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Identification of New Pharmacophore in Bioactive Palladium Schiff Base Metal Complexes of Cephalosporins: Synthesis, Characterization and Biological Activity

Satyendra Nath Shukla[1]*, Pratiksha Gaur[1], Jai Prakash Gupta[1], Sheela Mathews[1], Nidhi Rai[1], Bhaskar Chaurasia[1]
1. Department of Chemistry, Govt. Model Science College, Jabalpur (MP) 482001, India.

ABSTRACT

Growing numbers of antibiotic-resistant bacteria are putting this golden era of medicine at risk and stresses the need for regular monitoring of antibiotic susceptibility, and developing a new design being active against resist pathogens. In this view seven Schiff base ligands of Cephalosporin group antibiotics were synthesized by their condensation with salicylaldehyde in equimolar ratio. Complexes of these Schiff bases with Pd (II) metal were synthesized in 1:2 stoichiometric ratio. The complexes were formulated as $[Pd(L)_2].3H_2O$, where L is Schiff base of seven different cephalosporin antibiotics. Complexes were characterized by elemental analyses, molar conductance, UV-Visible, FT-IR, ^{1}H-NMR, $^{13}C\{^{1}H\}$-NMR, ^{2}D-NMR and ESI-Mass spectrometry. Schiff bases were coordinated with metal through phenolic oxygen and azomethine-N, giving simple square planar geometry to complexes. Complexes were tested for antibacterial activity and MIC against gram-negative bacteria *E. coli* and gram positive bacteria *S. aureus* and were found more potent than Schiff bases and precursor antibiotics.

Keywords: Cephalosporin groups, Palladium Complexes, Schiff base, Antibacterial activity, Pharmacophore.

*Corresponding Author Email: ccrl_2004@rediffmail.com
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INTRODUCTION

About a half of the last century, antibiotics have given us a powerful way to treat infections that once were life threatening. Yet, the growing numbers of antibiotic-resistant bacteria are putting this golden era of medicine at risk. Now, we find ourselves in a race to prevent bacterial infections from once again becoming one of humanity's major killers and that is the reason in the present scenario superbug bacteria becomes a real challenge not only to Indian sub-continent but to the whole world. Since, numbers of resist pathogens are increasing year by year probably due to misuse and overuse of antibiotics by doctors as well as patients, a search of broad range antibiotic is the necessity of the time.[1] However, despite a push for new antibiotic therapies, there has been a continued decline in the number of newly approved drugs. Antibiotic resistance therefore poses a significant problem. Cephalosporin constitute a class of antibiotics derived from parent compound cephalosporin C, a natural antibiotic produced by a strain of the mould *Cephalosporiumacremonium* first isolated in 1948.[2, 3] It resembles penicillin's in that they have a β-lactam structure, but the five-member thiazolidine ring characteristic of the penicillins is replaced by a six-member dihydrothiazine ring. This ring provides the molecule's ability to resist bacterial enzymes; the antibacterial activity comes from the β-lactam ring. Two side chains in position 3 and 7 affect the pharmacokinetics and antibacterial spectrum of the cephalosporins. The cephalosporins, like all β-lactams, act by inhibiting the enzymes that create the cross-linkage of the peptidoglycan polymer leading to interference with the cell wall structure. These enzymes are located beneath the cell wall and are known as "penicillin-binding proteins" (PBP). We have selected Cephalexin which is first generation, Cefuroxime a second generation and Cephotaxime, Ceftriaxone, Ceftazidime, Cefixime, Cefpodoxime which are third generation antibiotics.

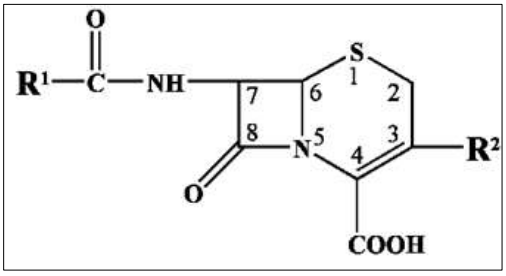

Figure 1.The basic cephalosporin molecule

Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial, antifungal, antitumor, antimicrobial activity and anti mouse hepatitis virus (MHV) activity. They have been studied extensively as a class of ligands and are known to coordinate with metal ions through the azomethine nitrogen

atom.[4-6] In the last two decades, considerable attention has been paid to the chemistry of the metal complexes of Schiff bases containing N and O donors. This may be attributed to their stability, biological activity and potential applications in many fields such as oxidation catalysis, electrochemistry etc.[7-9] Palladium compounds have found widespread application in organic synthesis. Coordination compounds of the type PdL_4, or PdL_2Cl_2 is used in many catalytic processes, particularly in the field of asymmetric catalysis.[10] Palladium (II) complexes have been found to cleave proteins with high level of stereo-specific selectively in good yields.[11] Some palladium complexes have recently been studied for their antibacterial,[12] antiproliferative,[13] antitrypanosomal,[14] anticancer, antimicrobial, antifungal and antitumor activity.[15] However, metal complexes of Schiff base derivatives of drugs are relatively less studied. Therefore, in anticipation of good chemistry and reactivity we have selected palladium as a metal and Schiff base of different Cephalosporins as a ligand and synthesized their complexes in desired molar ratio to explore their reactivity. These complexes were characterized by spectroscopic techniques to shed light on their structure and biological activity was also explored in order to establish structure activity relationship, with a hope that these new metalloantibiotic might throw a new light in this area.

MATERIALS AND METHOD

Cephalexin, Cephotaxime (both Ranbaxy), Ceftriaxone (Zuventus), Ceftazidime (Emcure), Cefixime, Cefpodoxime and Cefuroxime (All Mankind) were purchased from the market and used after purification. Salicylaldehyde, Palladium acetate (E. Merck), potassium hydroxide (CDH) and Mueller Hinton Agar media (Himedia) were used as received without further purification. Analytical reagent grade methyl alcohol, ethyl alcohol and other solvents were used as received. The ESI spectra were recorded on JEOL-Accut of JMS-T100 LC Mass spectrometer having a DART source. Rest of the experimental procedure is same as described earlier.[16]

Synthesis of Salicylidene Schiff base of Cephalosporin drugs

The drug (Cephalexin/ Cephotaxime/ Ceftriaxone/ Ceftazidime/ Cefixime, Cefpodoxime or Cefuroxime), dissolved in 30 mL methanol was mixed with Salicylaldehyde dissolved in 30 mL methanol in 1:1 molar ratio. To this reaction mixture, KOH (0.1% in methanol) was added drop wise to adjust the pH of the solution between 7 and 8, and the mixture was refluxed for 12 - 15 h. A clear yellowish-orange coloured solution was obtained which was reduced to one fourth of its volume and poured into ice cold water. A red brown/ dirty yellow/ brown/ dark yellow/ light

brown/ creamish yellow coloured precipitate was obtained in each case, which was filtered off, vacuum dried and recrystallized from acetonitrile : acetone : chloroform, solvent.

Synthesis of complexes

Palladium acetate and recrystallized salicylidene Schiff base of cephalosporin drug were mixed in 1:2 molar ratios in 30 mL of methanol and the reaction mixture were kept under stirring for 2 h in an inert atmosphere. The colour of reaction mixture changes from dark yellow to dark brown. Thereafter, reaction mixture was refluxed for 2-3 h. A dark brown/black solid was isolated after reduction of volume by evaporation, which was filtered off, washed with methanol and dried under vacuum. The solid obtained were recrystallized from acetonitrile : acetone : chloroform, 1 : 2 : 4; (v/v) solvent mixture.

Antibacterial Screening

All the drugs from **1a-7a,** their ligands **1b-7b**, complexes **1-7,** solvent **DMSO** and Palladium acetate were screened for antibacterial properties against gram negative bacteria ***Escherichia coli*** MTCC 1304 and gram positive bacteria ***Staphylococcus aureus*** ATCC 6538 at different concentrations. Mueller Hinton Agar plates (MHA) were prepared and 50 µL Suspension of ***Escherichia coli*** and ***Staphylococcus aureus*** containing approximately 10^5 - 10^6 CFC (colony forming unit) was applied to the plate by spread plate technique.[17-19] The wells are made on the plates and they were filled with 50 µL of sample solution of 0.03% concentration. The 0.03% drugs and 0.03% ligands were tested for comparison with complexes. These plates were incubated at 37±1 °C for 24 – 48 hours in refrigerated incubator shakers.

RESULTS AND DISCUSSION

Schiff base Ligands

Schiff base of Cephalexin, (SALCEPHAL)

Colour = Red brown, Yield: 0.334 g (24.66%); m.p.^{d} = 180°C; Anal. Calcd.for$C_{23}H_{21}N_3O_5S$ (M_τ= 451.50): C, 61.18; H, 4.69; N, 9.31. Found: C, 61.10; H, 4.65; N, 9.29; Selected infrared absorption (KBr, cm^{-1}): $\nu(OH)_{arom}$, 3448(br); ν(N-H), 3280(s); $\nu(C=O)_{carboxyllic}$, 1740(w); ν(CO-NH), 1666(br); ν(CH=N), 1616(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 10.98 (s, 1H); δ(CH=N), 8.10 (s, 1H); δ(CONH), 8.01(s, 1H); δ(Ar-H), 7.44(t, 2H); 7.27(t, 1H); 7.26(d, 2H); $\delta(Ar\text{-}H)_{phenol,}$ 7.15(d, 1H); 7.12(t, 1H); 6.85(t, 1H); 6.75(d, 1H); δ(HN-CH), 6.68(s, 1H); δ(Ar-OH), 5.0(s, 1H); δ(S-CH), 4.89(d, 1H); δ(CH-C=O), 4.45(d, 1H); $\delta(S\text{-}CH_a)$, 3.19(s, 1H); $\delta(S\text{-}CH_b)$, 3.06(s, 1H); $\delta(CH_3)$, 1.71(s, 3H). ^{13}C-NMR (δ value in ppm): δ(CONH), 175.2; δ(COOH), 168.3; δ(N-C=O), 166.3; δ(CH=N), 160.9; $\delta(Ar\text{-}C)_{phenolic}$, 161.1($C_1$),

121.5(C_2), 130.6(C_3), 124.6(C_4), 132.5(C_5), 116.01(C_6); δ(Ar-C), 147.3(C_1), 127(C_2, C_6), 128.6(C_3, C_5), 126.8(C_4); δ(C-CH_3), 136.1; δ(C-COOH), 121.1; δ(HN-CH), 71.4; δ(S-CH-N), 53.3; δ(N-CO-CH), 51.4; δ(S-CH_2), 29.7. ESI-Mass spectra, m/z: $[C_6H_5O]^+$= 93.10, $[C_7H_6NO]^+$ = 120.13, $[C_{14}H_{12}NO]^+$ = 210.25, $[C_{15}H_{13}N_2O_2]^+$ = 253.27, $[C_{18}C_{15}N_3O_3]^+$ = 321.33, $[C_5H_6O_2S]^+$= 130.16, $[C_8H_8NO_3S]^+$= 198.22, $[C_9H_9N_2O_4S]^+$= 241.24, $[C_{23}H_{21}N_3O_5S]^+$= 452.11.

