Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research

J. Chem. Pharm. Res., 2011, 3(5):390-398

ISSN No: 0975-7384
CODEN(USA): JCPRC5

Synthesis, characterization and evaluation of derivative of Ciprofloxacin (1-cyclopropyl-6-fluoro-4-oxo-7-[4-(phenyl carbonyl) piperazin-1-yl]-1, 4-dihydroquinoline-3-carboxylic acid) and their complexes

Y. M. Thakre* and M. D. Choudhary

**Department of Applied Chemistry of Engineering, DMIETR, Sawangi, Wardha*
Department of Applied Chemistry of Engineering, BDCOE, Sevagram, Wardha

ABSTRACT

Derivatives and their complexes from the ciprofloxacin fluoroquinoline family were synthesized, tested for antibacterial activity.The structure of derivative and their complex shows good antibacterial activity for the diagnostic aspects. Several reports have highlighted the interest of increasing the lipophilicityto improve the antitumor efficiency (2).These studies have led us to synthesize ciprofloxacin derivatives and to evaluate their activity by complex formation with metal ions. With an easy and cost-efficient procedure, derivatives of ciprofloxacin were prepared and yield had excellent .FTIR,Element Analysis, NMR analysis has been used to characterize the newly isolated complexes. This thesis intends to combine ciprofloxacin with metal ion, with the aim to improve the antibacterial activity. TheFTIR spectra of the isolated complexes suggest that ciprofloxacin derivative is act as bidentate ligands through the ring carbonyl oxygen atom and one of the oxygen atoms of the Carboxylic group. Derivative 06 showed enhanced activities than ciprofloxacin against all gram-positive and gram negative organisms likewise 2 & 5 showed highest activity against Pseudomonas spp. moreover 2 exhibited better activity against Salmonella spp, Salmonella typhi, Salmonella typhi Para-A, Salmonella typhi Para-B and Shigalla dysenteriae.

Author Keywords: Fluoroquinolines; Synthesis; Antimicrobial activity.

INTRODUCTION

Generally ciprofloxacin in THF was reacted with ciprofloxacin by simple substitution reaction with acyl chloride in the presence of trietyl amine as base to afford the acrylate derivative in moderate excellent yields. The structure of proposed derivative of ciprofloxacin and their complexes was determine by state of art spectrophotometric techniques like H-NMR, and IR.The structure of derivative and their complex shows good antibacterial activity for the diagnostic

aspects. During the bioassay we randomly screened the same compound for their antifungal potential .Ciprofloxacin derivatives an antibiotic has been shown to have antiproliferative and apoptotic activities in several cancer cell lines (1).All of the quinolone antibioticsshare 4-oxo-3-carboxylic acid groups which are essential for their bactericidal activity(1,2).Quinolone antibiotics are complexing agents for a variety of metal ions including alkaline earth metal ions. Although reports indicate that the coordination ofquinolones to metal ions such as Mg^{2+} and Ca^{2+} appear to be important for the activity ofthe quinolone antibiotics, [3-7] it has a detrimental effect on their absorption(8-13)Earlystudies by Nakano demonstrated the ability of the quinolone naldixic acid to complex avariety of metal ions(14).Probably the most widely studied cation,Since a host of low-molecular-weight complexes have been proven beneficial against several diseases such as tuberculosis, rheumatoid, gastric ulcers, and cancers [15-17].Since then, the exponential growth of this family has produced more than ten thousand analogues [18].Recently 5-methyl-7-piperazinyl-3"-methyl analogue of ciprofloxacin, was used to obtain stepwise-selected mutants of Streptococcus pneumonia 7785[22]. The coordination chemistry of these drugs with metal ions of biological and pharmaceutical importance is of considerable interest.

