

Synthesis, Characterization and Biological Evaluation of Mononuclear Dichloro-bis[2-(2-chloro-6,7-substituted Quinolin-3-yl)-1H-benzo[d]imidazole]Co(II) Complexes

Minaxi S. Maru^{a*} and Manish K. Shah^b^aChemical Research Laboratory, Department of Chemistry, Saurashtra University, Rajkot-360005, Gujarat, India.^bDepartment of Chemistry, Saurashtra University, Rajkot-360005, Gujarat, India.

Article history: Received: 14 November 2013; revised: 24 August 2014; accepted: 20 March 2015. Available online: 25 June 2015. DOI: <http://dx.doi.org/10.17807/orbital.v7i2.530>

Abstract: A series of Co(II) complexes **3'a-g** of 2-(2-chloro-6,7-substituted quinolin-3-yl)-1H-benzo[d]imidazole ligands **3a-g** were prepared and characterized by various spectroscopic and physico-chemical methods *viz.* FT-IR, ESI mass, ¹H NMR, ¹³C NMR and UV-Visible spectroscopy, Thermogravimetric analysis, Magnetic susceptibility, Molar conductance and Elemental analysis. The 2-(2-chloro-6,7-substituted quinolin-3-yl)-1H-benzo[d]imidazole ligands **3a-g** have been synthesized by cyclocondensation of benzene-1,2-diamine with 2-chloroquinoline-3-carbaldehydes by using ceric ammonium nitrate as a catalyst in presence of hydrogen peroxide as an oxidant. The structures of all ligands were confirmed by IR, Mass, UV-Visible, ¹H NMR and ¹³C NMR spectroscopy. All ligands **3a-g** and their Co(II) complexes **3'a-g** were screened for their *in vitro* antimicrobial activity using twofold serial dilution technique against standard MTCC strains of two Gram-positive *Staphylococcus aureus* and *Streptococcus pyogenes*, two Gram-negative *Escherichia coli* and *Pseudomonas aeruginosa* bacteria and three *Candida albicans*, *Aspergillus niger* and *Aspergillus clavatus* fungus in comparison with standard drugs. All ligands **3a-g** and complexes **3'a-g** also evaluated for antimycobacterial activity against standard *Mycobacterium tuberculosis* H₃₇Rv strain.

Keywords: Co(II) complexes; 1H-benzo[d]imidazoles; antimicrobial activity; antimycobacterial activity

1. INTRODUCTION

Generally, most of the infections and diseases caused in the human body are by fungus and bacteria. Recently it has been the challenge to overcome the diseases and infections which origins by the pathogenic microorganisms. Many organic compounds containing the heteroatoms in their structures were found as the potential drugs to fight against this kind of infections in the human body. By revering all the matters we have synthesized some novel benzimidazole molecules and their Co(II) complexes, which were then screened for anti-infective activities (*viz.*, antibacterial, antifungal and antimycobacterium activity) in this research article because benzimidazole compounds shows promising biological and pharmacological activities in organic and coordination chemistry. In this concern many benzimidazole compounds are reported as

antibacterial and antifungal agents in past literature [1-4], recently Chetan et al. have reported the antituberculosis activity of some benzimidazole molecules [5]. Further, the quinoline motifs have also good biological properties *viz.*, antitumor activity and DNA binding capability [6-8]. Because of these versatile biological properties of benzimidazole and quinoline motifs we have decided to prepare 2-(2-chloro-6,7-substituted quinolin-3-yl)-1H-benzo[d]imidazole molecules and their Co(II) complexes.

The cobalt ion and benzimidazole molecule both are the components of vitamin B₁₂, therefore, cobalt complexes containing benzimidazole ligands have attracted our attention due to their various biological properties and more especially, their structural similarity with vitamin B₁₂. It is well known that coordination compounds containing transition metal complexes have wide research area according to

*Corresponding author. E-mail: dr.maru139@gmail.com

their spectroscopic and structural representation for the active site of some metalloenzymes [9]. The Co(II) complexes of monodentate 2-substituted benzimidazole ligands by taking 1:2 mole ratio of cobalt(II)chloride salt and benzimidazole ligand respectively, were infrequently discussed in past literature, that is why in the present article, we reported the synthesis and characterization of the series of dichloro-bis[2-substituted benzimidazole]cobalt(II) complexes. The series of 2-chloro-6,7-disubstituted quinoline-3-carbaldehydes used for the synthesis of benzimidazole molecules were synthesized by previously published method [10]. The *in vitro* antimicrobial activity was determined by agar disc diffusion method against selected bacterial and fungal strains, also evaluated for *in vitro* antimycobacterial activity against *Mycobacterium tuberculosis* H₃₇Rv strain which was determined by broth micro dilution assay to identify their biological spectrum and strength.