3.1.2. Schiff base of Cephotaxime, (SALCEPHOT)

Colour = Dirty yellow, Yield: 0.293 g (22.31%); m.p. = 130°C; Anal. Calcd.for$C_{23}H_{21}N_5O_8S_2$ (M_τ= 559.60): C, 49.37; H, 3.78; N, 12.52. Found: C, 49.30; H, 3.72; N, 12.44; Selected infrared absorption (KBr, cm^{-1}): ν$(OH)_{arom}$, 3325(br), ν(N-H), 3306(br), ν(C=O), 1751(s), ν(CO-NH), 1666(w), ν(CH=N), 1635(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 10.95(s, 1H); δ(CH=N), 8.16(s, 1H); δ(CONH), 8.07(d, 1H); δ(S-CH), 7.35(s, 1H); δ$(Ar-H)_{phenolic,}$ 7.44(d, 1H); 7.18(t, 1H); 6.82(t, 1H); 6.78(d, 1H); δ(HN-CH), 5.49(d, 1H); δ(S-CH), 5.18(d, 1H); δ(Ar-OH), 5.19(s, 1H); δ(C-CH_2), 4.75(s, 1H); δ(O-CH_3), 4.01(s, 3H); δ(S-CH_a), 3.17(s, 1H); δ(S-CH_b), 3.09(s, 1H); δ(OCO-CH_3), 2.11(s, 3H). ^{13}C-NMR (δ value in ppm): δ(S-C=N), 171.7; δ(O-C=O), 170.3; δ(COOH), 169.8; δ(CONH), 165.4; δ(N-C=O), 164.2; δ(C=N), 164.12; δ(CH=N), 160.18; δ$(Ar-C)_{phenolic}$, 161.13(C_1), 118.54(C_2), 130.69(C_3), 121.51(C_4), 132.58(C_5), 116.08(C_6); δ(C=C), 130.95; δ(S-CH=C), 123.58; δ(N-C=C), 120.9; δ(O-CH_3), 61.8; δ(HN-CH), 58.58, δ(S-CH), 57.30; δ(C-CH_2), 56.9; δ(S-CH_2), 24.52; δ(OCO-CH_3), 21.8. ESI-Mass spectra, m/z; $[C_7H_8O_4]^+$ = 156.13, $[C_{10}H_{10}NO_5S]^+$ = 256.25, $[C_{13}H_{14}N_3O_7S]^+$ = 356.33, $[C_{16}H_{15}N_4O_7S_2]^+$ = 439.44, $[C_{12}H_{10}N_3O_2S]^+$ = 260.29, $[C_{15}H_{12}N_4O_4S]^+$ = 344.35, $[C_{16}H_{13}N_5O_4S_2]^+$ = 403.43, $[C_{21}H_{18}N_5O_7S_2]^+$ = 516.53, $[C_{23}H_{21}N_5O_8S_2]^+$ = 559.57.

Schiff base of Ceftriaxone, (SALCEFTRI)

Colour = Brown, Yield: 0.519 g (43.78%); m.p. = 160°C; Anal. Calcd.for$C_{25}H_{22}N_8O_8S_3$ (M_τ= 658.70): C, 45.59; H, 3.37; N, 17.01. Found: C, 45.52; H, 3.35; N, 16.98; Selected infrared absorption (KBr, cm^{-1}): ν$(OH)_{arom}$, 3350(w), ν(N-H), 3330(br), ν(C=O), 1750(w), ν(CO-NH), 1650(s), ν(CH=N), 1622(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 10.88(s, 1H); δ(CH=N), 8.15(s, 1H); δ(CONH), 8.02(s, 1H); δ$(CONH)_{cyclic}$, 8.0(s, 1H); δ$(Ar-H)_{phenolic,}$ 7.42(d, 1H); 7.18(t, 1H); 6.88(t, 1H); 6.82(d, 1H); δ(S-CH), 7.4(d, 1H); δ(HN-CH), 5.51(d, 1H); δ(S-CH), 5.11(d, 2H); δ(Ar-OH), 5.13(s, 1H); δ(O-CH_3), 4.01(s, 3H); δ(S-CH_2), 3.51(s, 1H); δ(S-CH_a), 3.21(s, 1H); δ(S-CH_b), 3.07(s, 1H); δ(N-CH_3), 2.49(s, 3H). ^{13}C-NMR (δ value in ppm): δ$(N-C=O)_{cyclic}$, 191.16; δ(S-C=N), 171.42; δ(COOH), 169.8; δ(CONH), 166; δ(N-C=O), 165.22; δ(C=N), 164.32; δ$(N-C-S)_{cyclic}$, 162.12; δ$(CONH)_{cyclic}$, 161.6; δ(CH=N), 160.19; δ$(Ar-C)_{phenolic}$, 161.18(C_1), 118.53(C_2), 130.61(C_3), 121.54(C_4), 132.56(C_5), 116.08(C_6); δ(C=C-

N), 143.21; δ(CH_2-C=C), 126.13; δ(S-C-H), 123.85; δ(C=C-N)$_{cyclic}$, 121.65; δ(O-CH_3), 61.29; δ(CH-NH), 59.5; δ(S-CH-N), 58.3; δ(N-CH_3), 37.26; δ(S-CH_2)$_{cyclic}$, 26.41; δ(S-CH_2), 20.66. ESI-Mass spectra, m/z; $[C_4H_4N_3O_2]^+$ = 126.09, $[C_5H_6N_3O_2S]^+$ = 172.185, $[C_9H_9N_3O_4S]^+$ = 255.25, $[C_{12}H_{12}N_5O_5S_2]^+$ = 370.38, $[C_{15}H_{15}N_6O_7S_2]^+$ = 455.45, $[C_{25}H_{21}N_8O_7S_3]^+$ = 641.68, $[C_{25}H_{22}N_8O_8S_3]^+$ = 658.69.

Schiff base of Ceftazidime, (SALCEFTAZI)

Colour = Dark yellow, Yield: 0.360 g (30.25%); m.p. = 180°C; Anal. Calcd.for$C_{29}H_{26}N_6O_8S_2$ (M_τ= 650.70): C, 53.53; H, 4.03; N, 12.92. Found: C, 53.51; H, 4.00; N, 12.88; Selected infrared absorption (KBr, cm^{-1}): ν(OH)$_{atom}$, 3404(br), ν(N-H), 3296(br), ν(C=O), 1750(w), ν(CO-NH), 1664(br), ν(CH=N), 1640(s), ν(COO^-), 1595(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 11.08(s, 1H); δ(CH)$_{pyridinium}$, 9.30(d, 1H); 9.26(d, 1H); 9.05(t, 1H); 8.41(t, 1H); 8.40(t, 1H); δ(CH=N), 8.18(s, 1H); δ(CONH), 8.14(s, 1H); δ(Ar-H)$_{phenolic,}$ 7.49(d, 1H); 7.13(t, 1H); 6.86(t, 1H); 6.82(d, 1H); δ(S-CH), 7.46(s, 1H); δ(HN-CH), 5.41(d, 1H); δ(S-CH), 5.13(d, 2H); δ(Ar-OH), 5.1(s, 1H); δ(S-CH_a), 3.17(s, 1H); δ(S-CH_b), 3.05(s, 1H); δ(CH_2-N^+), 2.09(s, 2H); δ(C-CH_3)$_a$, 1.41(s, 3H); δ(C-CH_3)$_b$, 1.37(s, 3H). ^{13}C-NMR (δ value in ppm): δ(COOH), 169.70; δ(S-C=N), 171.78; δ(COO^-), 169.93 δ(N-C=O), 164.21; δ(C-C=N), 164.10; δ(CONH), 163.22; δ(Ar-C)$_{phenolic}$, 161.16(C_1), 118.52(C_2), 130.63(C_3), 121.54(C_4), 132.51(C_5), 116.07(C_6); δ(CH=N), 160.19; δ(Ar-C)$_{pyridinium}$, 146.02(C_1), 128.52(C_2), 146.23(C_3), 128.52(C_4), 146.03(C_5); δ(N-C=C)$_a$, 143.12; δ(N-C=C)$_b$, 137.63; δ(S-C-C), 130.82; δ(S-C-H), 121.8; δ(N-O-C), 83.52; δ(HN-CH), 58.52; δ(S-CH), 57.36; δ(N^+-CH_2), 51.12; δ(S-CH_2), 26.32; δ(O-C-CH_3), 21.61. ESI-Mass spectra, m/z; $[C_6H_7N]^+$ = 93.12, $[C_{10}H_9NO_2]^+$ = 175.18, $[C_{13}H_{11}N_2O_3S]^+$ = 275.30, $[C_{19}H_{19}N_4O_7S]^+$ = 447.44, $[C_{23}H_{21}N_6O_7S_2]^+$ = 557.58, $[C_{29}H_{26}N_6O_8S_2]^+$ = 650.68.

Schiff base of Cefixime, (SALCEFIXI)

Colour = Dark yellow, Yield: 0.520 g (35.87%); m.p.^{d} = 170°C; Anal. Calcd.for$C_{23}H_{19}N_5O_8S_2$ (M_τ= 557.58): C, 49.55; H, 3.43; N, 12.56. Found: C, 49.51; H, 3.37; N, 12.53; Selected infrared absorption (KBr, cm^{-1}): ν(OH)$_{arom}$, 3450(w), ν(N-H), 3335(br), ν(C=O), 1747(s), ν(CO-NH), 1680(w), ν(CH=N), 1635(s), ν(C-O), 1047(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH)$_{exocyclic}$, 11.10(s, 1H); δ(COOH), 10.90(s, 1H); δ(CH=N), 8.13(s, 1H); δ(CONH), 8.06(s, 1H); δ(S-CH), 7.48(s, 1H); δ(Ar-H)$_{phenolic,}$ 7.42(d, 1H); 7.12(t, 1H); 6.86(t, 1H); 6.81(d, 1H); δ(C-CH), 6.49(d, 1H); δ(HN-CH), 5.53(t, 1H); δ(CH=CH_2)$_a$, 5.22(d, 1H); δ(CH=CH_2)$_b$, 5.20(d, 1H); δ(S-CH), 5.12(d, 2H); δ(Ar-OH), 5.10(s, 1H); δ(N-O-CH_2), 4.43(s, 2H); δ(S-CH_2)$_a$, 3.19(s, 1H); δ(S-CH_2)$_b$ 3.06(s, 1H); ^{13}C-NMR (δ value in ppm): δ(COOH), 173.44; δ(S-C=N), 171.73; δ(N-C=O), 164.6; δ(CONH), 164.13; δ(COOH)$_{exocyclic}$, 166.71; δ(Ar-C)$_{phenolic}$,

161.19(C_1), 118.51(C_2), 130.63(C_3), 121.55(C_4), 132.53(C_5), 116.09(C_6); δ(CH=N), 160.03; δ(N-C=C)$_a$, 143; δ(C-CH), 138.35; δ(C-C=C), 138.20; δ(S-C-H), 123.88; δ(N-C=C)$_b$, 121.8; δ(HC=CH_2), 117.2; δ(O-CH_2), 76.58; δ(HN-CH), 58.9; δ(S-CH), 58.2; δ(S-CH_2), 29.0. ESI-Mass spectra, m/z; $[C_7H_7NO_2S]^+$= 170.06, $[C_{10}H_7N_2OS]^+$ = 203.06, $[C_{11}H_9N_3O_4S]^+$ = 279.21, $[C_{11}H_9N_3O_5S]^+$ = 293.23, $[C_{15}H_{12}N_4O_5S_2]^+$ = 391.35, $[C_{15}H_{12}N_4O_4.O^{17}S_2]^+$ = 392.36, $[C_{15}H_{12}N_3O_6S_2]^+$ = 395.13, $[C_{18}H_{15}N_5O_6S_2]^+$ = 459.24, $[C_{20}H_{15}N_5O_6S_2]^+$ = 486.17, $[C_{20}H_{15}N_5O_5S_2.O^{17}]^+$ = 487.17, $[C_{21}H_{17}N_5O_7S_2]^+$ = 516.19, $[C_{23}H_{18}N_5O_5S_2.O^{17}O^{18}]^+$ = 543.21, $[C_{23}H_{19}N_5O_7S_2.O^{17}]^+$ = 558.24, $[C_{23}H_{19}N_5O_7S_2.O^{18}]^+$ = 559.25.

Schiff base of Cefpodoxime, (SALCEPHODO)

Colour = Light brown, Yield: 0.257 g (17.31%); m.p.^{d} = 135°C; Anal. Calcd.for$C_{22}H_{21}N_5O_7S_2$ (M_τ= 531.58) : C, 49.71; H, 3.98; N, 13.18. Found: C, 49.67; H, 3.95; N, 13.15; Selected infrared absorption (KBr, cm^{-1}): ν(OH)$_{arom}$, 3440(w), ν(N-H), 3296(br), ν(C=O), 1759(s), ν(CO-NH), 1680(sh), ν(CH=N), 1620(s), ν(C-O), 1041(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 10.91(s, 1H); δ(CH=N), 8.18(s, 1H); δ(CONH), 8.09(s, 1H); δ(S-CH)$_{ring}$, 7.46(s, 1H); δ(Ar-H)$_{phenolic,}$ 7.46(d, 1H); 7.13(t, 1H); 6.88(t, 1H); 6.84(d, 1H); δ(HN-CH), 5.51(t, 1H); δ(S-CH), 5.21(d, 2H); δ(Ar-OH), 5.12(s, 1H); δ(C-CH_2), 4.14(s, 2H); δ(N-O-CH_3), 4.10(s, 1H); δ(C-O-CH_3), 3.32(s, 3H); δ(S-CH_a), 3.21(s, 1H); δ(S-CH_b), 3.12(s, 1H). ^{13}C-NMR (δ value in ppm): δ(S-C=N), 173.41; δ(COOH), 169.8; δ(CONH), 167; δ(N-C=O), 165.2; δ(C=N), 164.54; δ(CH=N), 161.10; δ(Ar-C)$_{phenolic}$, 161.12(C_1), 123.5(C_2), 133.6(C_3), 124.5(C_4), 123.5(C_5), 118.33(C_6); δ(C=C)$_{thia}$, 132.93; δ(S-C-H), 125.8; δ(N-C=C), 118.90; δ(C-CH_2-O), 75.67; δ(N-O-CH_3), 62.2; δ(C-O-CH_3), 60.7; δ(HN-CH), 58.91; δ(S-CH), 57.64; δ(S-CH_2), 25.26. ESI-Mass spectra, m/z; $[C_6H_8O_3]^+$ = 128.13, $[C_7H_9NO_3S]^+$ = 187.22, $[C_9H_{11}N_2O_4S]^+$ = 243.26, $[C_{12}H_{14}N_3O_6S]^+$ = 328.32, $[C_{16}H_{16}N_5O_6S_2]^+$ = 438.46, $[C_{21}H_{10}N_3O_2S]^+$ = 260.29, $[C_{20}H_{16}N_5O_6S_2]^+$ = 486.50, $[C_{22}H_{21}N_5O_7S_2]^+$ = 531.56.