EXPERIMENTAL SECTION

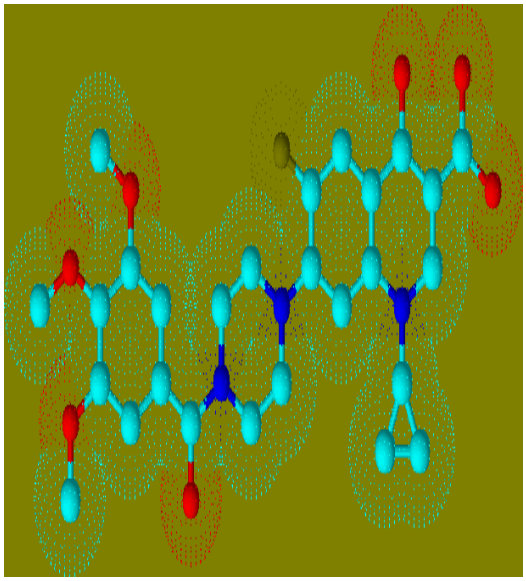
IR-spectra (KBR) were recorded on Bruker FT – IR IFS48 specrophotomeret.1H-NMR spectra were recorded in dd, doublets; dd, double; doublet; triplet; m, multiplate.Chemical shift are reported in δ(ppm) and coupling constant are given in Hz. the progress of all reaction monitored by TLC, which was performed on 2.0cmx5.0cm, aluminum sheet pre-coated with silica gel 60 f 254 to a thickness of 0.25mm (Merck).The chromatography were visualized under ultraviolet light (254~366 nm) or iodine vapor. Meltingpoint was determined by calorimeter on a buchi 434 melting point apperatus.The synthesized derivative complexes have excellent yield and antibacterial activity. In the agar well diffusion method wells were drugged in the media with the help of a sterile metallic borer. Two to eight hours old bacterial in columns containing approximately 104~106 colony forming units (CFU/mL) were spread on the surface in

(a)Regeneration of free ciprofloxacin:-

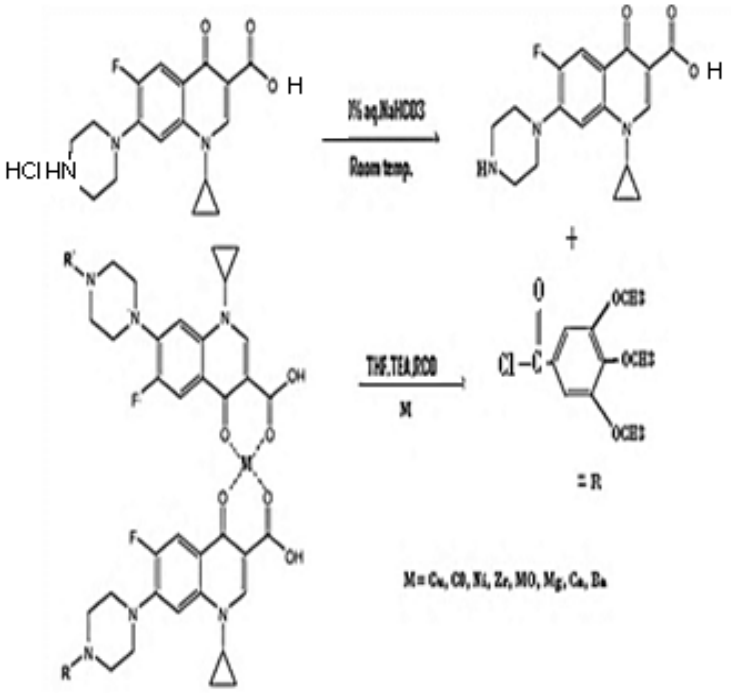
A solution of ciprofloxacin hydrochloride (l0 g) in water (50 ml) was treated with excess of 5% aqueous sodium bicarbonate solution resulting in the formation of white precipitates which were filtered through suction filtration and left to cry as a neutral ciprofloxacin (8.3 & 83%).

(b)Procedure for ciprofloxacin derivative

Ciprofloxacin was dissolve in one molar equivalent of appropriate 4-methoxy 1-chlorobenzen and result mixture was refluxed. The product was analyses by TLC .Cool the resultant mixture, remove excess solvent in vacuum and residue was suspended in brine and extracted with dichloromethane (3x50) the organic phase was dried over CaCl2 and evaporated in presence of chloroform to afford the solid product in pure form.



3D-Structure Derivative of Ciprofloxacin



Schematic scheme of synthesis Derivative of Ciprofloxacin

(c)Preparation of complexes:-

For complexes of 1,2,3,4

Take derivative of Ciprofloxacin of Concentration1mmol add in 2mmol Concentration Salt of Cupper Acetate , Cobalt Nitrate,Iron Nitrate, Nickel Acetate, with constant stirring, maintain PH 7.5 by acid and base($NH_4(OH)_2$).Reflux for 4-hour.All of the complexes were prepared by using the same procedure.

For complexes of 5,6,7,8.

0.6mmol (≈0.2 g) of ciprofloxacin derivative suspended in 30 mL of ethanol was mixed with another solution (water) containing 0.3 mmol of the salt of Magnesium perchlorate, calcium perchlorate and barium perchlorate 0.6 mmol in ethanol. The reaction mixture was stirred for 24

hours at room temperature. After that, the volume of the reaction mixture was reduced and the white precipitated complex was filtered off and washed with methanol and dichloromethane.

