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Designing and Synthesis of Some Transition Metal Complexes Derived from Schiff Bases for Anti-Bacterial Activity

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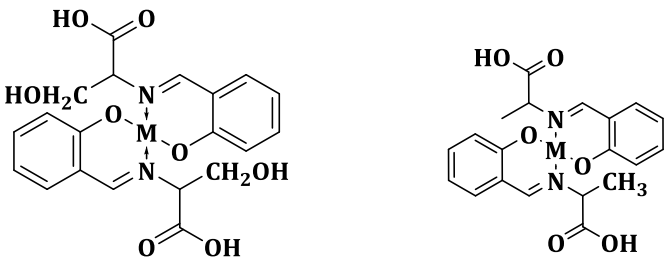
ABSTRACT

Condensation of salicylaldehyde with D-alanine and L-serine was carried out to obtain Schiff bases and treated with various metal chlorides to form metal complex derivatives. The metals chlorides used for the preparation of metal complexes derivatives were copper, cobalt, iron, manganese, and zinc, respectively and characterized by elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR, and LC-MS. Hence, a total of ten metal complexes derivatives was synthesized and screened for some tested bacterium organisms like *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa* and *Salmonella typhi*. The synthesized metal complexes derivatives showed significant activity compared with Schiff base and ciprofloxacin used as standard. The synthesized metal complexes derivatives showed a good effect on the selected antibacterial strains, indicating that the activity was depending on the structure of the compound. Amongst the selected five metals, cobalt showed the good antibacterial activity followed by other metals in dimethyl sulfoxide as a solvent. The Schiff bases synthesized also showed significant antibacterial activity.

GRAPHICAL ABSTRACT



M = Cu , Co, Fe, Zn, Mn

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Introduction

Metals are essential cellular components selected by nature to function in several indispensable biochemical processes for living organisms [1]. Formation of positive charged particles, which are freely soluble within biological fluids, is an important feature of metal ions that lose electrons substantially. This ion of metal is charged on for interacting and binding with biological molecules [2]. Electrons shuttling and oxygen carrying tasks are conducted by metals in the body. These metals are preferred due to a wide spectrum of anti-microbial activity, non-interference with the host defence mechanism [3]. Transition metal offers certain advantages such as DNA-binding agents. Hence, the research focused on the transition metal coordination compounds concerning with pharmacological activities such as "Zn(II), Cu(II), Mn(II), Fe(II) and, Co(II)" in the periodic table [4]. Additionally, within intracellular nature of living organisms are micro or macro essential components entailing these metals? Antibiotics, anti-bacterial [5], anti-viral [6], anti-parasitics [7], anti-HIV [8], anti-diabetes [9], radio-sensitizing agents [10] and anti-cancer [11] compounds are some of the mediates that are encouraged through the new metallo complex drugs and clinical use of metal complexes. Therefore, here in this study, we have decided to construct the metal complex ligands based on Schiff base synthesized from Salicylaldehyde and alanine and serine moieties using deficient-oxygen linkage with metal chlorides, which may circumvent the antibacterial drug resistance.

In the current research, metal complexes of Cu (II), Co (II), Zn (II), Fe (II) and Mn (II) bases have been synthesized from Schiff bases which were obtained from condensation of Salicylaldehyde with D-alanine & L-serine. These synthesized complexes of metal derivatives were further classified and evaluated by FT-IR, ^{1}H NMR and ^{13}C NMR analysis. Further, their anti-bacterial activities were screened with clinically important gram positive and gram-negative organisms.