Schiff base of Cefuroxime, (SALCEFURO)

Colour = Creamish yellow, Yield: 0.290 g (18.79%); m.p. = 102°C; Anal. Calcd.for$C_{23}H_{20}N_4O_9S$ (M_τ= 528.51) : C, 52.27; H, 3.81; N, 10.60. Found: C, 52.24; H, 3.76; N, 10.52; Selected infrared absorption (KBr, cm^{-1}): ν(OH)$_{arom}$, 3481(sh), ν(N-H), 3292(br), ν(C=O), 1761(br), ν(CO-NH), 1681(w), ν(CH=N), 1612(s), ν(C-O), 1011(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 11.07(s, 1H); δ(CH=N), 8.13(s, 1H); δ(CONH), 8.02(d, 1H); δ(Ar-H)$_{phenolic,}$ 7.53(d, 1H); 7.19(t, 1H); 6.85(t, 1H); 6.81(d, 1H); δ(Ar-H)$_{furan}$, 7.48(d, 1H); 6.38(t, 1H); 6.32(t, 1H); δ(HN-CH), 5.54(t, 1H); δ(S-CH), 5.26(d, 1H); δ(Ar-OH), 5.11(s, 1H); δ(C-CH_2), 4.83(s, 2H); δ(N-O-CH_3), 4.08(s, 3H); δ(S-CH_a), 3.19(s, 1H); δ(S-CH_b), 3.11(s, 1H). ^{13}C-NMR (δ

value in ppm): δ(COOH), 169.8; δ(CONH), 166; δ(N-C=O), 165.2; δ(C=N), 165.13; δ(CH=N), 161.76; δ(Ar-C)$_{phenolic}$, 162.12(C_1), 121.58(C_2), 132.65(C_3), 123.52(C_4), 135.52(C_5), 119.05(C_6); δ(N-CO-O), 158.16; δ(C-C=C), 131.93; δ(N-C=C), 120.9; δ(N-O-CH_3), 62.61; δ(HN-CH), 58.21; δ(S-CH), 57.65; δ(C-CH_2), 55.83; δ(S-CH_2), 26.11. ESI-Mass spectra, m/z; $[C_6H_6NO_2]^+$ = 124.12, $[C_7H_7N_2O_3]^+$ = 167.14, $[C_{10}H_9N_3O_4S]^+$ = 267.26, $[C_{14}H_{12}N_3O_6S]^+$ = 511.48, $[C_{16}H_{14}N_3O_8S]^+$ = 408.36, $[C_{23}H_{19}N_4O_8S]^+$ = 511.48, $[C_{13}H_{11}NO_5]^+$ = 261.23, $[C_{17}H_{14}N_3O_7S]^+$ = 404.37, $[C_{22}H_{17}N_4O_8S]^+$ = 497.46, $[C_{23}H_{20}N_4O_9S]^+$ = 528.50.

Complexes

[Pd(SALCEPHAL)$_2$].3H$_2$O; Complex 1

Colour = Sandy Black, Yield: 0.035g (53.68%); m.p. 260°C; Anal. Calcd.for$C_{46}H_{46}N_6O_{13}PdS_2$ (M_τ= 1061.12): C, 52.06; H, 4.33; N, 7.91. Found: C, 52.00; H, 4.28; N, 7.88; Molar conductance ($\Omega^{-1}cm^2mol^{-1}$): 12.0 in DMSO. Selected infrared absorption (KBr, cm^{-1}): ν(CH=N), 1595(s), ν(Pd-O), 460(s). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 11.02 (s, 1H); δ(CH=N), 8.32 (s, 1H); δ(CONH), 8.11(s, 1H); δ(Ar-H), 7.46(t, 2H); 7.29(t, 1H); 7.28(d, 2H); δ(Ar-H)$_{phenol}$, 7.17(d, 1H); 7.15(t, 1H); 6.89(t, 1H); 6.78(d, 1H); δ(HN-CH), 6.71(s, 1H); δ(S-CH), 4.93(d, 1H); δ(CH-C=O), 4.48(d, 1H); δ(S-CH_a), 3.23(s, 1H); δ(S-CH_b), 3.09(s, 1H); δ(CH_3), 1.74(s, 3H). ^{13}C-NMR (δ value in ppm): δ(CONH), 175.5; δ(COOH), 168.4; δ(N-C=O), 166.5; δ(CH=N), 162.35; δ(Ar-C)$_{phenolic}$, 161.3(C_1), 121.7(C_2), 130.7(C_3), 124.8(C_4), 132.7(C_5), 116.11(C_6); δ(Ar-C), 147.5(C_1), 127.4(C_2, C_6), 128.8(C_3, C_5), 126.9(C_4); δ(C-CH_3), 136.3; δ(C-COOH), 121.7; δ(HN-CH), 71.7; δ(S-CH-N), 53.4; δ(N-CO-CH), 51.8; δ(S-CH_2), 29.9. Electronic spectra (λ_{max}, nm (ε in M^{-1} cm^{-1})) in DMSO: 464(48), 424(69), 380(124). ESI-Mass spectra, m/z; $[C_9H_8NO_4S]^+$ = 226.23, $[C_{23}H_{20}N_3O_5PdS]^+$ = 556.91, $[C_{37}H_{31}N_4O_6PdS]^+$ = 766.15, $[C_{37}H_{32}N_5O_6PdS]^+$ = 781.16, $[C_{46}H_{40}N_6O_{10}PdS_2]^+$ = 1007.39.

[Pd(SALCEPHOT)$_2$].3H$_2$O; Complex 2

Colour = Brown, Yield: 0.310g (98.41%); m.p. 230°C; Anal. Calcd.for$C_{46}H_{46}N_{10}O_{19}PdS_4$ (M_τ = 1277.28): C, 43.25; H, 3.60; N, 10.96. Found: C, 43.23; H, 3.55; N, 10.90; Molar conductance ($\Omega^{-1}cm^2mol^{-1}$): 3.0 in DMSO. Selected infrared absorption (KBr, cm^{-1}): ν(CH=N), 1620(s), ν(Pd-O), 472(sh). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 10.99(s, 1H); δ(CH=N), 8.26(s, 1H); δ(CONH), 8.14(d, 1H); δ(S-CH), 7.40(s, 1H); δ(Ar-H)$_{phenolic}$, 7.46(d, 1H); 7.22(t, 1H); 6.85(t, 1H); 6.81(d, 1H); δ(HN-CH), 5.51(d, 1H); δ(S-CH), 5.22(d, 1H); δ(C-CH_2), 4.78(s, 1H); δ(O-CH_3), 4.08(s, 3H); δ(S-CH_a), 3.21(s, 1H); δ(S-CH_b), 3.12(s, 1H); δ(OCO-CH_3), 2.14(s, 3H). ^{13}C-NMR (δ value in ppm): δ(S-C=N), 171.9; δ(O-C=O), 170.5; δ(COOH), 169.9; δ(CONH), 165.7; δ(N-C=O), 164.4; δ(C=N), 164.24; δ(CH=N), 163.12; δ(Ar-

$C)_{phenolic}$, 161.33(C_1), 118.74(C_2), 130.78(C_3), 121.61(C_4), 132.71(C_5), 116.20(C_6); δ(C=C), 131.40; δ(S-CH=C), 123.78; δ(N-C=C), 121.11; δ(O-CH_3), 61.98; δ(HN-CH), 58.81, δ(S-CH), 57.62; δ(C-CH_2), 57.1; δ(S-CH_2), 25.32; δ(OCO-CH_3), 23.1. Electronic spectra (λ_{max}, nm (ε in M^{-1} cm^{-1})) in DMSO: 494(56), 435(78), 334(148). ESI-Mass spectra, m/z: $[C_8H_9NO_4S]^+$ = 215.23, $[C_{23}H_{20}N_5O_8PdS_2]^+$ = 664.98, $[C_{30}H_{25}N_6O_9PdS_2]^+$ = 784.10, $[C_{33}H_{26}N_7O_9PdS_3]^+$ = 867.22, $[C_{46}H_{40}N_{10}O_{16}PdS_4]^+$ = 1223.55.

$[Pd(SALCEFTRI)_2].3H_2O$; Complex 3

Colour = Red brown, Yield: 0.439g (90.33%); m.p. 270°C; Anal. Calcd.for$C_{50}H_{48}N_{16}O_{19}PdS_6$ (M_τ= 1475.50): C, 40.70; H, 3.25; N, 15.18. Found: C, 40.69; H, 3.22; N, 15.14; Molar conductance ($\Omega^{-1}cm^2mol^{-1}$): 8.0 in DMSO. Selected infrared absorption (KBr, cm^{-1}): ν(CH=N), 1610(s), ν(Pd-O), 480(w). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 10.93(s, 1H); δ(CH=N), 8.26(s, 1H); δ(CONH), 8.12(s, 1H); $\delta(CONH)_{cyclic}$, 8.08(s, 1H); $\delta(Ar\text{-}H)_{phenolic}$, 7.46(d, 1H); 7.21(t, 1H); 6.91(t, 1H); 6.84(d, 1H); δ(S-CH), 7.45(d, 1H); δ(HN-CH), 5.54(d, 1H); δ(S-CH), 5.16(d, 2H); δ(O-CH_3), 4.07(s, 3H); δ(S-CH_2), 3.54(s, 1H); δ(S-CH_a), 3.24(s, 1H); δ(S-CH_b), 3.11(s, 1H); δ(N-CH_3), 2.53(s, 3H). ^{13}C-NMR (δ value in ppm): $\delta(N\text{-}C{=}O)_{cyclic}$, 191.46; δ(S-C=N), 171.72; δ(COOH), 169.98; δ(CONH), 166.56; δ(N-C=O), 165.42; δ(C=N), 164.62; δ(CH=N), 162.54; $\delta(N\text{-}C\text{-}S)_{cyclic}$, 162.42; $\delta(CONH)_{cyclic}$, 161.8; $\delta(Ar\text{-}C)_{phenolic}$, 161.48($C_1$), 118.63($C_2$), 130.81($C_3$), 121.76($C_4$), 132.96($C_5$), 116.28($C_6$); δ(C=C), 143.41; δ($CH_2$-C=C), 126.35; δ(S-C-H), 124.1; $\delta(C{=}C\text{-}N)_{cyclic}$, 121.85; δ(O-$CH_3$), 61.40; δ(CH-NH), 59.71; δ(S-CH-N), 58.47; δ(N-CH_3), 37.66; $\delta(S\text{-}CH_2)_{cyclic}$, 26.76; δ(S-$CH_2$), 21.33. Electronic spectra (λ_{max}, nm (ε in M^{-1} cm^{-1})) in DMSO: 515(50), 438(86), 336(120). ESI-Mass spectra, m/z: $[C_{12}H_{11}N_4O_5S_2]^+$ = 355.37, $[C_{25}H_{21}N_8O_8PdS_3]^+$ = 764.10, $[C_{37}H_{30}N_{11}O_{10}PdS_4]^+$ = 1023.38, $[C_{45}H_{36}N_{13}O_{14}PdS_5]^+$ = 1259.59, $[C_{50}H_{42}N_{16}O_{16}PdS_6]^+$ = 1421.78.