2. MATERIAL AND METHODS

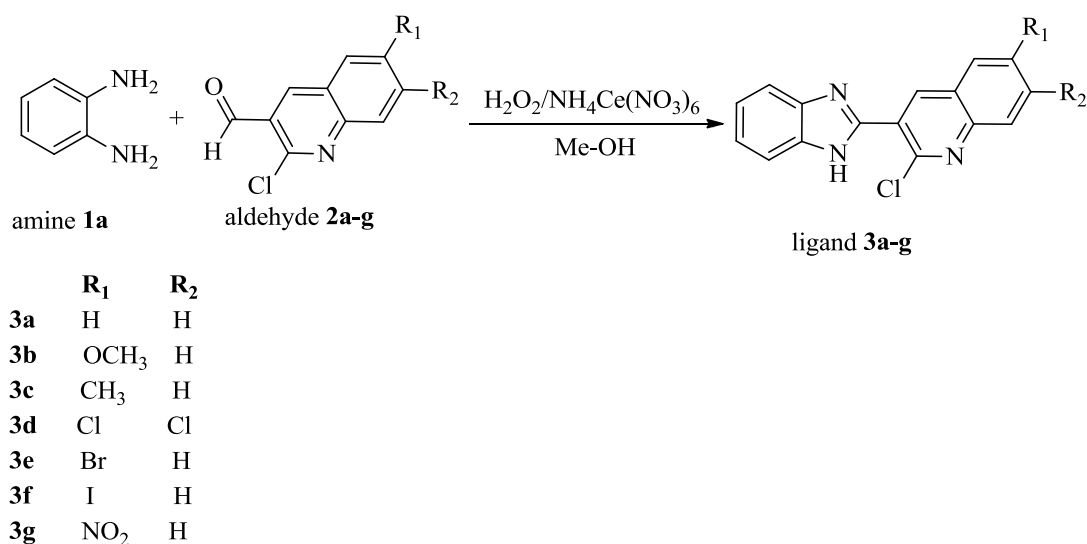
Nutrient agar was purchased from Himedia. All chemicals, acetic anhydride, *N,N*-dimethylformamide, hydrated cobalt(II) chloride salt (Allied chemical corporation), anilines (Sisco chem. Pvt. Ltd.), phosphorous oxychloride, hydrogen peroxide (Spectrochem), ceric ammonium nitrate and benzene-1,2-diamine (LOBA Chemie), were of the analytical reagent grade (AR) and of highest purity available. All organic solvents were from Merck used as received.

Pathogens

The pathogenic bacterial and fungal strains were procured from Institute of Microbial Technology, Chandigarh. The bacteria were subcultured on Nutrient agar whereas, fungi were subcultured on Sabouraud's dextrose agar (SDA) and were incubated aerobically at 37 °C.

Physical methods

Elemental analysis was done for C, H, N and Co on a Euro EA Elemental Analyzer, EA-3000, RS-232. Infrared spectra were recorded on a Shimadzu FT-IR 8400 spectrophotometer using KBr pellets in the range 4000-400cm⁻¹. The ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were measured in DMSO-*d*₆ solutions on a Bruker Av spectrophotometer using TMS as an internal reference (chemical shifts in δ ppm). The mass spectra were recorded on GC-MS QP-2010 Gas Chromatograph Shimadzu. Electronic spectra were recorded in DMF solution on a Shimadzu UV mini-1240 spectrophotometer. ESI mass spectral study were recorded on Micromass Q-ToF Micro having mass Range of 4000 amu in quadruple and 20000 amu in ToF at SAIF, IIT Bombay, India. The TG analysis curves were obtained on the Perkin Elmer the Diamond Thermogravimetric/Differential Thermal Analyzer (TG/DTA) model at a heating rate of 20 °C per minute in nitrogen atmosphere at SAIF, IIT Bombay, India.