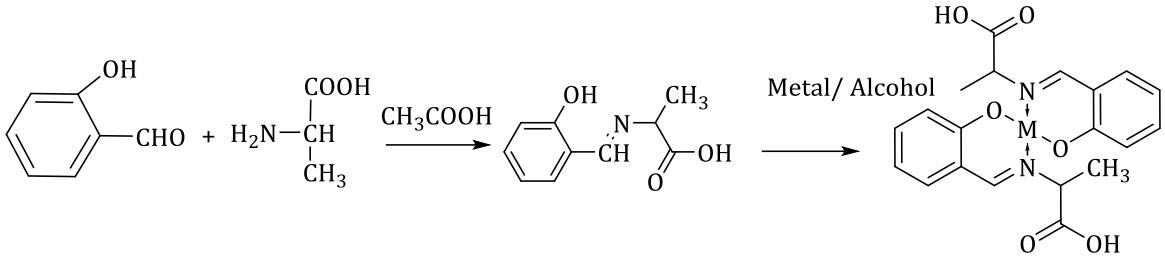
Material and methods

The compositions of carbon, hydrogen, and nitrogen contents were determined by microanalyses (Perkin Elmer elemental analyzer, USA) and FR-IR spectra. These compositions were recorded on a Perkin-Elmer Fourier Transform-Infrared Spectrometer using KBr pellets (L160000I,USA), ^{1}H NMR spectra ($CDCl_3$/DMSO-d_6) on a Bruker NMR Spectrometer (Billerica, MA, USA) at 300 MHz Frequency and mass spectra on a Shimadzu mass spectrometer LC-MS (LC/MS-8040,USA). These utilized synthesizing chemicals were of pure grade procured from Merck, India. The metal chloride such as"$CuCl_2$, $ZnCl_2$, $FeCl_2$, $MnCl_2$ and $CoCl_2$ were of pure grade obtained from Merck, India.

Synthesis of Schiff bases derived from salicylaldehyde

D-Alanine (0.8 g, 0.1 *mmol*) and *L*-Serine (1.08 g, 0.1 *mmol*) was taken in a round bottom flask separately and salicylaldehyde (1.22 g, 0.1 *mmol)* was added to each followed by 25 ml of ethanol and three drops of acetic acid, stirred for 10 min and refluxed for 6-7 h on an electric water bath and cooled. The precipitate obtained was filtered through whatman filter paper, washed with cool water and kept over anhydrous calcium chloride under vacuum, and dried to obtain the Schiff bases, respectively (AL1 & SE1). Their spectral data are given as AL1 IR (KBr, cm^{-1}): OH (stretching): 3477, OH (bending): 1323, C=N– (stretching): 1633 CH, (stretching, Ar): 3023. Combustion analysis for $C_{11}H_{13}NO_3$: Calculated. C= 62.76, H= 6.32, N= 6.76, O= 23.16; Found C= 62.80, H= 6.32, N= 6.77, O= 23.19. ^{1}H NMR (300 MHz, DMSO, δ): 10.21 (*s*, 1H, H-1), 13.08 (*s*, 1H, H-1) 8.66 (*d*, N-CH), 1.56 (*d*, 1H, H-3), 6.65 -7.30 (*m*, 1H, H-7), 4.55 (*d*, N-CH). ^{13}C NMR (300 MHz, DMSO-d_6, δ): 178.37, 161.27, 158.47, 133.21, 118.97, 132.34, 133.14, 63.56, 16.45.LC/MS (*m/z*): calculated for $[C_{10}H_{11}NO_3+H]^+$ = 193.074, observed 193.075. SE1: IR (KBr, cm^{-1}): OH (stretching): 3500–3300, OH (bending): 1349, C=N (stretching): 1625. Combustion analysis for $C_{10}H_{11}NO_4$: Calculated. C = 57.41, H =5.30, N= 6.70, O=30.59; Found: C = 57.42, H= 5.32, N= 6.72, O30.60. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.21 (*s*, 1H, H-2), 8.66 (*d*, 1H, H-2), 13.08 (*s,* 1H, H-1), 4.08 (*d,* N=CH), 6.85 -7.29 (*m*, 2H, H-4), 3.89 (*d*, CH_2). ^{13}C NMR (300 MHz, DMSO-d6, δ):

176.57, 165.03, 161.27, 132.34, 118.97, 69.57, 62.06.LC/MS (*m*/*z*): calculated for $[C_{10}H_{11}NO_4 + H]^+$= 209.202, observed 209.210.