$[Pd(SALCEFTAZI)_2].3H_2O$; Complex 4

Colour = Black, Yield: 0.211g (73.26%); m.p. 240°C; Anal. Calcd.for$C_{58}H_{56}N_{12}O_{19}PdS_4$ (M_τ= 1459.44): C, 47.73; H, 3.84; N, 11.51. Found: C, 47.71; H, 3.81; N, 11.44; Molar conductance ($\Omega^{-1}cm^2mol^{-1}$): 6.0 in DMSO. Selected infrared absorption (KBr, cm^{-1}): ν(CH=N), 1608(br), ν(Pd-O), 472(sh). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 11.16(s, 1H); $\delta(CH)_{pyridinium}$, 9.37(d, 1H); 9.29(d, 1H); 9.11(t, 1H); 8.46(t, 1H); 8.41(t, 1H); δ(CH=N), 8.31(s, 1H); δ(CONH), 8.11(s, 1H); $\delta(Ar\text{-}H)_{phenolic}$, 7.53(d, 1H); 7.17(t, 1H); 6.88(t, 1H); 6.83(d, 1H); δ(S-CH), 7.48(s, 1H); δ(HN-CH), 5.44(d, 1H); δ(S-CH), 5.16(d, 2H); δ(S-CH_a), 3.20(s, 1H); δ(S-CH_b), 3.08(s, 1H); δ(CH_2-N^+), 2.12(s, 2H); $\delta(C\text{-}CH_3)_a$, 1.48(s, 3H); $\delta(C\text{-}CH_3)_b$, 1.38(s, 3H). ^{13}C-NMR (δ value in ppm): δ(COOH), 175.97; δ(S-C=N), 171.89; δ(COO^-), 170.13;

δ(N-C=O), 164.32; δ(C-C=N), 164.19; δ(CONH), 163.42; δ(CH=N), 161.71; δ(Ar-C)$_{phenolic}$, 161.26(C$_1$), 118.72(C$_2$), 130.93(C$_3$), 122.54(C$_4$), 132.81(C$_5$), 116.32(C$_6$); δ(Ar-C)$_{pyridinium}$, 146.32(C$_1$), 128.71(C$_2$), 146.36 (C$_3$), 128.61(C$_4$), 146.23(C$_5$); δ(N-C=C)$_a$, 143.42; δ(N-C=C)$_b$, 137.83; δ(S-C-C), 131.12; δ(S-C-H), 121.98; δ(N-O-C), 83.82; δ(HN-CH), 59.40; δ(S-CH), 57.42; δ(N$^+$-CH$_2$), 51.32; δ(S-CH$_2$), 26.56; δ(O-C-CH$_3$), 22.37. Electronic spectra (λ_{max}, nm (ε in M^{-1} cm^{-1})) in DMSO: 486(34), 440(88), 346(150). ESI-Mass spectra, m/z: [C$_{19}$H$_{19}$N$_4$O$_7$S]$^+$ = 447.44, [C$_{29}$H$_{25}$N$_6$O$_8$PdS$_2$]$^+$ = 756.09, [C$_{36}$H$_{30}$N$_7$O$_9$PdS$_2$]$^+$ = 875.21, [C$_{39}$H$_{31}$N$_8$O$_9$PdS$_3$]$^+$ = 958.33, [C$_{58}$H$_{50}$N$_{12}$O$_{16}$PdS$_4$]$^+$ = 1405.77.

[Pd(SALCEFIXI)$_2$].3H$_2$O; Complex 5

Colour = Brown, Yield: 0.369g (88.07%); m.p.^{d} 290°C; Anal. Calcd.forC$_{46}$H$_{42}$N$_{10}$O$_{19}$PdS$_4$ (M$_\tau$ = 1273.28): C, 43.39; H, 3.30; N, 11.00. Found: C, 43.36; H, 3.26; N, 10.96; Molar conductance ($\Omega^{-1}cm^2mol^{-1}$): 4.4 in DMSO. Selected infrared absorption (KBr, cm^{-1}): ν(CH=N), 1610(s), ν(Pd-O), 440(w). ^{1}H-NMR (DRX-300 MHz, DMSO-d$_6$, 25°C) spectra (δ value in ppm): δ(COOH)$_{exocyclic}$, 11.18(s, 1H); δ(COOH), 10.94(s, 1H); δ(CH=N), 8.45(s, 1H); δ(CONH), 8.12(s, 1H); δ(S-CH), 7.49(s, 1H); δ(Ar-H)$_{phenolic,}$ 7.45(d, 1H); 7.18(t, 1H); 6.88(t, 1H); 6.84(d, 1H); δ(C-CH), 6.53(d, 1H); δ(HN-CH), 5.58(t, 1H); δ(CH=CH$_2$)$_a$, 5.26(d, 1H); δ(CH=CH$_2$)$_b$, 5.21(d, 1H); δ(S-CH), 5.14(d, 2H); δ(N-O-CH$_2$), 4.54(s, 2H); δ(S-CH$_2$)$_a$, 3.24(s, 1H); δ(S-CH$_2$)$_b$3.13(s, 1H); ^{13}C-NMR (δ value in ppm): δ(COOH), 173.64; δ(S-C=N), 171.93; δ(N-C=O), 164.8; δ(CONH), 164.43; δ(COOH)$_{exocyclic}$, 162.97; δ(CH=N), 161.22; δ(Ar-C)$_{phenolic}$, 161.29(C$_1$), 118.73(C$_2$), 130.74(C$_3$), 121.75(C$_4$), 132.66(C$_5$), 116.19(C$_6$); δ(N-C=C)$_a$, 143.38; δ(C-CH), 138.73; δ(C-C=C), 138.48; δ(S-C-H), 123.95; δ(N-C=C)$_b$, 122.18; δ(HC=CH$_2$), 117.92; δ(O-CH$_2$), 76.74; δ(HN-CH), 59.29; δ(S-CH), 58.41; δ(S-CH$_2$), 29.74. Electronic spectra (λ_{max}, nm (ε in M^{-1} cm^{-1})) in DMSO: 566(54), 438(94), 339(138). ESI-Mass spectra, m/z; [C$_5$H$_5$S]$^+$ = 99.47, [C$_6$H$_5$OS]$^+$ = 126.05, [C$_7$H$_7$NO$_2$S]$^+$ = 170.07, [C$_{10}$H$_8$N$_2$O$_3$S]$^+$ = 239.19, [C$_{10}$H$_9$N$_2$O$_4$S]$^+$ = 256.22, [C$_8$H$_5$N$_2$OPdS]$^+$ = 285.11, [C$_{10}$H$_7$N$_4$O$_5$S$_2$]$^+$ = 325.16, [C$_{10}$H$_7$N$_4$O$_4$S$_2$O^{17}]$^+$ = 326.16, [C$_{14}$H$_{10}$N$_2$O$_2$Pd]$^+$ = 344.29, [C$_{15}$H$_{12}$N$_4$O$_5$S$_2$]$^+$ = 397.43, [C$_{17}$H$_{14}$N$_5$O$_7$S$_2$]$^+$ = 467.44, [C$_{21}$H$_{12}$N$_5$O$_3$PdS$_2$]$^+$ = 551.61, [C$_{23}$H$_{15}$N$_5$O$_5$PdS]$^+$ = 577.65, [C$_{23}$H$_{17}$N$_5$O$_7$PdS$_2$]$^+$ = 643.84, [C$_{23}$H$_{24}$N$_5$O$_{11}$PdS$_2$]$^+$ = 718.02, [C$_{30}$H$_{29}$N$_6$O$_{12}$PdS$_2$]$^+$ = 839.14, [C$_{33}$H$_{24}$N$_7$O$_9$PdS$_3$]$^+$ = 868.05, [C$_{35}$H$_{25}$N$_9$O$_{13}$PdS$_3$]$^+$ = 982.48, [C$_{35}$H$_{26}$N$_{10}$O$_{12}$PdS$_4$]$^+$=1015.89.

[Pd(SALCEPHODO)$_2$].3H$_2$O; Complex 6

Colour = Dark brown, Yield: 0.147g (61.00%); m.p.^{d} 285°C; Anal. Calcd.forC$_{44}$H$_{46}$N$_{10}$O$_{17}$PdS$_4$ (M$_\tau$ = 1221.26): C, 43.27; H, 3.76; N, 11.46. Found: C, 43.22; H, 3.75; N, 11.43; Molar conductance ($\Omega^{-1}cm^2mol^{-1}$): 10.5 in DMSO. Selected infrared absorption (KBr, cm^{-1}): ν(CH=N),

1606(sh), ν(Pd-O), 440(w). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 10.95(s, 1H); δ(CH=N), 8.41(s, 1H); δ(CONH), 8.13(s, 1H); δ(S-CH)$_{ring}$, 7.48(s, 1H); δ(Ar-H)$_{phenolic,}$ 7.49(d, 1H); 7.18(t, 1H); 6.91(t, 1H); 6.86(d, 1H); δ(HN-CH), 5.57(t, 1H); δ(S-CH), 5.26(d, 2H); δ(C-CH_2), 4.19(s, 2H); δ(N-O-CH_3), 4.15(s, 1H); δ(C-O-CH_3), 3.37(s, 3H); δ(S-CH_a), 3.24(s, 1H); δ(S-CH_b), 3.15(s, 1H). ^{13}C-NMR (δ value in ppm): δ(S-C=N), 173.67; δ(COOH), 169.91; δ(CONH), 167.88; δ(N-C=O), 165.43; δ(C=N), 164.73; δ(CH=N), 162.22; δ(Ar-C)$_{phenolic}$, 161.32(C_1), 123.6(C_2), 133.8(C_3), 124.72(C_4), 123.68(C_5), 118.53(C_6); δ(C-N) $_{cyclic}$, 144.37; δ(C=C)$_{thia}$, 133.14; δ(S-C-H), 125.93; δ(N-C=C), 119.34; δ(C-CH_2-O), 71.87; δ(N-O-CH_3), 62.41; δ(C-O-CH_3), 60.87; δ(HN-CH), 59.17; δ(S-CH), 57.83; δ(S-CH_2), 25.82. Electronic spectra (λ_{max}, nm (ε in M^{-1} cm^{-1})) in DMSO: 496(72), 444(88), 346(146). ESI-Mass spectra, m/z: $[C_9H_{10}NO_4S]^+$ = 228.25, $[C_{22}H_{20}N_5O_7PdS_2]^+$ = 636.97, $[C_{29}H_{25}N_6O_8PdS_2]^+$ = 756.09, $[C_{34}H_{29}N_8O_9PdS_3]^+$ = 896.26, $[C_{44}H_{40}N_{10}O_{14}PdS_4]^+$ = 1167.53.

[Pd(SALCEFURO)$_2$].3H$_2$O; Complex 7

Colour = Black, Yield: 0.148g (61.67%); m.p.^{d} = 140°C; Anal. Calcd.for$C_{46}H_{44}N_8O_{21}PdS_2$ (M_τ= 1215.13): C, 45.46; H, 3.62; N, 9.22. Found: C, 45.41; H, 3.60; N, 9.17; Molar conductance ($\Omega^{-1}cm^2mol^{-1}$): 8.5 in DMSO. Selected infrared absorption (KBr, cm^{-1}): ν(CH=N), 1592(s), ν(Pd-O), 480(w). ^{1}H-NMR (DRX-300 MHz, DMSO-d_6, 25°C) spectra (δ value in ppm): δ(COOH), 11.11(s, 1H); δ(CH=N), 8.36(s, 1H); δ(CONH), 8.07(d, 1H); δ(Ar-H)$_{phenolic,}$ 7.58(d, 1H); 7.22(t, 1H); 6.89(t, 1H); 6.83(d, 1H); δ(Ar-H)$_{furan}$, 7.51(d, 1H); 6.42(t, 1H); 6.33(t, 1H); δ(HN-CH), 5.57(t, 1H); δ(S-CH), 5.28(d, 1H); δ(C-CH_2), 4.88(s, 2H); δ(N-O-CH_3), 4.15(s, 3H); δ(S-CH_a), 3.23(s, 1H); δ(S-CH_b), 3.14(s, 1H). ^{13}C-NMR (δ value in ppm): δ(COOH), 169.94; δ(CONH), 166.54; δ(N-C=O), 165.47; δ(C=N), 165.21; δ(CH=N), 162.12; δ(Ar-C)$_{phenolic}$, 162.32(C_1), 121.71(C_2), 132.84(C_3), 123.67(C_4), 135.63(C_5), 119.23(C_6); δ(N-CO-O), 158.33; δ(C-C=C), 132.38; δ(N-C=C), 121.27; δ(N-O-CH_3), 62.94; δ(HN-CH), 58.63; δ(S-CH), 57.92; δ(C-CH_2), 56.1; δ(S-CH_2), 27.32. Electronic spectra (λ_{max}, nm (ε in M^{-1} cm^{-1})) in DMSO: 482(45), 430(80), 350(122). ESI-Mass spectra, m/z: $[C_{14}H_{12}N_3O_6S]^+$ = 350.33, $[C_{23}H_{19}N_4O_9PdS]^+$ = 633.90, $[C_{30}H_{24}N_5O_{10}PdS]^+$ = 753.02, $[C_{39}H_{32}N_7O_{15}PdS_2]^+$ = 1009.26, $[C_{46}H_{38}N_8O_{18}PdS_2]^+$ = 1161.39.