Scheme 1. Reaction scheme for the synthesis of 2-(2-chloro-6,7-disubstituted quinolin-3-yl)-1H-benzo[d]imidazole ligands **3a-g**.

Procedures

Synthesis of 2-chloro-6,7-substituted quinoline-3-carbaldehydes 2a-g: 2-chloro-6,7-substituted quinoline-3-carbaldehydes **2a-g** have been synthesized by the typical vilsmeier-haack reaction [10].

Synthesis of 2-(2-chloro-6,7-substituted quinolin-3-yl)-1H-benzo[d]imidazole ligands 3a-g: The benzene-1,2-diamine (0.01 mol) **1a** was added to the solution of 2-chloro-6,7-substituted quinoline-3-carbaldehydes **2a-g** (0.01 mol in 30 mL methanol). Ceric ammonium nitrate (0.001 mol) and hydrogen peroxide (30 %, 15 mL) were then added to this solution. The reaction mixture was refluxed on water bath for 6-8 h (Scheme 1). After completion of reaction monitored by TLC, the reaction mixture was cooled at room temperature and poured into crushed ice, separated solid product was collected by suction and washed with cold saturated sodium bisulphite solution and recrystallized with methanol to get 59-79% yield of benzimidazole ligands **3a-g**.

2-(2-chloro quinolin-3-yl)-1H-benzo[d]imidazole (3a): Yield: 68 %, m.p.: 210-215 °C. IR (KBr) ν cm⁻¹: 3356-3254 (N-H), 3178-3053 (C-H of Ar), 1666 (C=N of benzimidazole), 1583-1519 (C=N of quinoline), 1481, 1390 and 1240 (C-N), 819 and 750 (C-Cl). ¹H NMR (400 MHz, DMSO-*d*₆) δ in ppm: 6.91-6.93 (d, 2H, Ar-H of benzimidazole ring; *J* = 7.88 Hz), 7.07-7.09 (d, 1H, Ar-H of quinoline ring; *J* = 7.8 Hz), 7.15-7.19 (m, 1H, Ar-H of quinoline ring), 7.21-7.29 (m, 2H, Ar-H of quinoline ring), 7.56-7.58 (d, 1H, Ar-H of quinoline ring; *J* = 7.76), 7.71-7.73 (d, 1H, Ar-H of benzimidazole ring; *J* = 7.76 Hz), 8.08-8.10 (d, 1H, Ar-H of benzimidazole ring; *J* = 7.68 Hz), 12.56 (s, 1H, H of imidazole ring). ¹³C NMR (100 MHz, DMSO-*d*₆) δ in ppm: 117.96, 118.69, 123.87, 127.36, 128.43, 129.03, 129.69, 134.25, 138.54, 138.78, 147.16, 148.89, 158.67. Mass *m/z*: 281 (M+2). Mol. Wt.: 279. Anal.Ca. for C₁₆H₁₀ClN₃; Ca. for C, 68.70; H, 3.60; N, 15.02; Found: C, 68.52; H, 3.48; N, 14.89 %.

2-(2-chloro-6-methoxyquinolin-3-yl)-1H-benzo[d]imidazole (3b): Yield: 70 %, m.p.: 200-207 °C. IR (KBr) ν cm⁻¹: 3342-3174 (N-H), 3101 and 3041 (C-H of Ar), 2993, 2937 and 2883 (Assy. and sym. C-H of alkane), 1685 and 1660 (C=N of benzimidazole), 1589 and 1537 (C=N of quinoline), 1438, 1344 and 1288 (C-N), 1240 and 1057 (C-O of methoxy), 854 and 686 (C-Cl). ¹H NMR (400 MHz, DMSO-*d*₆) δ in ppm: 3.79 (s, 3H, -OCH₃), 7.19-7.21