All the isolated complexes were desiccated over calcium chloride under reduced pressure for several days. The isolation of a single complex was checked using thin layer chromatography.

Ciprofloxacin Derivative; yield: 0.76g (76%); M.P=170^{o}C-172^{o}C;
Colure-:LightBrown;IR:(KBr,cm^{-1}): 3418.36, 1719, 1602, 1467, 1433, 1387.66, 1338.51, 1255.57, 1217.OO, 1011.50, 707.83. 1H NMR (DMSO-d6)d: 8.97 (s, 1H, H-2); 7.54 (d, 1H, H-5); 4.90 (m, 1H, NHþ); 4.59 (m, 1H,CH2–O); 4.39 (m, 1H, CH2–O); 3.92 (m, 1H, CH); 3.41 (s, 4H, CH2-10;CH2-30); 2.85 (m, 1H, CH2-40); 2.77 (m, 1H, CH2-40); 2.61 (s, 3H, CH3–N); 2.36 (s, 2H, CH2-20); 1.44 (d, 3H, CH3–CH). 13C NMR (DMSO-d6)d: 176.3 (C4); 166.1 (COOH); 157.2 (C2); 153.8 (C6); 146.2 (C8); 124.8(C7); 120.0 (C8a); 106.7 (C4a); 103.3 (C3 and C5); 68.2 (O–CH2); 59.8 (CH); 54.9 (C20 and C40); 49.5 (C10 and C30); 44.6 (N–CH3); 17.9(CH3)

Ciprofloxacin –Derivative Complexes.
1. Yield: 0.72g (72%); M.P=174^{0}C-176^{0}C; Colure-: Blue. IR: (KBr, cm1) -:3412Cm-^{1}, 3016Cm-1,2930 Cm-^{1},1719 Cm-^{1},1602 Cm-^{1}1521.75 Cm-^{1},1467 Cm-^{1},1255 Cm-^{1},1143 Cm-^{1},757Cm-^{1}.1H NMR (DMSO-d6)d: 8.97 (s, 1H, H-2); 7.54 (d, 1H, H-5); 4.90 (m, 1H, NHþ); 4.59 (m, 1H,CH2–O); 4.39 (m, 1H, CH2–O); 3.92 (m, 1H, CH); 3.41 (s, 4H, CH2-10;CH2-30); 2.85 (m, 1H, CH2-40); 2.77 (m, 1H, CH2-40); 2.61 (s, 3H, CH3–N); 2.36 (s, 2H, CH2-20); 1.44 (d, 3H, CH3–CH). 13C NMR (DMSO-d6)d: 176.3 (C4); 166.1 (COOH); 157.2 (C2); 153.8 (C6); 146.2 (C8); 124.8

2) Yield: 0.52g (52%); M.P=172^{0}C-173^{0}C; Colure-:Pink solid. IR: (KBr, cm1) 3473, 3418, 1628, 1585, 1473, 1384, 1266, 1115,1019, 947, 316, 302. 1H NMR (DMSO-d6)d: 8.97 (s, 1H, H-2); 7.54 (d, 1H, H-5); 4.90 (m, 1H, NHþ); 4.59 (m, 1H,CH2–O); 4.39 (m, 1H, CH2–O); 3.92 (m, 1H, CH); 3.41 (s, 4H, CH2-10;CH2-30); 2.85 (m, 1H, CH2-40); 2.77 (m, 1H, CH2-40); 2.61 (s, 3H, CH3–N); 2.36 (s, 2H, CH2-20); 1.44 (d, 3H, CH3–CH). 13C NMR (DMSO-d6)d: 176.3 (C4); 166.1 (COOH); 157.2 (C2); 153.8 (C6); 146.2 (C8); 124.8(C7); 120.0 (C8a); 106.7 (C4a); 103.3 (C3 and C5); 68.2 (O–CH2);59.8 (CH); 54.9 (C20 and C40); 49.5 (C10 and C30); 44.6 (N–CH3); 17.9(CH3)