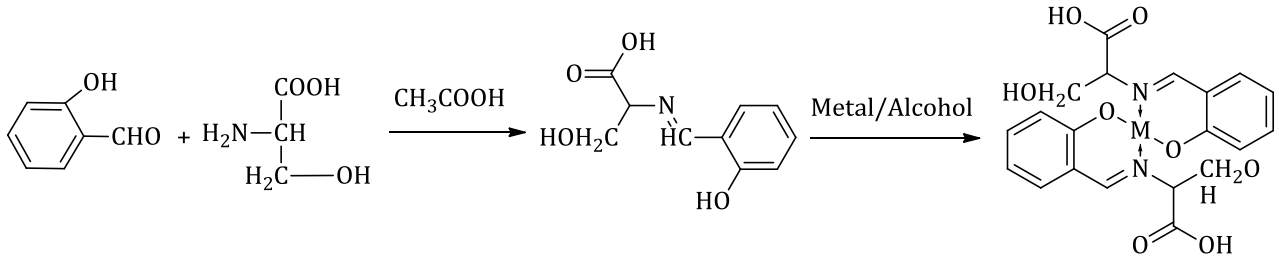


D-Alanine AL1 AL2-AL6

Scheme 1: Synthesis of metal complexes from D-Alanine

Table 1: List of compounds in Scheme1

Compound	Metals (M)
AL2	$CuCl_2$
AL3	$CoCl_2$
AL4	$FeCl_2$
AL5	$ZnCl_2$
AL6	$MnCl_2$



L-Serine SE 1 SE2-SE6

Scheme 2: Synthesis of metal complexes from L-Serine

Table 2: List of compounds in Scheme 2

Compound	Metals (M)
SE2	$CuCl_2$
SE3	$CoCl_2$
SE4	$FeCl_2$
SE5	$ZnCl_2$
SE6	$MnCl_2$

Where for 1) L-Alanine (AL1) yield 65% for 2) *L*-Serine (SE1) yield 68%

The metal ion was bonded to imine nitrogen and oxygen of the phenolic OH group, forming a co-ordination bond [12]. The metal ions incorporated for the synthesis were copper, manganese, cobalt, iron, and zinc, respectively, and various salts of metal solutions were developed in alcohol and synthesize as shown in Tables 1 and 2.

Synthesis of copper complexes

An ethanolic solution of $CuCl_2.2H_2O$ (1.34 g, 0.01 mmol) was added to each Schiff bases (1.8 g, 0.2 mmol) in 15 ml of ethanol, stirred for 15 min and refluxed for 5-6 h on an electric water bath. The blue coloured precipitate obtained was filtered through whatman filter paper, rinsed with lukewarm water and 1, 4-dioxane to take out excess of metal ions present in the solutions to obtain metal complexes AL2 and SE2, respectively. It was then kept over anhydrous calcium chloride under vacuum, and dried. Their spectral data are given as AL2: IR (KBr, cm^{-1}): OH (stretching): 3327, OH (bending): 1350, C=N (stretching): 1596, M–N: 630, M–O: 422. Combustion analysis for $C_{20}H_{20}Cl_2CuN_2O_6$: Calculated. C= 46.33, H= 3.89, Cl= 13.67, N= 5.40, O= 18.50, Cu= 12.18; Found: C= 46.30, H= 3.87,

N= 18.54, O= 5.41, Cu= 12.19. ^{1}H NMR (300MHz, DMSO-d_6, δ): 10.21 (*s*, 1H, H-2), 5.23 (*m*, 1H, H-4), 1.99 (*d*, 1H, H-6), 8.02 (*d*, N=CH), 6.87 -7.28 (*m*, 2H, H-8). ^{13}C NMR (300 MHz, DMSO-d_6, δ): 177.25, 153.42, 132.08, 129.09, 116.09, 114.82, 53.91, 17.48. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2CuN_2O_6 + H]^+$ 518.835, observed: 518.90. SE2: IR (KBr, cm^{-1}): OH (stretching): 3340, OH (bending): 1360, C=N– (stretching): 1600, M–N: 637, M–O: 428. Combustion analysis for $C_{20}H_{20}Cl_2CuN_2O_8$: Calculated. C= 43.61, H= 3.66, C= l12.87, N= 5.09, O= 23.24, Cu= 11.54; Found: C= 43.62, H= 3.67, Cl= 12.88, N= 5.10, O= 23.25, Cu= 11.54. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.21, (*s*, 1H, H-2), 8.14 (*d*, CH-N), 5.23 (*t*, C-NH), 3.61, (*s*, 1H, H-1), 7.14-8.14, (*m*, 2H, H-8). ^{13}C NMR (300 MHz, DMSO-d_6, δ): 175.46, 161.91, 153.56, 132.08, 129.04, 119.14, 116.26, 114.78, 61.20, 59.75. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2CuN_2O_8+ H]^+$ 548.989, observed: 548.98.