(d, 1H, Ar-H of quinoline ring; *J* = 7.2 Hz), 7.43-7.47 (t, 1H, Ar-H of quinoline ring), 7.57-7.66 (m, 2H, Ar-H of benzimidazole ring), 7.99-8.01 (d, 2H, Ar-H of benzimidazole ring; *J* = 8 Hz), 8.25-8.29 (t, 1H, Ar-H of quinoline ring), 8.34-8.37 (t, 1H, Ar-H of quinoline ring), 12.63 (s, 1H, H of imidazole ring). ¹³C NMR (100 MHz, DMSO-*d*₆) δ in ppm: 56.40, 108.72-109.59, 124.26, 126.49, 128.63, 128.84, 141.25, 142.31, 145.44, 148.52, 149.81, 160.64. Mass *m/z*: 309 (M). Mol. Wt.: 309. Anal.Ca. for C₁₇H₁₂ClN₃O; Ca. for C, 65.92; H, 3.90; N, 13.57; Found: C, 65.45; H, 3.41; N, 13.03 %.

2-(2-chloro-6-methylquinolin-3-yl)-1H-benzo[d]imidazole (3c): Yield: 65 %, m.p.: 220-225 °C. IR (KBr) ν cm⁻¹: 3288-3230 (N-H), 3091 and 3064 (C-H of Ar), 2980 and 2810 (C-H of alkane), 1639 (C=N of benzimidazole), 1556 and 1492 (C=N of quinoline), 1448, 1329 and 1282 (C-N), 796 and 756 (C-Cl). ¹H NMR (400 MHz, DMSO-*d*₆) δ in ppm: 2.84 (s, 3H, -CH₃), 7.18-7.21 (m, 2H, Ar-H of benzimidazole ring), 7.38-7.44 (m, 2H, Ar-H of quinoline ring), 7.56-7.60 (t, 2H, Ar-H of benzimidazole ring), 7.87-7.89 (d, 1H, Ar-H of quinoline ring; *J* = 9.2 Hz), 7.95-7.97 (d, 1H, Ar-H of benzimidazole ring; *J* = 7.6 Hz), 12.63 (s, 1H, H of imidazole ring). ¹³C NMR (100 MHz, DMSO-*d*₆) δ in ppm: 18.22, 125.91, 126.33, 127.64, 127.57, 131.43, 135.55, 136.32, 136.84, 146.03, 147.52, 158.40. Mass *m/z*: 293 (M). Mol. Wt.: 293. Anal.Ca. for C₁₇H₁₂ClN₃; Ca. for C, 69.51; H, 4.12; N, 14.30; Found: C, 69.39; H, 3.93; N, 14.10 %.

2-(2,6,7-trichloroquinolin-3-yl)-1H-benzo[d]imidazole (3d): Yield: 74 %, m.p.: 200-215 °C. IR (KBr) ν cm⁻¹: 3325 and 3252 (N-H), 3174 and 3055 (C-H of Ar), 1664 and 1618 (C=N of benzimidazole), 1568 and 1500 (C=N of quinoline), 1429 and 1315 (C-N) and 750 (C-N). ¹H NMR (400 MHz, DMSO-*d*₆) δ in ppm: 7.25 (s, 1H, Ar-H of quinoline ring), 7.34-7.37 (m, 1H, Ar-H of benzimidazole ring), 7.45-7.52 (m, 1H, Ar-H of benzimidazole ring), 7.73-7.77 (m, 1H, Ar-H of benzimidazole ring), 7.83-7.85 (d, 1H, Ar-H of benzimidazole ring; *J* = 7.6 Hz), 8.04 (s, 1H, Ar-H of quinoline ring), 8.78 (s, 1H, Ar-H of quinoline ring), 12.41 (s, 1H, H of imidazole ring). ¹³C NMR (100 MHz, DMSO-*d*₆) δ in ppm: 117.28, 118.51, 127.04, 127.88, 128.72, 129.62, 129.76, 130.94, 133.32, 134.66, 138.91, 150.03, 157.59. Mass *m/z*: 348 (M). Mol. Wt.: 348. Anal.Ca. for C₁₆H₈Cl₃N₃; Ca. for C, 55.12; H, 2.31; N, 12.05; Found: C, 55.00; H, 2.11; N, 11.92 %.