3) Yield: 0.52g (82%); M.P=173^{0}C-176^{0}C; Colure-: Green solid. IR: (KBr, cm1) 3466, 1624, 1579, 1515,1462, 1397, 1271, 1113,1089, 981, 800, 748, 328, 326. 1H NMR (DMSO-d6)d: 8.97 (s, 1H, H-2); 7.54 (d, 1H, H-5); 4.90 (m, 1H, NHþ); 4.59 (m, 1H,CH2–O); 4.39 (m, 1H, CH2–O); 3.92 (m, 1H, CH); 3.41 (s, 4H, CH2-10;CH2-30); 2.85 (m, 1H, CH2-40); 2.77 (m, 1H, CH2-40); 2.61 (s, 3H, CH3–N); 2.36 (s, 2H, CH2-20); 1.44 (d, 3H, CH3–CH). 13C NMR (DMSO-d6)d: 176.3 (C4); 166.1 (COOH); 157.2 (C2); 153.8 (C6); 146.2 (C8); 124.8(C7); 120.0 (C8a); 106.7 (C4a); 103.3 (C3 and C5); 68.2 (O–CH2);59.8 (CH); 54.9 (C20 and C40); 49.5 (C10 and C30); 44.6 (N–CH3); 17.9(CH3)3)) 3474, 3031, 2851, 2751, 1624,1586, 1515, 1465, 1401, 1275, 1091, 980, 799, 325, 322.

4)Yield: 0.84g (84%); M.P=170^{0}C-171^{0}C; Colure-Pale-yellow. IR: (KBr, cm1) 3466, 1635,1578 ,1372,1127,800, 748, 328, 3261HNMR(DMSO-d6) d: 8.95 (s, 1H, H-2); 7.53 (d, 1H, H-5); 4.90 (m, 1H, NHþ);4.56 (m, 1H, CH2–O); 4.39 (m, 1H, CH2–O); 4.15 (m, 1H, CH); 3.42 (m,4H, CH2-10; CH2-30); 2.77 (m, 4H, CH2-20; CH2-40); 2.47 (s, 3H, CH3–N); 1.46 (d, 3H, CH3–CH). 13C NMR (DMSO-d6) d: 176.3 (C4); 166.1(COOH); 157.1 (C2); 153.8 (C6); 146.1 (C8); 124.7 (C7); 120.0 (C8a);106.7 (C4a); 103.2 (C3 and C5); 68.2 (O–CH2); 54.8 (C20 and C40);54.5 (CH); 48.8 (C10 and C30); 44.6 (N–CH3); 17.9 (CH3).