Synthesis of cobalt complexes

An ethanolic solution of $CoCl_2.2H_2O$ (1.02 g, 0.01 mmol) was added to each Schiff bases (1.8 g, 0.02 mmol) in 15 ml of ethanol, stirred for 15 min and refluxed for 5-6 h on an electric water bath. The orange-blue precipitate obtained was filtered through whatman filter paper and rinsed with cooled water and 1,4-dioxane to take out excess of metal ions present in the solutions to obtain metal complexes AL3 and SE3, respectively. It was then kept over anhydrous calcium chloride under vacuum and dried. Their spectral data are given as AL3: IR (KBr, cm^{-1}): OH (stretching): 3292, OH (bending): 1354, C=N (stretching): 1614, M–N: 597, M–O: 430. Combustion analysis for $C_{20}H_{20}Cl_2CoN_2O_6$: Calculated. C= 46.71, H= 3.92, Cl= 13.79, N= 5.45, Co= 11.46; Found: C= 46.72, H= 3.94, Cl= 13.80, N= 5.46, Co= 11.47. ^{1}H NMR (300MHz, DMSO-*d6, δ*): 10.21 (s, 1H, H-2), 5.23 (*m*, 1H, H-4), 1.99 (*d*, 1H, H-6), 8.02 (*d*, N=CH), 6.87 -7.28 (*m*, 2H, H-8), 1.79 (*d*, 1H, H-2). ^{13}C NMR (300 MHz, DMSO-*d6, δ*): 177.25, 153.42, 132.08, 129.09, 116.09, 114.82, 53.91, 17.48. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2CoN_2O_6 + H]$+ 514.222, observed 514.233.

SE3: IR (KBr, cm^{-1}): OH (stretching): 3341, OH (bending): 1360, C=N (stretching): 1605, M–N: 643, M–O: 432.Combustion analysis for $C_{20}H_{20}Cl_2CoN_2O_8$: Calculated. C= 43.98, H= 3.69, Cl= 12.98, N= 5.13, O= 23.43, Co= 10.79; Found: C= 43.92, H= 3.69, N= 5.14, O= 23.25, Cl= 12.98, Co= 10.80. ^{1}H NMR (300 MHz, DMSO-*d6, δ*): 10.23 (*s*, 1H, H-2), 8.16 (*d*, CH-N), 5.24 (*t*, C-NH), 3.63, (*s*, 1H, H-1), 7.18-8.16, (*m*, 2H, H-8). ^{13}C NMR (300 MHz, DMSO-d_6, δ): 175.47, 161.91, 153.56, 132.08, 129.04, 119.14, 116.26, 114.81, 61.25, 59.75. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2CoN_2O_8$ +H]+ 544.989, observed 544.98.

Synthesis of iron complexes

An ethanolic solution of $FeCl_2.2H_2O$ (1.62 g, 0.01 *mmol*) was added to each Schiff bases (1.8 g, 0.02 *mmol*) in 15 ml of ethanol, stirred for 15 min and refluxed for 5-6 h on an electric water bath. The reddish white precipitate obtained was filtered through whatman filter paper and cleaned with warm water and 1,4-dioxane to take out excess of metal ions present in the solutions excess ions of metal to obtain metal complexes AL4 and SE4, respectively. It was then kept over anhydrous calcium chloride under vacuum and dried. Their spectral data are given as AL4: IR (KBr, cm^{-1}): OH (stretching): 3377, OH (bending): 1383, C=N (stretching): 1634, M–N: 657, M–O: 501. Combustion analysis for $C_{20}H_{20}Cl_2FeN_2O_6$: Calculated. C= 47.00, H= 3.94, Cl= 13.87, N= 5.48, O= 18.78, Fe= 10.93; Found: C= 47.10, H= 3.95, N= 5.49, O= 18.78, Fe= 10.94. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.22 (*s*, 1H, H-2), 5.26 (*m*, 1H, H-4), 1.99 (*d*, 1H, H-6), 8.13 (*d,* N=CH), 6.88 -7.29 (*m*, 2H, H-8). ^{13}C NMR (300 MHz, DMSO-d_6, δ): 177.25, 153.42, 132.08, 129.10, 116.19, 114.82, 53.94, 17.48. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2FeN_2O_6 + H]^+$ 511.134, observed 512.13. Shown in figure 1.

SE4: IR (KBr, cm^{-1}): OH (stretching): 3353, OH (bend.): 1370, C=N (stretching): 1620, M–N: 636, M–O: 427. Combustion analysis for $C_{20}H_{20}Cl_2FeN_2O_8$: Calculated. C= 44.23, H= 3.71, Cl= 13.06, N= 5.16, O= 23.57, Fe= 11.83; Found: C= 44.24, H= 3.72, N= 5.17, O= 23.58, Cl= 13.08, Fe= 11.84.