Characterization of Ligands

ESI-MS spectra of Ligands

The C, H, N analytical data for the synthesized ligands were in full agreement with the proposed empirical formula. ESI-Mass spectra of all the seven ligands exhibit several peaks depending upon the fragmentation pattern. Isotopic pattern of molecular ion peak gave clear evidence about molecular mass. The ESI-MS spectra (Figure. 1 and Figure. 2of supplementary material) of one of

the ligand, SALCEFIXI exhibit peaks at 170.06; 203.06; 279.21; 293.23; 391.35; 392.36; 395.13; 459.24; 486.17; 487.17; 516.19; 543.21; 558.24; 559.25 attributed for $[C_7H_7NO_2S]^+$; $[C_{10}H_7N_2OS]^+$; $[C_{11}H_9N_3O_4S]^+$; $[C_{11}H_9N_3O_5S]^+$; $[C_{15}H_{12}N_4O_5S_2]^+$; $[C_{15}H_{12}N_4O_4.O^{17}S_2]^+$; $[C_{15}H_{12}N_3O_6S_2]^+$; $[C_{18}H_{15}N_5O_6S_2]^+$; $[C_{20}H_{15}N_5O_6S_2]^+$; $[C_{20}H_{15}N_5O_5S_2.O^{17}]^+$; $[C_{21}H_{17}N_5O_7S_2]^+$; $[C_{23}H_{18}N_5O_5S_2.O^{17}O^{18}]^+$; $[C_{23}H_{19}N_5O_7S_2.O^{17}]^+$; $[C_{23}H_{19}N_5O_7S_2.O^{18}]^+$. The peak observed at 391.35, 392.36, 486.17, 487.17 were probably due to the isotopic pattern of the fragments shown in the Figure.2. However peaks at 558.24 and 559.25 appeared due to the isotopic pattern of the molecular ion. Similar ESI-MS assignment and fragmentation pattern were proposed in other ligands which gave idea about molecular ion peak.

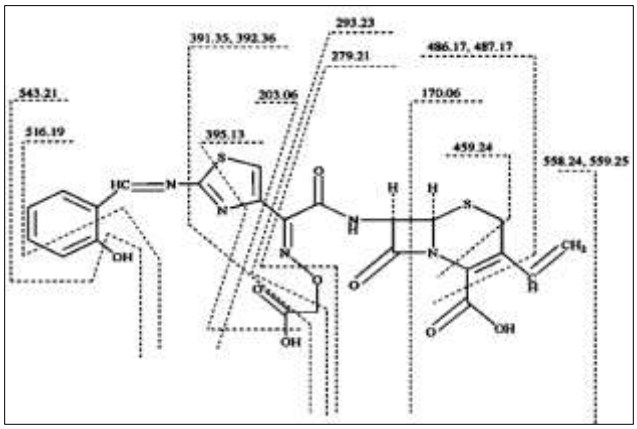

Figure 2.ESI-MS fragmentation pattern of SALCEFIXI Schiff base ligand

FT-IR spectra of ligands

FT-IR spectra of ligands display a sharp signal, between 1612-1635 cm^{-1} attributed to ν (HC=N) which was not present in the precursor antibiotic. All the ligands exhibit significant bands at about 3500 cm^{-1}, 3300 cm^{-1}, 1750 cm^{-1} and 1680 cm^{-1} assigned to ν (OH), ν (N-H), ν (C=O) and ν (CONH) respectively.[20, 21] These bands are approximately at the same place as it was observed in the antibiotic precursors.

^{1}H-NMR spectra of ligands

^{1}H-NMR of the ligands exhibit a signal at about δ 11.00 ppm for 1H, assigned for -COOH group. Another signal at δ 8.15 ppm for 1H was assigned for one azomethine (-CH=N) proton. It is confirmatory evidence for the formation of Schiff base. All the seven Schiff base ligands exhibits singlet at ~ δ 8.00 ppm for one proton assigned to CONH group. In SALCEPHAL a triplet at δ 7. 44 ppm for two protons, a triplet at δ 7.27 ppm for one proton and a doublet observed at δ 7.26 ppm for two protons was attributed to the phenyl group present. All the ligands exhibit multiplet between δ 7.53 – 6.75 ppm assigned for an aromatic ring of phenolic moiety. A signal at about δ

5.50 ppm was anticipated for HN-CH group present, however in SALCEPHAL ligand this was observed at δ 6.68 ppm. The signal at δ 5.10 ppm was attributed to phenolic –OH. A doublet observed between δ 4.89 - 5.26 ppm was attributed for S-CH group present. Two signals observed at about ~ δ 3.20 ppm were assigned to S-CH_a and S-CH_b of the S-CH_2 group. In SALCEFTRI ligand one more signal was observed for S-CH_2 group. The SALCEPHOT, SALCEFTRI, SALCEFTAZI, SALCEFIXI Schiff base ligands have displayed one signal at about ~ δ 7.40 ppm attributed to S-CH group present. The Schiff base ligand SALCEPHOT, SALCEFIXI, SALCEPHODO, SALCEFURO exhibit a doublet in between δ 4.14 - 4.83 ppm assigned for the C-CH_3 group. However, a singlet observed at about ~ δ 4.00 ppm in SALCEPHOT, SALCEFTRI, SALCEPHODO and SALCEFURO was assigned to O-CH_3 group. In SALCEPHODO ligand, one more signal was observed for O-CH_3 group. The Schiff base SALCEPHAL and SALCEFTAZI exhibits one signal at δ 1.71 ppm and two signals at ~δ 1.40 ppm for the three protons of the methyl group. Apart from these signal SALCEPHAL exhibited one more signal at δ 4.45 ppm assigned for CH-C=O group, SALCEPHOT exhibited a signal at δ 2.11 ppm assigned for OCO-CH_3 group, SALCEFTRI exhibited signals at δ 8.00 ppm and δ 2.49 ppm for one and three proton each assigned for (-CONH) and N-CH_3 group proton and SALCEFTAZI ligand exhibited a doublet at δ 9.30 ppm, a triplet at δ 8.40 ppm for one proton each and a singlet δ 2.09 ppm for two protons attribute for $(CH)_{pyridinium}$ and CH_2N^+ group proton. In SALCEFIXI Schiff base ligand a singlet at δ 11.10 ppm, a doublet at δ 6. 49 ppm and a doublet at ~ δ 5.20 ppm was observed, which were assigned for -COOH, C-CH and CH=CH_2 group protons respectively. In SALCEPHODO ligand a signal was observed at δ 7.46 ppm assigned to $(S\text{-}CH)_{ring}$ similarly SACEFURO ligand exhibit a doublet at δ 7.48 ppm and a triplet at δ 6.32 ppm for one proton each attributed for the aromatic proton of furan.[20]

^{13}C-NMR spectra of ligands

$^{13}C\{^1H\}$-NMR spectra of Schiff base ligands exhibit a signal in between δ 167.00 – δ163.22 ppm assigned for CO-NH carbon. However, in SALCEPHAL ligand this signal was shifted down field and observed at δ 175.20 ppm, probably due to the absence of the C=N group in the vicinity. The signal observed in between δ 173.41 - δ 171.42 ppm was attributed to S-C=N carbon. However, this signal was absent in SALCEPHAL and SALCEFURO ligands. A signal observed between δ 169.88 - δ 166.71 ppm was assigned to COOH carbon. One signal observed between δ 166.30 – δ 164.20 ppm was attributed to N-C=O carbon. A signal observed at ~ δ 160 ppm assigned for azomethine carbon, was confirmatory evidence for the formation of the Schiff base. The signals observed between δ 162.12 – δ 116. 00 ppm was assigned to phenolic-C. A signal observed at ~ δ

170 ppm in SALCEPHOT and SALCEFTAZI was attributed for O=C-O carbon. However, this signal was upfield shifted in SALCEFURO and appeared at δ 158.16 ppm probably due to presence of CH=N group in the vicinity. A signal observed at ~ δ 164.20 ppm in SALCEPHOT, SALCEFTRI, SALCEFTAZI and SALCEPHODO was attributed to C=N group carbon. A new signal observed at ~ δ 131.00 ppm in SALCEPHOT, SALCEFTAZI, SALCEPHODO and SALCEFURO was assigned for C=C group carbon of thiazine ring. However, this signal was downfield shifted in SALCEFTRI and SALCEFIXI and appeared at δ 143.21 ppm and δ 138.20 ppm, respectively. A signal observed in SALCEPHOT, SALCEFTRI, SALCEFTAZI, SALCEFIXI and SALCEPHODO at ~ δ 143.00 ppm was assigned for N-C=C group for thiazole ring. A signal observed at ~ δ 123.80 ppm in SALCEPHOT, SALCEFTRI, SALCEFTAZI, SALCEFIXI and SALCEPHODO was attributed for S-CH carbon group. A signal observed at ~ δ 121.00 ppm was assigned for N-C=C carbon of thiazine moiety. However, this signal was downfield shifted in SALCEFTAZI and appeared at δ 143.12 ppm probably due to the presence of carboxylate anion one side and pyridiniumcation on the other. In SALCEFEXI and SALCEPHODO a signal was observed at ~ δ 75.00 ppm were assigned to O-CH_2 carbon. In SALCEPHOT, SALCEFTRI, SALCEPHODO, and SALCEFURO a signal was observed at ~ δ 62.00 ppm attributed to O-CH_3 carbon. However, in SALCEPHODO one more signal was observed at δ 60.00 ppm for the same carbon assigned for another methoxy carbon. A signal observed at ~ δ 58.00 ppm was attributed for carbon attached to azetidine-2-one moiety. In SALCEPHAL a signal observed at δ 71.40 ppm was assigned to the –CH carbon flanked by an azomethine group on one side and amide groups on the other. A signal observed at ~ δ 58.00 ppm was assigned to CH group carbon joining the thiazine and azetidine ring. This signal was found upfield shifted in the SALCEPHAL and appeared at δ 53.30 ppm, probably due to the presence of a C=O group of the amide in the vicinity. A signal observed at δ 55.00 ppm in SALCEPHOT and SALCEFURO was attributed for -CH_2 carbon linked with thiazine ring. This signal was upfield shifted and appeared at δ 51.12 ppm probably due to the presence of pyridiniumcation in the vicinity. Another signal observed in between δ 29.70 -δ 20.20 ppm was attributed for S-CH_2group of thiazine ring. A signal observed in SALCEPHAL at δ 136.10 ppm was attributed to the C-CH_3 group carbon of thiazine ring. The four signals observed between δ 147.30 - δ 126.80 ppm in SALCEPHAL were attributed for phenyl group carbon. A signal observed in SALCEPHOT and SALCEFTAZI at ~ δ 21.70 ppm was assigned for methyl group carbon of OCO-CH_3 attached to thiazine ring. A signal observed at δ 191.16 ppm in SALCEFTRI was attributed for –C=O group of azetidine ring. A signal observed at δ 162.12 ppm in SALCEFTRI was assigned for N-C=N

carbon of triazine ring. A signal observed at δ 161.60 ppm in SALCEFTRI was attributed for -CO-NH carbon of triazine ring. A signal observed at δ 37.26 ppm in SALCEFTRI was attributed for -N-CH_3 carbon attached to triazine ring. A signal observed at δ 26.41 ppm in SALCEFTRI was attributed for S-CH_2 carbon sandwiched between thiazine and triazine ring. The three signals observed between δ 146.02 - δ 128.52 ppm in SALCEFTAZI were assigned for pyridinium carbon. A signal observed at δ 83.52 ppm in SALCEFTAZI was assigned to C_2 carbon of isobutyric acid. A signal observed at ~ δ 175.00 ppm in SALCEFTAZI and SALCEFIXI was assigned to the carboxylic carbon of isobutyric acid and oxymeacetic acid, respectively. Two signals observed at δ 138.35 ppm and δ 117.20 ppm in SALCEFIXI were assigned for CH and CH_2 carbon of CH=CH_2 group attached with thiazine ring.[20-22] Thus on the basis of C,H,N analyses, ESI-MS, FT-IR, ^{1}H-NMR, ^{13}C{^{1}H}-NMR and HETCOR-NMR probable structure of the ligands were suggested as below in Figure 3 – Figure 9.