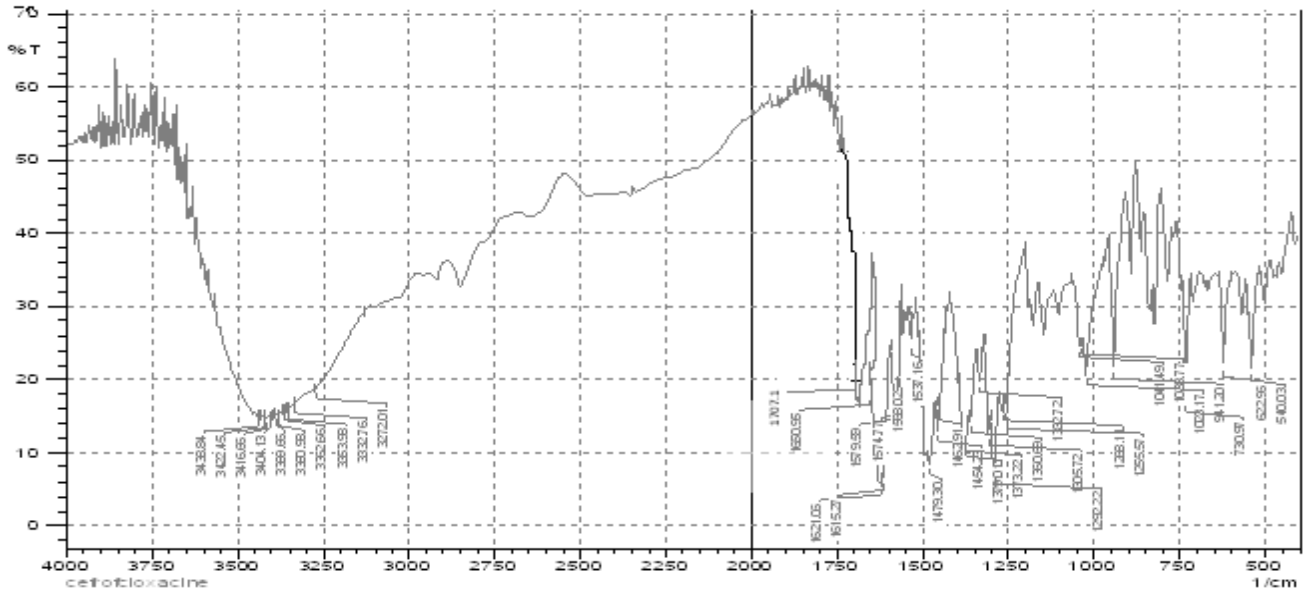


Fig2-ciprofloxacin

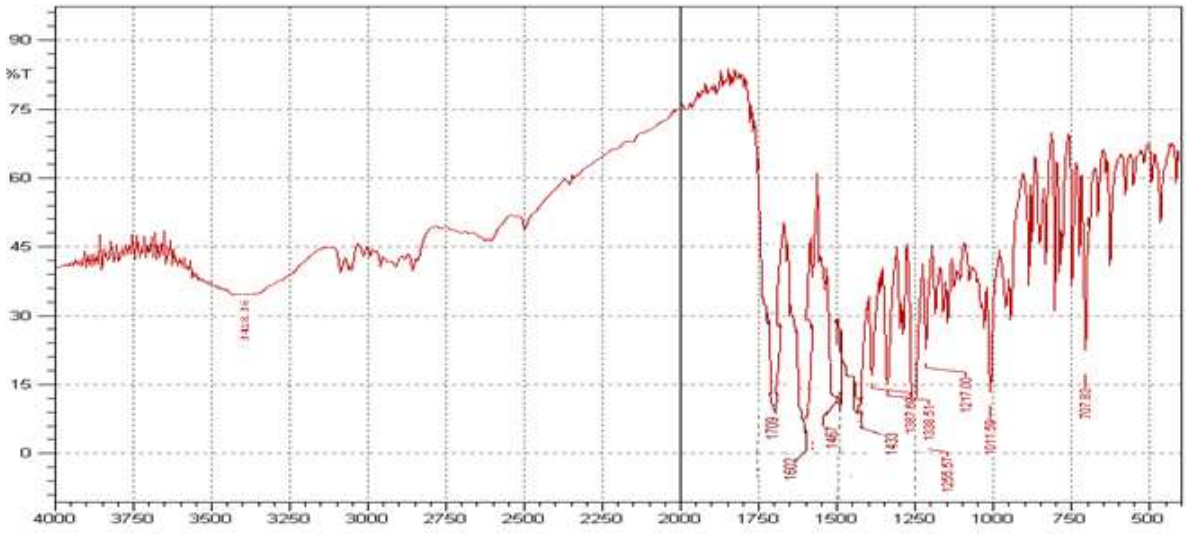


Fig3-Ciprofloxacin Derivative

Table 1-Elemantal analysis of C,H,N

Main IR absorptions (cm^{-1}).

Sr.No.	nCOOH	nC–Oas	nC=O	nC–Os
Ciprofloxacin derivative	1719	1602	1467	1255
Complexes of CIPD				
1	-----	1628	1521.75	
2	------	1624	1525	1397
3	------	1624	1526.23	1401
4	------	1635	1551.17	1372
5	------	1629	1530.11	1322
6	-----	1628	1526.31	1391
7	-------	1624	1525.34	1377
8	--------	1628	1528.22	1390

5)Yield: 0.64g (64%); M.P=170^{0}C-171^{0}C; Colure-.Colorless IR: (KBr, cm1) 3474, 3031, 2851, 2751, 1624, 1586, 1515, 1465, 1401, 1275, 1086, 980, 799, 325, 322. 1H NMR(DMSO-d6) d: 8.95 (s, 1H, H-2); 7.53 (d, 1H, H-5); 4.90 (m, 1H, NHþ);4.56 (m, 1H, CH2–O); 4.39 (m, 1H,

CH2–O); 4.15 (m, 1H, CH); 3.42 (m,4H, CH2-10; CH2-30); 2.77 (m, 4H, CH2-20; CH2-40); 2.47 (s, 3H, CH3–N); 1.46 (d, 3H, CH3–CH). 13C NMR (DMSO-d6) d: 176.3 (C4); 166.1(COOH); 157.1 (C2); 153.8 (C6); 146.1 (C8); 124.7 (C7); 120.0 (C8a); 106.7 (C4a); 103.2 (C3 and C5); 68.2 (O–CH2); 54.8 (C20 and C40); 54.5 (CH); 48.8 (C10 and C30); 44.6 (N–CH3); 17.9 (CH3).

6)Yield: 0.72g (72%); M.P=167^{o}C-168^{o}C; Colure-.Light brown IR: (KBr, cm^{-1}) 3466, 1628, 1580, 1526, 1462, 1391, 1271, 1080, 981, 800, 744, 327, 326. 1H NMR (DMSO-d6)d: 8.97 (s, 1H, H-2); 7.54 (d, 1H, H-5); 4.90 (m, 1H, NHþ); 4.59 (m, 1H,CH2–O); 4.39 (m, 1H, CH2–O); 3.92 (m, 1H, CH); 3.41 (s, 4H, CH2-10;CH2-30); 2.85 (m, 1H, CH2-40); 2.77 (m, 1H, CH2-40); 2.61 (s, 3H, CH3–N); 2.36 (s, 2H, CH2-20); 1.44 (d, 3H, CH3–CH). 13C NMR (DMSO-d6)d: 176.3 (C4); 166.1 (COOH); 157.2 (C2); 153.8 (C6); 146.2 (C8); 124.8(C7); 120.0 (C8a); 106.7 (C4a); 103.3 (C3 and C5); 68.2 (O–CH2);59.8 (CH); 54.9 (C20 and C40); 49.5 (C10 and C30); 44.6 (N–CH3); 17.9(CH3).