^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.26, (*s*, 1H, H-2), 8.17 (*d*, CH-N), 5.34 (*t*, C-NH), 3.67 (*s*, 1H, H-1), 7.19-8.23, (*m*, 2H, H-8). ^{13}CNMR (300 MHz, DMSO-d_6, δ): 177.48, 161.89, 153.59, 132.13, 130.14, 119.04, 117.36, 114.82, 71.27, 60.77. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2FeN_2O_8 + H]^+$ 543.132, observed 543.12.

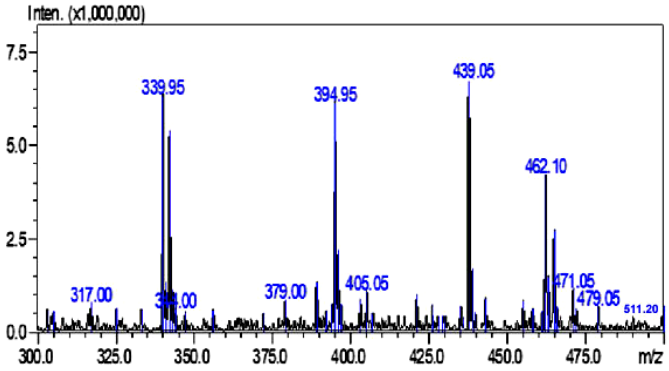


Figure1: LC/MS (m/z) AL5 metal complex

Synthesis of zinc complexes

An ethanolic solution of $ZnCl_2.2H_2O$ (1.36 g, 0.01 *mmol*) was added to a Schiff bases (1.8 g, 0.2 *mmol*) in 15 ml of ethanol, stirred for 15 min and refluxed for 5-6 h in on an electric water bath. The blue-white precipitate obtained was filtered through whatman filter paper and prepared with warm water and 1,4-dioxane to take out excess of metal ions present to obtain metal complexes AL5 and SE5, respectively. It was then kept over anhydrous calcium chloride under vacuum and dried. Their spectral data are given as AL5: IR (KBr, cm^{-1}): OH (stretching): 3294, OH (bend): 1356, C=N (stretching): 1625, M–N: 601, M–O: 435. Combustion analysis for $C_{20}H_{20}Cl_2ZnN_2O_6$: Calculated. C= 46.14, H= 3.87, Cl= 13.62, N= 38, O= 18.44, Zn= 12.56; Found: C= 46.16, H= 3.65, N= 5.40, O= 18.45, Zn= 12.60. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.22 (*s*, 1H, H-2), 5.25 (*m*, 1H, H-4), 1.99 (*d*, 1H, H-6), 8.03 (*d* N=CH), 6.88 -7.29 (*m*, 2H, H-8). ^{13}CNMR (300 MHz, DMSO-d_6, δ): 177.25, 153.42, 132.08, 129.10, 116.19, 114.82, 53.94, 17.48. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2ZnN_2O_6 + H]^+$ 520.669, observed 520.10. SE5 IR (KBr, cm^{-1}): OH (stretching): 3346, OH (bending): 1373, C=N (stretching): 1610, M–N: 646, M–O: 437.Combustion analysis for $C_{20}H_{20}Cl_2ZnN_2O_8$: Calculated. C= 43.46, H= 3.65, Cl= 12.83, N= 5.07. ,O= 23.16, Zn= 11.83; Found: C= 43.47, H= 3.69, N= 5.10, O= 23.18, Cl= 12.84, Zn= 11.84. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.25, (*s*, 1H, H-2), 8.17 (*d*, CH-N), 5.28 (*t*, C-NH), 3.65, (*s*, 1H, H-1), 7.19-8.23, (*m*, 2H, H-8). ^{13}C NMR (300 MHz, DMSO-d_6, δ): 175.48, 161.89, 153.59, 132.13, 129.14, 119.04, 116.36, 114.82, 61.27, 59.77. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2ZnN_2O_8 + H]^+$ 549.989, observed 549.95. Shown in Figure 2.