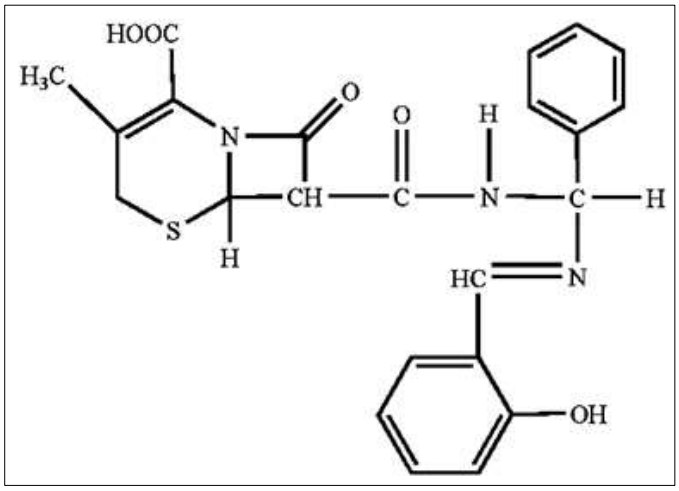

Figure 3.Schiff base of Cephalexin (SALCEPHOT)

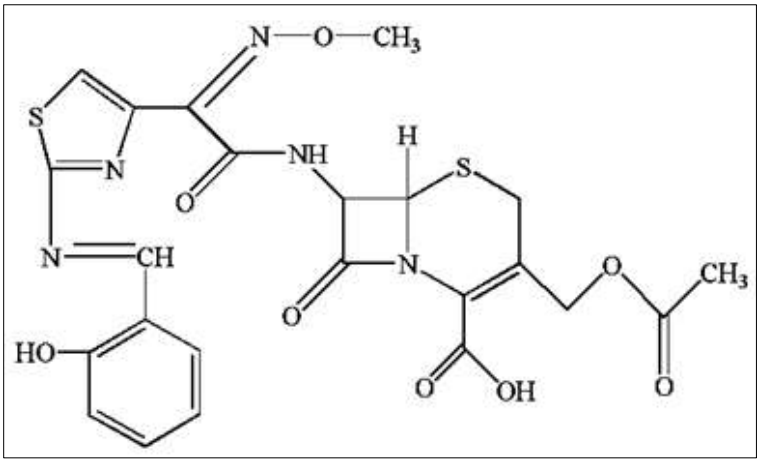

Figure 4.Schiff base of Cephotaxime (SALCEPHAL)

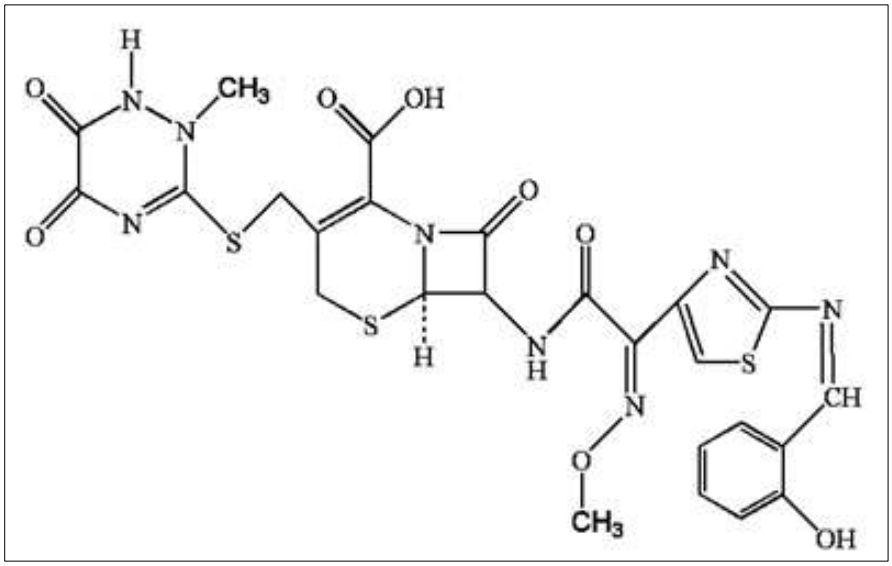

Figure 5.Schiff base of Ceftriaxone (SALCEFTRI)

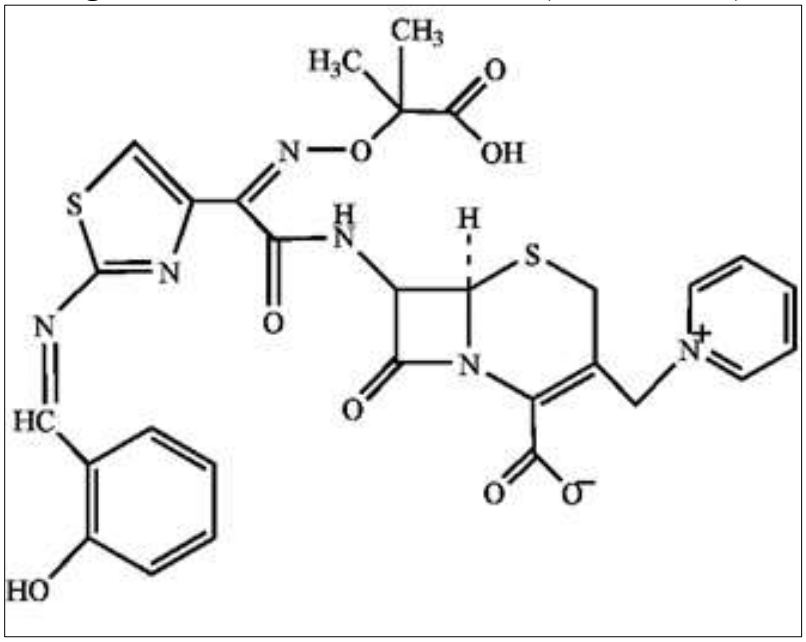

Figure 6.Schiff base of Ceftazidime (SALCEFTAZI)

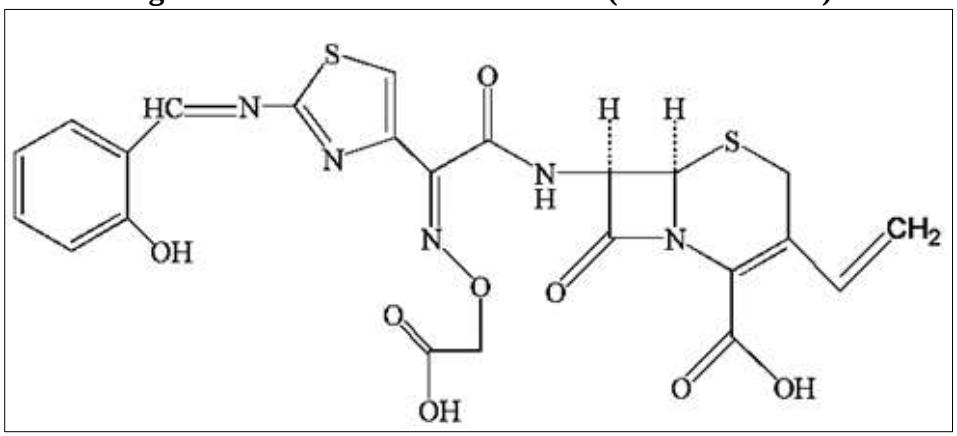

Figure 7.Schiff base of Cefixime (SALCEFIXI)

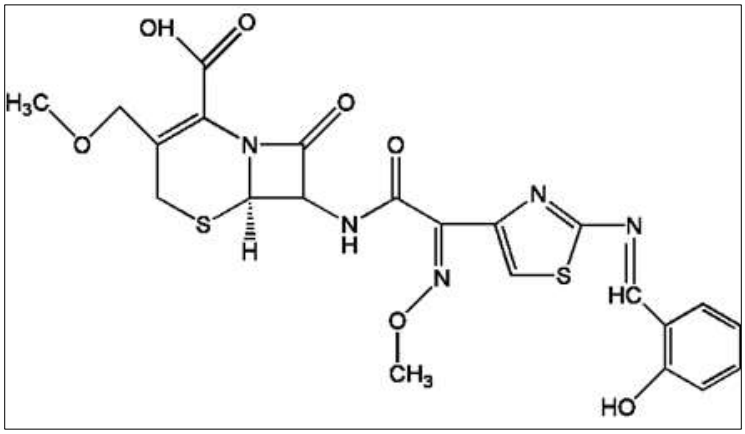

Figure 8.Schiff base of Cefpodoxime (SALCEPHODO)

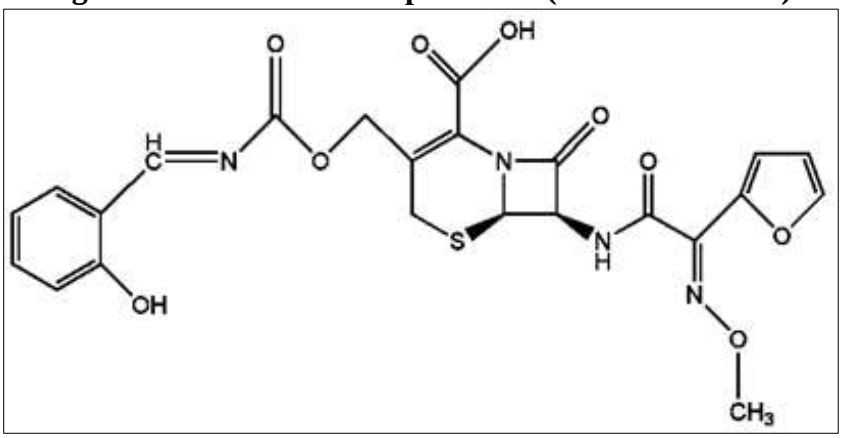

Figure 9.Schiff base of Cefuroxime (SALCEFURO)

Characterization of Complexes

The stoichiometries of the complexes were in agreement with elemental analyses data. The molar conductance of complexes is in range 3 – 13 Ω^{-1} cm^2 mol^{-1} indicating their non-electrolytic nature.

ESI-MS spectra of Complexes

ESI-Mass spectra of all the seven complexes exhibit several peaks depending upon the fragmentation pattern. Isotopic pattern of molecular ion peak gave clear evidence about molecular mass. The ESI-MS spectra of $[Pd(SALCEFIXI)_2].3H_2O$, Complex 5, (Figure. 3of supplementary material)exhibit peaks at 99.47; 126.05; 170.07; 239.19; 256.22; 285.11; 325.16; 326.16; 344.29; 397.43; 467.44; 551.61; 577.65; 643.84; 718.02; 839.14; 868.05; 982.48; 1015.89 attributed for $[C_5H_5S]^+$; $[C_6H_5OS]^+$; $[C_7H_7NO_2S]^+$; $[C_{10}H_8N_2O_3S]^+$; $[C_{10}H_9N_2O_4S]^+$; $[C_8H_5N_2OPdS]^+$; $[C_{10}H_7N_4O_5S_2]^+$; $[C_{10}H_7N_4O_4S_2O^{17}]^+$; $[C_{14}H_{10}N_2O_2Pd]^+$; $[C_{15}H_{12}N_4O_5S_2]^+$; $[C_{17}H_{14}N_5O_7S_2]^+$; $[C_{21}H_{12}N_5O_3PdS_2]^+$; $[C_{23}H_{15}N_5O_5PdS]^+$; $[C_{23}H_{17}N_5O_7PdS_2]^+$; $[C_{23}H_{24}N_5O_{11}PdS_2]^+$; $[C_{30}H_{29}N_6O_{12}PdS_2]^+$; $[C_{33}H_{24}N_7O_9PdS_3]^+$; $[C_{35}H_{25}N_9O_{13}PdS_3]^+$; $[C_{35}H_{26}N_{10}O_{12}PdS_4]^+$. The peak observed at 325.16 and 326.16 was probably due to isotopic pattern of the fragments $[C_{10}H_7N_4O_5{}^{16}S_2]^+$ and $[C_{10}H_7N_4O_4{}^{16}S_2O^{17}]^+$(Figure. 10). Similar ESI-MS assignment and

fragmentation pattern were proposed for other complexes which gave idea about molecular ion peak.