TABLE2-Elemental analysis

Compounds	Colour	M.P.	Yield	Elemental analysis					
				% Found			% Calculated		
				% C	% H	% N	% C	% H	% N
Ciprofloxacin derivative (CIPD)	light brown	166^{O}C-168^{O}C	76%	61	5.24	7.33	61.79	5.37	7.9
1. [Cu $_2$(Cip.D)$_2$]	blue	174^{0}C-176^{0}C	72%	59.12	5.18	7.46	59.27	3.327	7.67
2. [C0 (Cip.D)$_2$]	pink	172^{0}C-173^{0}C	52%	59	5.52	7.92	59.52	3.33	7.72
3.[Ni 2(Cip.D)$_{2}$]	green	173^{0}C-176^{0}C	82%	55.34	7.52	7.52	56.483193	3.16	7.32
4.[ZrO (Cip.D)$_2$]3H$_2$O	pale yellow	170^{0}C-171^{0}C	84%	55.45	5.052	7.25	56.9	3.18	7.38
5.[MO$_2$(CipD)$_2$]	colorless	170^{0}C-171^{0}C	64%	52.11	2.95	6.66	53.05	2.966	6.87
6.[Mg $_2$(CIP.D)2](ClO4)2.xH2O	light brown	167^{o}C-168^{o}C	72%	60.01	3.33	6.77	60.08	3.36	7.78
7.[Ca$_2$(CIP.D)2](ClO4)2.xH2O	light brown	169^{0}C-171^{0}C	74%	57.15	3.10	6.73	58.38	3.26	7.56
8.[Ba $_2$(CIP.D)2](ClO4)2.xH2O	light brown	170^{0}C	76%	49.52	2.74	6.13	49.67	2.76	6.44

7) Yield: 0.75g (74%); M.P=169^{0}C-171^{0}C; Colure-Light brown IR: (KBr, cm1) 3466, 1624, 1586, 1525.34, 1462,1377, 1271, 1091, 954, 800, 748, 328, and 326. 1H NMR (DMSO-d6)d: 8.97 (s, 1H, H-2); 7.54 (d, 1H, H-5); 4.90 (m, 1H, NHþ); 4.59 (m, 1H,CH2–O); 4.39 (m, 1H, CH2–O); 3.92 (m, 1H, CH); 3.41 (s, 4H, CH2-10;CH2-30); 2.85 (m, 1H, CH2-40); 2.77 (m, 1H, CH2-40); 2.61 (s, 3H, CH3–N); 2.36 (s, 2H, CH2-20); 1.44 (d, 3H, CH3–CH). 13C NMR (DMSO-d6)d: 176.3 (C4); 166.1 (COOH); 157.2 (C2); 153.8 (C6); 146.2 (C8); 124.8(C7); 120.0 (C8a); 106.7 (C4a); 103.3 (C3 and C5); 68.2 (O–CH2);59.8 (CH); 54.9 (C20 and C40); 49.5 (C10 and C30); 44.6 (N–CH3); 17.9(CH3)3))

8) Yield: 0.76g (76%); M.P=170^{0}C; Colour- Light brown IR: (KBr, cm1) 3466,1628, 1580, 1528.22, 1462, 1390, 1271, 1083, 964, 800, 748, 328, 326. 1H NMR (DMSO-d6)d: 8.97 (s, 1H, H-2); 7.54 (d, 1H, H-5); 4.90 (m, 1H, NHþ); 4.59 (m, 1H,CH2–O); 4.39 (m, 1H, CH2–O); 3.92 (m, 1H, CH); 3.41 (s, 4H, CH2-10;CH2-30); 2.85 (m, 1H, CH2-40); 2.77 (m, 1H, CH2-40); 2.61 (s, 3H, CH3–N); 2.36 (s, 2H, CH2-20); 1.44 (d, 3H, CH3–CH). 13C NMR (DMSO-d6)d: 176.3 (C4); 166.1 (COOH); 157.2 (C2); 153.8 (C6); 146.2 (C8); 124.8(C7); 120.0 (C8a); 106.7 (C4a); 103.3 (C3 and C5); 68.2 (O–CH2);59.8 (CH); 54.9 (C20 and C40); 49.5 (C10 and C30); 44.6 (N–CH3); 17.9(CH3).