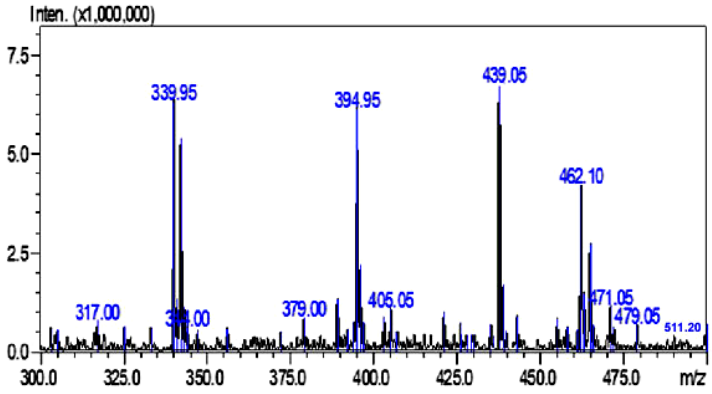


Figure 2: LC/MS (*m*/*z*) SE5 metal complex

Synthesis of manganese complexes

An ethanolic solution of $MnCl_2.2H_2O$ (1.25, 0.01 *mmol*) was added to each Schiff bases (1.8 g, 0.02 *mmol*) in 15 ml of ethanol, stirred for 15 min, and refluxed for 5-6 h on an electric water bath. The purple white precipitate obtained was filtered through whatman filter paper and washed with hot water and 1,4-dioxane to take out excess of metal ions to obtain metal complexes AL6 and SE6, respectively. It was then kept over anhydrous calcium chloride under vacuum and dried. Their spectral data are given as AL6: IR (KBr, cm^{-1}): OH (stretching): 3383, OH (bending): 1383, C=N (stretching): 1635, M–N: 658, M–O: 510. Combustion analysis for $C_{20}H_{20}Cl_2MnN_2O_6$: Calculated. C= 47.08, H= 3.95, Cl= 13.90, N= 5.49, O= 18.81, Mn= 10.77; Found: C= 47.10, H= 3.97, N= 5.50, O= 18.78, Mn= 10.79. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.22 (*s*, 1H, H-2), 5.26 (*m*, 1H, H-4), 1.99 (*d*, 1H, H-2), 8.13 (*d* N=CH), 6.88 -7.29 (*m*, 2H, H-8). ^{13}CNMR (300 MHz, DMSO-d_6, δ): 177.25, 153.42, 132.08, 129.10, 116.19, 114.82, 53.94, 17.48. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2MnN_2O_6 + H]^+$ 510.227, observed 510.30.

SE6: IR (KBr, cm^{-1}): OH (stretching): 3343, OH (bending): 1365, C=N (stretching): 1615, M–N: 627, M–O: 427. Combustion analysis for $C_{20}H_{20}Cl_2MnN_2O_8$: Calculated. C= 44.30, H= 3.72, Cl= 13.08, N= 5.17, O= 23.61, Mn= 10.14; Found: C= 44.31, H= 3.74, N= 5.18, O= 23.63, Mn= 10.14. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 10.26, (*s*, 1H, H-2), 8.27 (*d*, CH-N), 5.44 (*t*, C-NH), 3.77 (*s*, 1H, H-1), 7.19-8.23, (*m*, 2H, H-8). ^{13}CNMR (300 MHz, DMSO-d_6, δ): 75.49, 161.91, 153.60, 132.14, 129.16, 119.14, 116.36, 114.82, 61.27, 59.79. LC/MS (*m*/*z*): calculated for $[C_{20}H_{20}Cl_2FeN_2O_8 + H]^+$ 542.22, observed 542.12.

Antibacterial activity

Dextrose agar medium was used for anti-bacterial activity [13]. The pathogenic microorganisms used for investigations were *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Salmonella typhi*. After being dissolved in the DMF, these metal complexes provided a final concentration level of 1 mg/0.1 ml. Approximately *25 ml* broth of nutrient was inoculated with the loop full of provided test strain for about 24 hours at 37°C to activate the strain of bacteria. Around *28 ml* of the nutrient medium was implemented into 100 mm diameter Petri-plate. Inoculation was conducted by Pour-plate technique. The activated strain of 0.2 ml reached a temperature of 40-45º*C* after it was injected into the media. This entire process of the plate preparation was executed in a laminar airflow to maintain aseptic conditions, allowing the medium to solidify has generated viable results. After media solidification, substantial wells in the plates were made with the assistance of a cup-borer (0.85 cm), these wells were then implemented with one of the test sample solutions and control sample ciprofloxacin were executed, for each solvent and every bacterial strain, where the solvent was incorporated into these well. These plates were reserved for twenty-four hours at 37 °C. Moreover, the zones of inhibition formed by these metal complexes derivatives against the particular test bacterial strain were used to determine the antibacterial potency of the base ligands [14]. The average range acquired for three each replicate was utilised to indicate the zone of inhibition of every metal complex derivative.