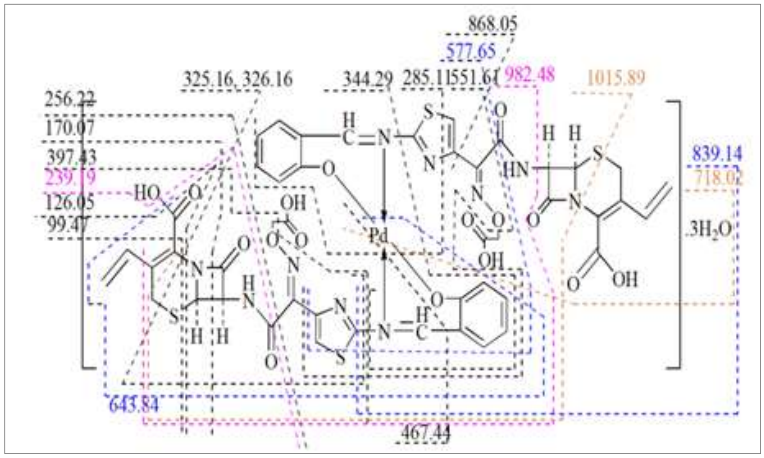

Figure 10.ESI-MS Fragmentation pattern of complex-5

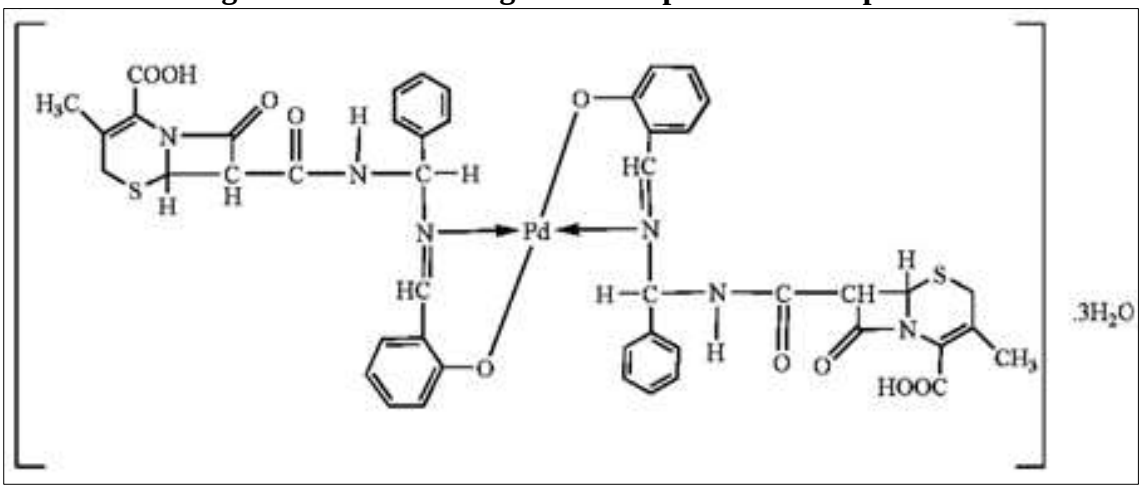

Figure 11.Complex-1

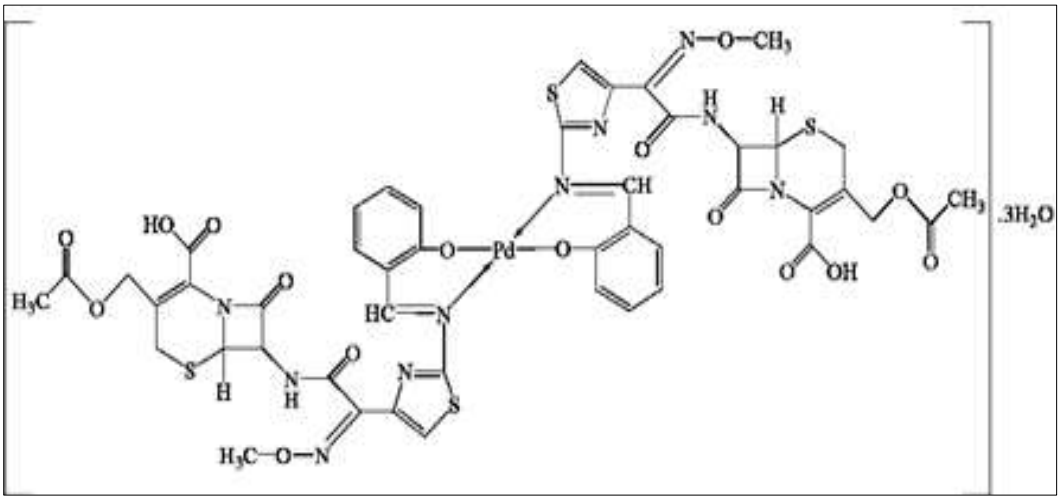

Figure 12.Complex-2

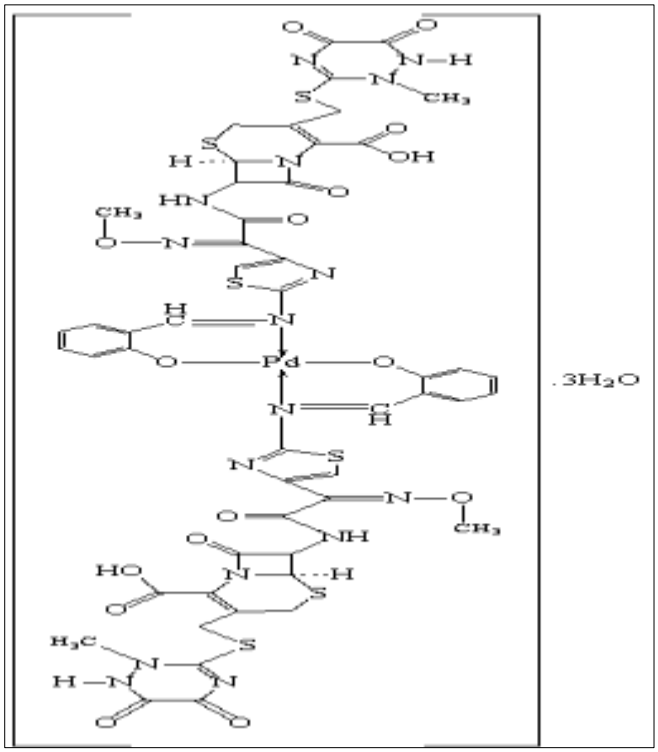

Figure 13.Complex-3

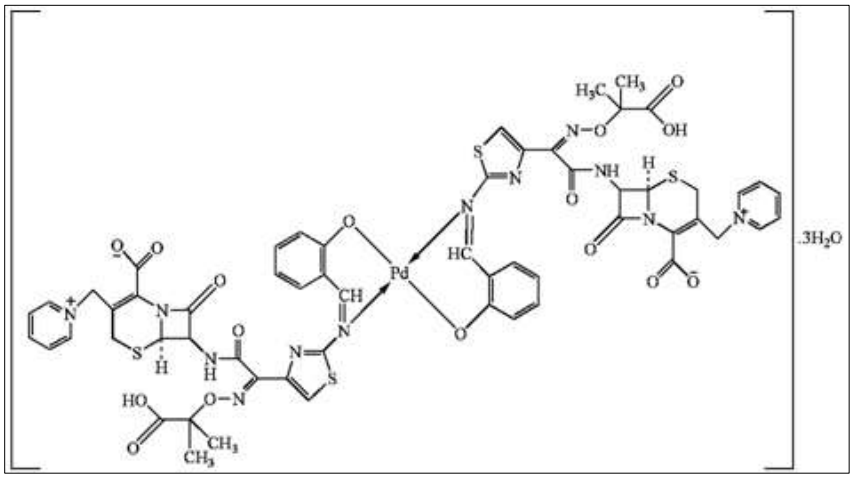

Figure 14.Complex-4

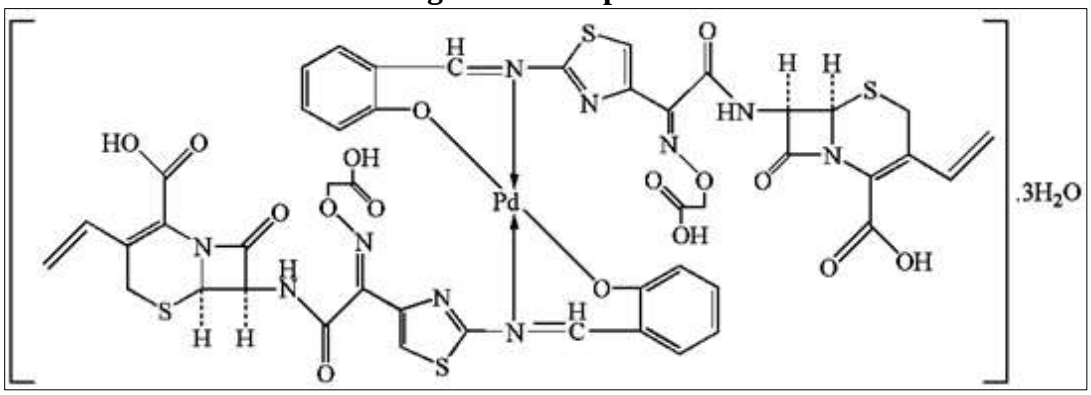

Figure 15.Complex-5

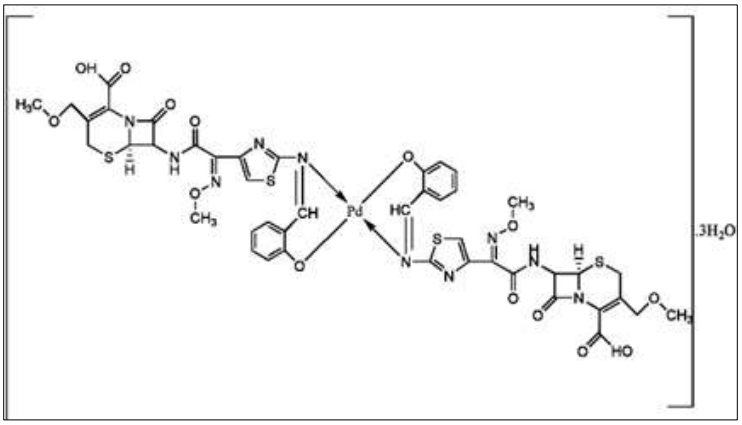

Figure 16.Complex-6

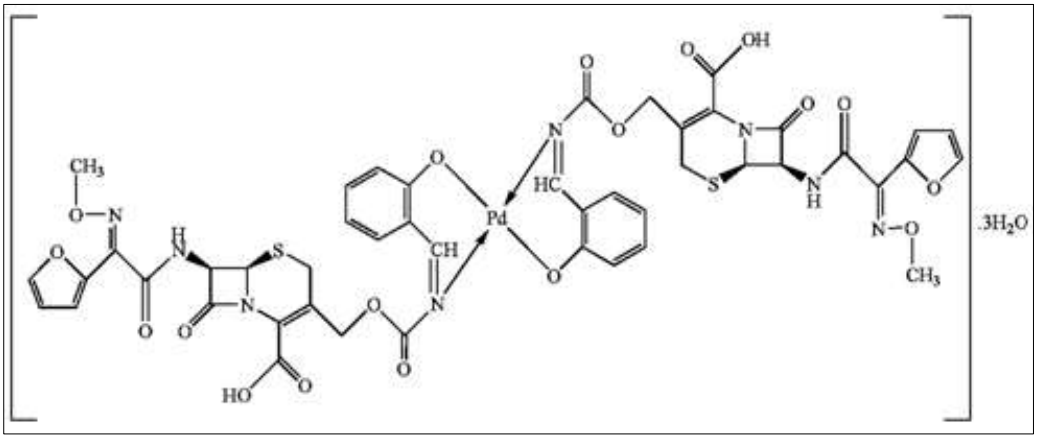

Figure 17.Complex-7

FT-IR Spectra of Complexes

A strong peak appeared in between 1635 – 1612 cm^{-1} in the ligands assigned for azomethine (–CH=N) group, was shifted downwards and appeared in between 1620 – 1592 cm^{-1} in the complexes, confirming coordination of metal to azomethine nitrogen.[23, 24] A band of medium to low intensity appeared between 3520 – 3325 cm^{-1}, assigned for ν(OH), was vanished completely in the complexes and at the same time a new peak of medium intensity was appeared between 480 – 440 cm^{-1}, was assigned for new Pd-O bond, indicates the bonding of metal to the oxygen by removal of phenolic-H.

