}, 1259.52 cm^{-1}, 1037.70 cm^{-1} (amine group) among others (Fig. 2D).

DSC thermograms of gentamicin sulfate and its complexes

Based on the DSC thermograms of gentamicin sulfate and its metal complexes (Fig. 3), significant alterations in thermal behavior confirmed the successful formation of new coordination compounds. Gentamicin sulfate

exhibited a sharp endothermic peak at ~220°C, corresponding to its melting/decomposition point. In contrast, the metal complexes displayed distinct thermal profiles: the Sr-complex showed a shifted endotherm at ~204°C, the Co-complex exhibited exceptional stability with a high-temperature transition at ~395°C, and the Ni-complex melts at ~246°C. Complexes with Mg, Ba, Cu, Zn, and Pb demonstrated no thermal events below 400°C, indicating superior thermal robustness. Minor endothermic peaks below 200°C in some complexes (*e.g.*, Ca, Ni) suggested dehydration of coordinated water molecules or stepwise decomposition. These shifts in melting/decomposition temperatures reflected structural reorganization due to metal-ligand coordination, aligning with FTIR evidence of bond formation.

Antimicrobial studies

Table 3 and Table 4 show the antibacterial and antifungal activities of the metal compounds, respectively. Gentamicin and its metal complexes were found to be very active against some of the

Table 3 — Antibacterial activity of some drug-metal complexes of gentamicin sulfate at 30 µg/disc

Complex/Drug	Zone of Inhibition (mm)							
	Gram positive bacteria				Gram negative bacteria			
	S. aureus	*B. subtilis*	*B. cereus*	*Ps. aeruginosa*	*S. typhi*	*S. abony*	*E. coli*	*K. pneumoniae*
Manganese-gentamicin complex	24.33±0.88	19.33±0.67	19.33±0.67	0	22.33±0.88	23.33±0.88	22.67±0.88	22±0.58
Strontium-gentamicin complex	23.67±1.20	0	0	25.33±1.20	23.67±1.20	31.67±26.67	0	19.67±0.88
Cobalt-gentamicin complex	30.83±0.88	26.67±0.88	19.33±0.88	0	26±1.15	26±1.15	26±1.15	26±1.15
Calcium-gentamicin complex	18.33±0.88	0	0	26.33±0.88	25±0.58	0	0	19.33±0.67
Nickel-gentamicin complex	24.67±0.88	0	0	0	22.33±0.88	0	0	0
Magnesium-gentamicin complex	0	0	0	28.33±0.88	20.33±0.67	0	0	0
Barium-gentamicin complex	28±1	0	0	0	26.67±0.88	0	0	17.67±0.67
Copper (II)-gentamicin complex	0	20±0.58	0	18±0.58	26±1	22±0.58	0	18.67±0.88
Zinc-gentamicin complex	28±0.58	23.33±0.88	26.33±0.88	31±0.11	0	6	24.67±1.20	24.67±0.88
Iron (II)-gentamicin complex	18.33±0.88	0	0	23.67±0.88	0	0	0	21±0.58
Magnesium-gentamicin complex	18.67±0.88	0	16.67±0.88	21.67±0.88	0	0	0	20±0.58
Lead-gentamicin complex	0	0	0	16.67±1.20	0	0	0	18±0.58
Gentamicin (30 µg/disc)	30.33±0.88	29.67±0.88	29.67±0.33	29±0.58	30±0.58	30.67±0.33	29.33±1.20	32.33±0.88

Values are presented as the Mean ± SEM (n=3)

Table 4 — Antifungal activity of some drug-metal complexes of gentamicin sulfate

Complex/Drug (50 µg/disc)	Zone of Inhibition (mm)			
	Penicillium species	*C. albicans*	*A. fumigatus*	*A. niger*
Manganese-gentamicin complex	30.33±0.33	20±0.58	27.33±0.19	0
Strontium-gentamicin complex	29±0.58	0	27±0.11	15.67±0.88
Cobalt-gentamicin complex	27.33±0.33	0	27±0.11	28±0.58
Calcium-gentamicin complex	17.33±0.33	0	29±0.37	16.33±0.88
Nickel-gentamicin complex	27±0.58	0	30±0.11	20.33±0.33
Magnesium-gentamicin complex	17.67±0.88	20.33±0.67	14±0.11	0
Barium-gentamicin complex	29.67±0.88	0	0	16±1.15
Copper (II)-gentamicin complex	0	0	0	19±0.58
Zinc-gentamicin complex	31±0.58	0	31±0.18	30.33±0.33
Iron (II)-gentamicin complex	30±0.58	0	30±0.11	29.33±0.88
Magnesium-gentamicin complex	27.67±1.20	0	30.33±0.13	30.33±0.88
Lead-gentamicin complex	16.67±0.88	19.67±1.21	13.33±0.13	0
Ketoconazole (200 µg/disc)	30.33±0.88	30±0.58	29.33±0.19	28.67±1.21

Values are showed as the Mean ± SEM (n=3)

bacterial species assayed with inhibition zones higher than the standard one. Sr-gentamicin complex, Co-gentamicin and Zn-gentamicin complexes showed significant effects with zone of inhibition of 31.67 mm, 30.83 mm and 31 mm against *S. abony*, *St. aureus* and *Ps. Aeruginosa*, respectively. Other complexes exhibited moderate inhibitory effects. But some of the complexes were not active against both Gram-positive and Gram-negative bacteria.