Result and Discussion

Metals play a crucial role within the biological system through enzymatic process. The interaction of these metals within the active ligands plays an important role within the biological system . Some biologically active metal act through chelation, but generally metal coordination compounds influences their activity. It is noticeable in Table 1 that the two bases of Schiff and ten complexes of metal derivatives along with their drug standard assimilated dissimilar zones against the assessed bacterial strains. The complexes of metal with an activity of antibacterial activity of AL1 and SE1 in DMF against *S. aureus* is shown in Fig.3, the bases of Schiff AL1 and SE1 displayed considerably greater antibacterial nature of activity than their metal format of complexes. Of those bases regarding Schiff, SE1 denoted greater range of

activity than AL1 in DMF. Within DMF, the Cobalt form of complex based on SE3 indicated the simplest activity against *S. aureus*, followed by the zinc. Therefore, it is noticeable that the metal complex ion influences the antibacterial nature of activity.

Substantially, antibacterial nature of activity against *B. subtilis* is indicated in Fig.4. The bases of Schiff highlighted promising action compare with metal form of complexes. Consequently, AL1 and SE3 determined significantly comparable antibacterial form of activity in DMF. Nonetheless Zn metal complex of SE3 illustrated the greater antibacterial range of activity, followed by metal form complex of Cu and Fe, while other metal complexes showed significant outcomes. On the contrary, all the other forms of complexes highlighted no significant activity. It is suggested that the activity is more influenced by the ligands, metal, and therefore the solvent used for the investigation of the antibacterial activity.

Table 1: Anti-bacterial Activity

Test compound	Inhibition Zone, (*mm*)							
	S. aureus		*B.subtilis*		*P.aeruginosa*		*S.typhi*	
	100 mg	*200mg*	*100 mg*	*200mg*	*100 mg*	*200mg*	*100 mg*	*200mg*
AL1	38	42	48	50	42	51	45	47
AL2	52	58	62	68	61	64	62	69
AL3	63	68	58	69	32	41	67	70
AL4	58	60	59	53	45	47	56	59
AL5	48	54	53	51	60	63	54	57
AL6	37	43	47	49	50	53	50	51
SE1	47	54	50	53	53	55	43	49
SE2	59	64	57	60	65	67	57	59
SE3	69	73	66	74	73	85	65	73
SE4	62	64	57	59	51	55	54	55
SE5	53	58	55	61	53	57	59	63
SE6	53	59	58	60	54	59	58	62
Standard*	51	*60*	56	57	55	57	60	63

*Ciprofloaxcin

However, antibacterial activity against *B. subtilis* is highlighted in Figure 4, the Schiff bases indicated significant antibacterial form of activity in comparison to metal type of complexes and therefore the solvent in DMF, the Zn complex of SE3 displayed the greater antibacterial form of activity, followed by the Cu and Fe of SE3. Nevertheless, all of metal complexes developed significant changes. These outcomes again denoted the antibacterial form of activity of the ligands, metal, and therefore the solvent used for the investigation of the antibacterial type of activity was affected.