Electronic spectra

Magnetic susceptibility data shows diamagnetic behavior of the complexes. Electronic spectra of the complexes exhibit three bands attributed to the three d-d spin allowed transition corresponding to the three lower lying d-levels to the empty $d_{x^2-y^2}$. The three d-d bands obtained are in the region 464 - 566 nm, 424 - 444 nm and 334 - 380 nm are attributed to $^1A_{1g} \rightarrow {}^1A_{2g}$ (ν_1); $^1A_{1g} \rightarrow {}^1B_{1g}$ (ν_2)

and $^1A_{1g} \rightarrow {}^1E_g$ (ν_3) transitions respectively. These assignments suggest a square planar geometry around Pd (II) metal ion in the complexes.[25]

^{1}H-NMR spectra of Complexes

A singlet observed at ~ δ 8.15 ppm, assigned for –CH=N group was down field shifted in all the complexes and appeared at ~ δ 8.45 ppm, confirming the transfer of one lone pair electron from nitrogen to metal and coordination of azomethine-N to metal. A signal appeared at ~ δ 5.00 ppm in the ligands, disappeared in the complexes confirming the removal of phenolic-H facilitating the coordination of ligand from oxygen to metal and formation of the Pd-O bond.

^{13}C-NMR spectra of Complexes

A signal observed at ~ δ 160.50 ppm in ligands assigned for –CH=N group was downfield shifted in all the complexes and appeared at ~ δ 162.00 ppm, confirming the transfer of one lone pair electron from nitrogen to metal and coordination of azomethine-N to metal.

HETCOR NMR of ligand and complex

One ligand SALCEFIXI and its complex **5** was studied by {^{13}C-^{1}H}^{2}D-NMR (HETCOR)(Figure. 4 and 5 in supplementary material). ^{2}D-NMR of the complex exhibit signal observed at δ 161.22 ppm, assigned for azomethine carbon was connected with H at δ 8.45 ppm. The signal at δ 138.35 ppm in ligand assigned for the carbon attached to thiazine ring was connected with H at δ 6.49 ppm. The signal observed at δ 138.73 ppm for the carbon attached to thiazine ring was connected with H at δ 6.53 ppm. A signal at δ 123.88 ppm in ligand assigned for the carbon for a thiazole ring was connected with H at δ 7.48 ppm. The signal observed at δ 123.95 ppm for the thiazole carbon was connected with H at δ 5.14 ppm. Four signals observed at about δ 118.00, δ 130.00, δ 121.00 and δ 132.00 in the ligand and complexes assigned for phenolic carbon C_2, C_3, C_4 and C_5 were found connected with protons at about δ 6.80, δ 7.10, δ 7.40 and δ 6.80 ppm. A signal observed at δ 117.00 ppm assigned for alkene carbon was found tied with two protons at δ 5.25 and δ 5.20 ppm. A signal observed at δ 76.00 ppm in the ligand and complex assigned for O-CH_2 group flanked by C=N and COOH group was found connected with the two protons at about δ 4.50 ppm. A signal observed at δ 59.00 ppm in the ligand and complex assigned to a CH group of azetidine ring connected with the proton at δ 5.50 ppm. A signal observed at δ 58.30 ppm in the ligand and complex assigned for CH group present between azetidine and thiazine ring connected with the proton at about δ 5.10 ppm. A signal observed at δ 29.0 ppm in the ligand and complex assigned for CH_2 group of thiazine ring connected with two protons at about δ 3.20 and δ 3.10 ppm.[26]

TGA analysis

Complex **5** was also studied by Thermogravimetric method (Figure. 6 in supplementary material). TGA showed weight loss in four steps. First loss of weight takes place between 25°C - 118°C, accompanied by a weight loss of 4.35% (expected 4.24%), easily attributable for the entire three water molecules. The maximum loss takes place at 58.25°C. In second step weight loss occurs between 119°C - 342°C, accompanied with a weight loss of 30.38% (expected 30.97%) assigned for $C_{16}H_{14}N_2O_6S_2$ moiety. In this step maximum weight loss occurs at 271.99°C. In third step weight loss occurs between 343°C - 480°C, accompanied with a weight loss of 31.32% (expected 30.65%) assigned for $C_{14}H_{10}N_6O_4S_2$ moiety. Maximum weight loss occurs at 383.48°C. In fourth step weight loss occurs between 481°C - 578°C, accompanied with a weight loss of 4.65% (expected 7.069%) assigned for $C_2H_2O_4$ moiety. Maximum weight loss in this step occurs at 535.77°C. Lastly a residue of 26.00% was obtained (expected 27.06%) assigned for $C_{14}H_{10}N_2O_2Pd$, which was actually bis(2-salcylidimine)palladium chelate ring moiety.[27, 28]

Biological activity

Antibacterial activity and Structure activity relationship

Antibacterial activity results in the form of zone inhibition were measured in mm and presented in Table1. Cephalexin is the first generation antibiotic containing phenylmethanamine group along with CONH attached to the side chain at 7th position, is active against both ***E. coli*** and ***S. aureus***. Introduction of azomethine group exhibited considerable effect on activity as demonstrated by the increased activity in the Schiff base. However, chelation of Schiff base with Pd (II) exhibits more effect on activity in ***S. aureus*** in comparison to ***E. coli***. Cephotaxime is a third generation drug consists of (Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamide moiety as R^1 at 7th and methyl acetate as R^2 at 3rd position exhibit quite good activity against ***E. coli*** and ***S. aureus***. The addition of azomethine group shows pronounced effect on the activity of Schiff base particularly against ***S. aureus***. However, on chelation with Pd (II) probably increased in lipophilicity expressed a remarkable increase in activity against both the microorganism particularly in ***S. aureus.*** Ceftriaxone is a third generation antibiotic containing (Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamide moiety as R^1 at 7th position and 1,2-dihydro-2-methyl-3-(methylthio)-1,2,4-triazine-5,6-dione moiety as R^2 nucleus exhibit good activity against both the bacteria. Introduction of azomethine group exhibit little impact on activity against ***E. coli*** but good increase in activity against ***S. aureus***. However, chelation of Schiff base drug with Pd (II) exhibit good activity against the both bacteria. Ceftazidime is also a third generation drug containing 2-{amino-(Z)-2-(2-aminothiazol-4-yl)-2-(hydroxyimino)acet}-2-methylpropanoic acid as R^1 and methyl

pyridinium group as R^2, was quite active against both the bacteria. Its Schiff base and Pd (II) chelate activity increases considerably but the increase in activity was much higher in the case of ***S. aureus***. Cefixime is a third generation drug consisting 2-(amino (Z)-2-(2-aminothiazol-4-yl)-2-(hydroxyimino)acet)acetic acid as R^1 and $CH=CH_2$ moiety as R^2, found active on ***E. coli***, but it was inactive against ***S. aureus***. Introduction of azomethine group and chelation with Pd (II) have marked effect on antibacterial activity against ***E. coli***, but surprisingly, both Schiff base and Pd (II) chelate were found inactive against ***S. aureus***. Cefpodoxime is another third generation broad spectrum antibiotic which consist of (Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamide as R^1 and methoxy methane moiety as R^2, is quite active against the both organism. Introduction of azomethine group and chelation with Pd (II) have obvious effect on antibacterial activity against both ***E. coli*** and ***S. aureus***. Another drug Cefuroxime is a second generation drug containing (E)-2-(furan-2-yl)-2-methoxyiminoacetamide as R^1 and methyl carbamate moiety as R^2 is quite active against the both bacteria. Introduction of azomethine group and chelation with Pd (II) demonstrated noticeable effect on the inhibition zone in both the bacteria.

Table 1: Antibacterial screening against *Escherichia coli* and *Staphylococcus aureus.*

	Compounds	***Diameter of inhibition zone(in mm.) ± SEM**		**MIC (µg/mL)**	
		E. coli	***S. aureus***	***E. coli***	***S. aureus***
1a.	Cephalexin drug	24±1.5	22±0.8	-	-
1b.	SALCEPHAL	26±1.2	28±0.8	-	-
1.	$[Pd(SALCEPHAL)_2].3H_2O$	29±0.8	34±1.5	0.35	0.86
2a.	Cephotaxime drug	23±0.5	27±1.2	-	-
2b.	SALCEPHOT	26±1.5	34±0.5	-	-
2.	$[Pd(SALCEPHOT)_2].3H_2O$	32±1.5	38±1.5	0.48	0.94
3a.	Ceftriaxone drug	24±0.8	24±0.8	-	-
3b.	SALCEFTRI	25±0.8	29±1.0	-	-
3.	$[Pd(SALCEFTRI)_2].3H_2O$	30±0.5	34±1.2	0.42	0.67
4a.	Ceftazidime drug	26±0.9	20±0.9	-	-
4b.	SALCEFTAZI	29±1.2	24±0.5	-	-
4.	$[Pd(SALCEFTAZI)_2].3H_2O$	34±1.5	34±0.9	0.44	0.78
5a.	Cefixime drug	25±0.8	-	-	-
5b.	SALCEFIXI	30±0.5	-	-	-
5.	$[Pd(SALCEFIXI)_2].3H_2O$	35±1.2	-	0.39	-
6a.	Cefpodoxime drug	21±0.8	24±1.5	-	-
6b.	SALCEPHODO	31±1.5	30±1.2	-	-
6.	$[Pd(SALCEPHODO)_2].3H_2O$	35±0.9	38±0.8	0.48	0.87
7a.	Cefuroxime drug	22±1.2	32±1.5	-	-
7b.	SALCEFURO	28±1.5	36±0.8	-	-
7.	$[Pd(SALCEFURO)_2].3H_2O$	36±1.5	39±1.2	0.39	0.97

8.	DMSO (solvent)	05±1.0	06±1.0	-	-
9.	$Pd(CH_3COO)_2$	04± 1.5	05±1.2	-	-

*Values as mean ±Standard Error Mean.

Minimum Inhibitory Concentration (MIC)

Since the appearance of resistance is common in pathogen, it lays the responsibility on investigator to report, an antibiotic sensitivity pattern accurately and rapidly, at reasonable cost.[29]Seven complexes which have shown promising antibacterial activity were selected for MIC evaluation. A commonly used method, Successive Dilution Method was employed for MIC evaluation as described earlier.[30] MIC is the concentration of the highest dilution tube, in which bacterial growth was absent and results are presented in Table 1. Complex **1** was the most active to inhibit bacterial growth at 0.35 µg/mL for E. *coli* and for *S. aureus*, complex **3** was observed as most active at 0.67µg/mL.

CONCLUSION

Seven Schiff bases were prepared by equimolar reaction of different Cephalosporin antibiotics viz. Cephalexin, Cephotaxime, Ceftriaxone, Ceftazidime, Cefixime, Cefpodoxime and Cefuroxime. The resulting Schiff bases SALCEPHAL, SALCEPHOT, SALCEFTRI, SALCEFTAZI, SALCEFIXI, SALCEPHODO and SALCEFURO on reaction with $(CH_3COO)_2Pd$ in 1:2 molar ratio yielded seven new complexes. These complexes were square planar and coordination was observed through the azomethine-N and phenolic–O of the salcylidimine moiety. All the complexes and Schiff bases have exhibited good antibacterial activity against ***E. coli*** and ***S. aureus,*** except complex **5** and **SALCEFIXI** Schiff base, which were actually inactive against ***S. aureus.*** It means, introduction of azomethine group and chelation with Pd (II) have no reasonable effect on antibacterial activity of the Cefixime drug against *S. aureus*, due to which **SALCEFIXI** and its complex were still inactive. It has been observed that biological activity is not a conglomeration of several toxophoric functions but only synergic effect is observed in a bigger molecule rather than the additive effect. Minimum inhibitory concentrations (MIC) of complexes were in between 0.35 - 0.48 µg/mL for *E. coli* and between 0.67 - 0.97 µg/mL for *S. aureus*. It is pragmatic to state that the introduction of the azomethine group in most cases result in Schiff bases with increased biological activity and chelation of these Schiff bases with Palladium has shown optimistic results. Thus metallo antibiotics may pave a new way to achieve relatively good biological activity in the future and may serve as the new alternative to inhibit the growth of resistant pathogens.

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