Table3: Minimum Inhibiting Concentration (mm) values against Gram-positive bacteria

Sample name Dose (µg) CiproD	CIPD	(1)	2	3	4	5	6	7	8
Staphylococcus aureus 100	17.15	6	20	5.5	5.5	6.5	22	21	21.1
Streptococci 100	11.5	13	16.5	11.5	11	13.8	18.5	14	16
Bacillus spp 100	12.14	16.5	21.2	12.4	12	13.5	21.5	20	20.5

Table4: Minimum Inhibiting Concentration (mm) values against Gram-negative and Gram positive bacteria

Sample name Dose (µg) Cipro	CIP-D	(1)	2	3	4	5	6	7	8
E. coli 100	18.5	11.5	8	10	9	8.5	20	20	21
Klebsiellapneumoniae 100	20	31	33	32.5	23	24	34.5	30	31
Pseudomonas spp 100	23.7	34	44	25.1	16	42.3	42	40	29.3
Salmonella spp 100	15.6	38.1	24.2	14.3	11.6	12.1	39	38.1	33
Salmonella typhi 100	22	32.1	34	27	26	27.5	36	37.1	36.2
Salmonella typhipara-A 100	26.6	34.2	4.51	30.1	27.52	30.33	38	38.4	36
Shigalla dysenteriae 100	26	32	36.5	32.5	31	34	38.5	30	31
Sample name Dose (µg) Cipro		(1)	2	3	5	5	6	7	8
Candida albicans (antifungal)	13.8	44	12.1	26	16	14	15.2	16	15.4

RESULTS AND DISCUSSION

Table 2 summarizes the carbon, hydrogen and nitrogen elemental analysis of the isolated complexes. The results obtained indicate that all of the isolated complexes are formed from the reaction of the metal salt with drug in 1:2 molar ratios. The IR spectra for the complexes of Ciprofloxacin with Cu,Co,Ni,Zr,Mo calcium, magnesium and barium perchlorate And show three strong bands at1143, 1115 ,1113,1127,and 1086 ,1080,1091,1083cm-1,these Seven bands are absent in the spectrum of the derivative of ciprofloxacin. The The band at the 1709cm^{-1} is found in derivative of ciprofloxacin to be absent in the complexes of ciproflixacin derivatives. Band shows in ciprofloxacin at 3419.56 cm-1 is because of secondary amine present in ciprofloxacin, the broad band found near the3418.36 cm-1 of amide group attached in derivative of ciprofloxacin. All of those experiments compared with parent antibiotic ciprofloxacin derivatives, then we observed that two complex 2,and 6 showed enhanced activities than ciprofloxacin against gram positive organisms (Table 3) which we screened such as Staphylococcus aureus, Streptococci and Bacillus spp. Whereas 6 exhibited similar activity against Staphylococcus and 5 & 3 also showed similar activities against Streptococci. Two derivatives 3 and 6 exhibited enhanced activities than ciprofloxacin against all gram negative organisms(Table 4) which we tested including E. coli, Klebsiella pneumoniae,Pseudomonas spp, Salmonella spp,Salmonella typhi,Salmonellatyphi Para-A, Salmonella typhi Para-B and Shigalladysenteriae.Whereas 2 & 5 showed highest activity against Pseudomonas spp, moreover 2 exhibited better activity against Salmonella spp, Salmonella typhi,Salmonellatyphi Para-A, Salmonella typhi Para-B and Shigalla dysenteriae likewise 3 showed similar activity against Shigalla dysenteriae .In generally, we can say derivative 06 showed enhanced activities than ciprofloxacin against all grampositive and gram negative organisms likewise 2 & 5 showed highest activity against Pseudomonas spp moreover 2 exhibited better activity against Salmonella spp,Salmonellatyphi,Salmonellatyphi Para-A, Salmonella typhi Para-B and Shigalla dysenteriae All of the synthesized compounds (2-6) were screened for their antifungal affects against Candida albicans and compared with parent antibiotic, ciprofloxacin. We observed all of the synthesized compounds showed enhanced activities than ciprofloxacin and derivative 6 showed the highest activity.