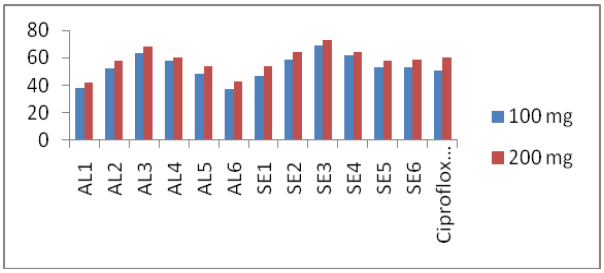


Figure 3: Anti-bacterial Activity of *S. aureus*

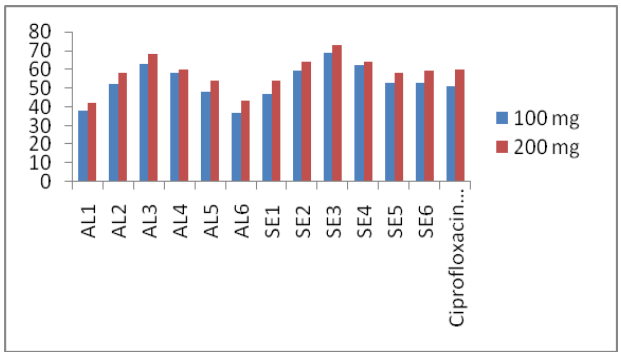


Figure 4: Anti-bacterial Activity of *B. subtilis*

Significantly, antibacterial type of activity against the gram-negative strain of *P.aeruginosa* is highlighted in Figure 5. In this scenario, the Schiff bases displayed a critical antibacterial activity than their metal complexes and the outcomes were substantially more when DMF was utilised as the solvent. Amongst the metal form of complexes, the best antibacterial type of action was indicated again by the cobalt complex of SE3, followed by the other metal complex. In DMSO, the nature of metal complexes of AL1 displayed

significant antibacterial format of activity. These activities against *P. aeruginosa* again determined the same conclusions developed for *B. Subtilis.*

The antibacterial activities of the synthesized metal complexes in contradiction of *S. typhi* are revealed in Figure 6. Extreme antibacterial type of activity was indicated by AL1 followed by SE1 in DMF. Approximately, every type of metal complex of both the Schiff bases in the solvents indicated remarkable activity. Overall, it was noticed that this gram-negative bacterium was significant to the synthesized compounds.

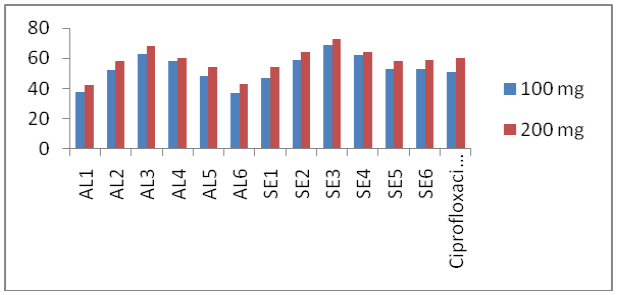


Figure 5: Anti-bacterial Activity of *P.aeruginosa*

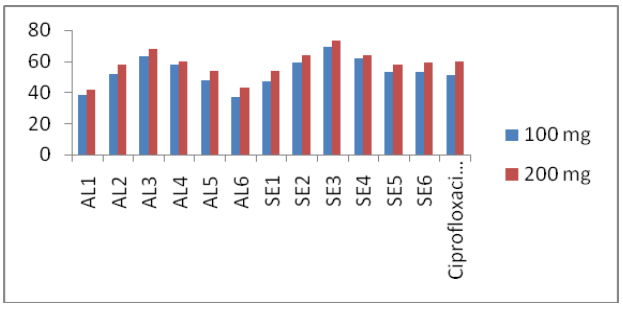


Figure 6: Anti-bacterial Activity of *S. typhi*

It was clearly indicated that metal complexes derivatives have a more significant range of antibacterial format of activity than free type of ligands due increase in the permeability of cell. The lipid form of membrane surrounds the cell that favour the passage of lipid soluble materials and its solubility is an important factor for controlling biological activity. However, in the present study, the higher activity of the metal complexes derivatives was observed and visualized. Another cause for the increase action of the metal nature of complexes may be the range relevance within lipophilicity of these types, metal complexes that have a penetration range of the complexes within the lipid form of membrane that could neither inhibit nor block the development of the microorganism. This approach again confirms that antibacterial format of activity is highly reliant on the molecular structure of the compound, the employed solvent, and the bacterial strain under consideration [15]. Therefore, the metal complexes derivatives synthesized have the active type of agents crucial for the successful anticipation of a lead molecule and drug-like properties.

Conclusion

Ten metal complex ligands were synthesized by condensing Schiff bases with the metal chloride in the ratio of 1:2 the nitrogen of the Schiff base and deficient oxygen atom form a bond with the metal. The Spectral and analytical data of the metal complexes derivatives are in relation with the dibasic tetra dentate coordination of the Schiff bases with stoichiometry (M= Cu(II), Zn(II), Co(II), Fe(II),and Mn(II)) in which both the phenolic protons of the ligands are replaced by the divalent metal cations. The anti-bacterial activity was carried out for schiff bases and ten metal complexes derivatives with standard ciprofloxacin among these cobalt complexes showed good activity when compared with other metal complexes derivatives for antibacterial activity.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

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