The complexes were also found to be active against fungi and showed zone of inhibition from 17-31 mm in diameter. Co-gentamicin complex showed 28 mm zone of inhibition against *A. niger*, Zn-gentamicin exhibited 31 mm and 30 mm zone of inhibition against *Penicillium* species and *A. niger*, respectively. Fe-gentamicin complex showed 30 mm and 29 mm zone of inhibition against *Penicillium* species and *A. niger*, respectively. Mg-gentamicin complex produced 30 mm and 30 mm against *A. fumigatus* and *A. niger,* respectively. Besides, most of them were inactive against *C. albicans.* Because generally *Candida* species are not susceptible to the traditional aminoglycosides except at high concentrations[16].

The FTIR spectra of gentamicin sulfate and metal complexes exhibited strong broad bands ranging from 2879 cm^{-1} to 2079 cm^{-1} due to the presence of coordinated water molecules, the hydroxyl group, and the primary and secondary amine stretching vibrations. All the complexes showed a shift of the C-O stretching bands to a lower wavenumber compared to the IR spectrum of gentamicin sulfate, indicating the coordination of metal ions through deprotonated oxygen from the hydroxyl group. Gentamicin sulfate exhibited a band at 1620 cm^{-1} corresponding to the N-H bending. For every metal complex, this band was moved to a higher wave number, demonstrating the amine group's involvement in coordinating with the metal ions to form metal complexes[17]. The presence of coordinated water molecule in the metal complexes was evidenced with the bands in the region of 746 cm^{-1} to 755 cm^{-1} corresponding to the rocking vibration of the coordinated water molecules[18,19]. A strong intensity of the S=O stretching bands in the region of 1045 cm^{-1} to 1051 cm^{-1} and the medium-to-weak bands of SO_2 bending at 615 cm^{-1} were attributed to the presence of sulfuric acid molecules in the metal complexes, which was identical to gentamicin sulfate[20,21]. The DSC thermograms provided decisive evidence of new compound formation through significant alterations in thermal behavior compared to gentamicin sulfate. The variable thermal stabilities reflect differences in metal-ligand bond strengths and structural arrangements, which correlate with the observed antimicrobial enhancements. Notably, complexes with higher thermal stability (*e.g*., Co, Zn) demonstrated superior bioactivity, suggesting thermal robustness may indicate stronger metal coordination and enhanced drug delivery potential[22,23].

According to How *et al*. (2021), the interaction of gentamicin sulfate with transition metals is a promising approach to increasing antibiotic efficacy against resistant pathogens. Their findings revealed that, while gentamicin's fundamental antibacterial spectrum remained intact, certain metal complexes exhibited significantly increased activity. The copper(II) complex, in particular, showed a broad-spectrum increase in bactericidal efficacy against all tested Gram-positive and Gram-negative bacteria, which the authors attributed to increased lipophilicity, which promotes membrane penetration and disrupts microbial enzyme activity. Furthermore, the chromium(III) complex exhibited selective and enhanced bactericidal activity, particularly against Streptococcus pyogenes and Klebsiella pneumoniae, indicating that metal ion selection can influence antibiotic selectivity and potency. Complexation with zinc(II) and nickel(II) ions, on the other hand, resulted in similar or even decreased antimicrobial activity, demonstrating that the enhancement is dependent on the metal used and is not a universal result of complexation. These findings highlight the potential of specific gentamicin-metal complexes, particularly those involving copper and chromium, as effective antimicrobial resistance strategies, requiring further investigation into their mechanisms of action and therapeutic development potential[24]. Gentamicin, the parent drug, is effective against a wide range of bacterial infections, especially Gram-negative bacteria. Though gentamicin is not commonly used as an antifungal agent (is not a standard antifungal medication), some derivatives and formulations, such as gentamicin B1, have shown antifungal activity against plant pathogens such as *Fusarium, Aspergillus, Microsporum*, and *Cryptococcus* species[25]. That is why the parent drug's activity against fungi was not tested.

Conclusion

This research illustrates that the coordination of metals can significantly improve the antimicrobial

efficacy of gentamicin sulfate. Specific complexes, especially those involving strontium, cobalt, zinc, iron, nickel, and magnesium, showed enhanced antibacterial or antifungal properties, indicating that the choice of metal ions can influence the performance of the drug. These results underscore the potential of metalloantibiotics as a viable strategy to rejuvenate current antibiotics and broaden their therapeutic range against different pathogens. The successful formation of gentamicin–metal complexes was validated through FTIR, DSC, and thermal analyses, which confirmed structural modifications consistent with metal–ligand coordination. Future investigations should be directed toward mechanistic elucidation, assessment of *in vivo* efficacy, and comprehensive toxicity profiling, whereby these complexes may subsequently be advanced toward clinical applications against drug-resistant infections.

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Author contributions

Conception and design, or design of the research; or the acquisition, analysis, or interpretation of data: MAS, MZS, MAR. Drafting the manuscript or revising it critically for important intellectual content: MAS, MZS, MMM, MAR. Final approval of the version to be published: MAR. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: MAR.

Conflicts of Interest

The authors declare no conflict of interest.

Ethical approval

Not Applicable.

Data availability statement

We confirm that data supporting the study's findings will be shared upon reasonable request.

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