Structure of the Isolated Complexes

Figure 2 shows the FTIR spectra of Ciprofloxacin derivative (CIPD)and its all complexes with metal ion .The strong bands observed at1719 and1602 cm-1 in the spectrum of the Ciprofloxacin derivative have been assigned before to the stretching vibration of the carboxylic (νCOOH) and the carbonyl groups (νCO), respectively.The measured spectrum for the free ciprofloxacin is similar to that reported by Turelet. al.[20] The νCO of ciprofloxacin was observed 1623 cm-1.[1.40]and same band observed for derivative 0f ciprofloxacin at1602 cm-1.The IR spectra of their complex are νcooh band observed at 1719cm^{-1} for cip disappears, a behavior that is indicative of the involvement of the carboxyl group in the interaction with metal ion. The intense band at 1628,1624,1624,1635,1629,1628,1624 in the spectra of all the complexes appears to be reasonably assigned to the asymmetric stretching vibration of the ligated COO- group. The spectra 0f all the complexes of derivative also show another medium intensity bands at1521.75cm^{-1}, 1585cm^{-1},1526.23 cm^{-1},1578.17 cm^{-1} ,1515.11 cm^{-1},1526.23 cm^{-1} ,1525.34 cm^{-1},1528.22 cm^{-1} respectively, these bands are absent in spectrum of ciprofloxacin derivatives most likely due to the symmetric vibration of the ligatedCOO^{-}group .

Acknowledgments

This Work Was Supported By Dattameghe College Of Engineering And Research Technology Institute, Sawangi (Wardha)&Institute Of Pharmacetical Education And Resarch, BDCOE College Of Engineering Sevagram,Wardha.

REFERENCES

[1] BN Lomaestero; G R Bailie; *Ann, Pharmacother*. **1991**, 25, 1249-1558.
[2] JH Paton ;DS Reeves; *Drugs* **1988**, 36, 193-228
[3] M Gellert; K Mizuuchi; MO Dea; H Nash, *Proc. Natl. Acad. Sci. USA* **1976**, 73, 3872-3876.
[4] M Gellert; K Mizuuchi; MO Dea;T. Itoh,J. Tomizawa, *Proc. Natl. Acad. Sci*., USA **1977**, 74,4772-4776.
[5] M Gillert; *An Rev; Biochem*., **1981**,50, 879-910.
[6] NRCozarelli, *Science*., **1980**, 207, 953-960.
[7] G Palu; S Valisena; G Ciarrocchi; B Gatto;M Palumbo; *Proc. Natl. Acad. Sci. USA*., **1992**, 89,9671-9675.
[8] RW Frost;JD Carlson; AJ Dietz; A Heyd; JT Lettieri; *J. Clin.Pharmacol*., **1989**, 29, 953-955.
[9] DE Nix; WA Watson; ME Lener; RW Frost; G Krol; H Goldstein; J. Lettieri, *Clin. Pharmacol.,Ther.* **1992**, 46, 830-836.
[10] RW Frost; KC Leasseter; AJ Noe; EC Shamblen; JT Lettieri; *Antimicrob. Agents Chemother.*,**1992**, 36, 830-832.
[11] RE Polk; DP Healy; J Sahai; L drawl; E Racht; *Antimicrob. Agents Chemother*., **1989**, 33,
[12] 18411844.
[13] M Kara; BB Hasinoff; DW Mckay; NRC Campell; *Brit. J. Clin. Pharmac*., **1991**, 31, 257-261.
[14] T Motoya; M Niyashita; A Kawachi; K Yamada; J. *Pharm. Pharmacol*., **2000**, 52, 397-401.
[15] JRJ Sorenson*; J. Med. Chem*., **1976**, 19, 135-148.
[16] DH Brown; AJ Lewis; WE Smith; JW Teape., *J. Med. Chem*. **1980**, 23, 729-734.
[17] DR Williams. The Metals of Life, Van Nostrand Reinhold: London, **1971**.
[18] M Ruiz; L Perello;R Ortiz; A Castineiras; C Maichlemossmer; *J. Inorg. Biochem*. ,**1995**, 59, 801-810.
[19] SE Castillo-Blum; N Barba-Behrens; *Coord. Chem. Rev*. **2000**, 196, 3-30.
[20] 19 RM Silverstein; GC Bassler; TC Morril. Spectroscopic Identification of Organic compounds,5th edit,Wiley,**1991**.

[21] I Turel; P Bukovec ;M Quiros, *Int. J.Pharm*., **1997**, 152, 59-65.
[22] YM. Thakre,.MDChoudhary; RD Raut.Synthesis and evaluation of Ciprofloxacin complexes as diagnostic tools for bacterial infection.International conference. Innovative ideas2011.
[23] JE Morris; XS Pan; LM Fisher, *Antimicrobial Agents and Chemotherapy*, February **2002**, p. 582-585, Vol. 46, No.