2-(2-chloro-6-bromoquinolin-3-yl)-1H-

benzo[d]imidazole (3e): Yield: 60 %, m.p.: 250-255 °C. IR (KBr) ν cm⁻¹: 3416, 3298, 3238 and 3190 (N-H), 3061 and 3005 (C-H of Ar), 1676 and 1651 (C=N of benzimidazole), 1521 and 1487 (C=N of quinoline), 1446, 1396 and 1313 (C-N), 821 and 688 (C-Cl), 626 (C-Br). ¹H NMR (400 MHz, DMSO-*d*₆) δ in ppm: 7.31-7.33 (dd, 1H, Ar-H of benzimidazole ring; *J* = 8.72 Hz), 7.40-7.43 (m, 1H, Ar-H of quinoline ring), 7.45-7.47 (m, 2H, Ar-H of quinoline ring), 7.53-7.54 (dd, 1H, Ar-H of benzimidazole ring; *J* = 5.4 Hz), 7.58-7.62 (m, 2H, Ar-H of benzimidazole ring), 8.01 (s, 1H, Ar-H of quinoline ring), 11.69 (s, 1H, H of imidazole ring). ¹³C NMR (100 MHz, DMSO-*d*₆) δ in ppm: 117.51, 118.75, 126.92, 127.64, 128.08, 128.52, 128.67, 129.62, 132.07, 134.90, 138.99, 152.32, 157.92. Mass *m/z*: 356 (M). Mol. Wt.: 356. Anal.Ca. for C₁₆H₉BrClN₃; Ca. for C, 47.38; H, 2.24; N, 10.36; Found: C, 47.18; H, 2.09; N, 10.20 %.

2-(2-chloro-6-iodoquinolin-3-yl)-1H-

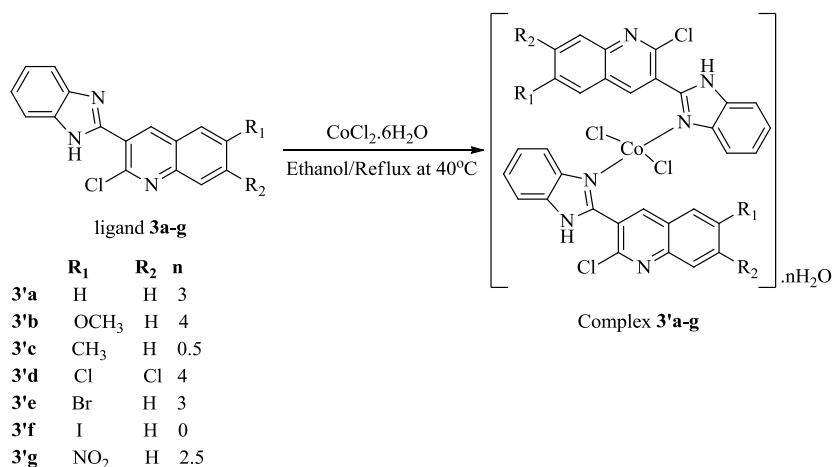
benzo[d]imidazole (3f): Yield: 59 %, m.p.: 190-195 °C. IR (KBr) ν cm⁻¹: 3444, 3379, 3329 and 3290 (N-H), 3099, 3034 and 2964 (C-H of Ar), 1691 and 1604 (C=N of benzimidazole), 1533 and 1483 (C=N of quinoline), 1394 and 1307 (C-N), 821 and 730 (C-Cl), 607 and 584 (C-I). ¹H NMR (400 MHz, DMSO-*d*₆) δ in ppm: 6.89-6.91 (d, 1H, Ar-H of benzimidazole ring; *J* = 8.32 Hz), 7.21-7.24 (d, 1H, Ar-H of benzimidazole ring; *J* = 10.04 Hz), 7.26-7.34 (m, 1H, Ar-H of quinoline ring), 7.40-7.52 (m, 2H, Ar-H of benzimidazole ring), 7.60-7.63 (d, 2H, Ar-H of quinoline ring; *J* = 8.68 Hz), 8.09 (s, 1H, Ar-H of quinoline ring), 11.67 (s, 1H, H of imidazole ring). ¹³C NMR (100 MHz, DMSO-*d*₆) δ in ppm: 126.15, 126.96, 127.70, 127.82, 128.42, 131.49, 135.98,

136.74, 146.90, 148.40, 158.40. Mass *m/z*: 404 (M+1). Mol. Wt.: 405. Anal.Ca. for C₁₆H₉IClN₃; Ca. for C, 47.38; H, 2.24; N, 10.36; Found: C, 47.18; H, 2.09; N, 10.20 %.

2-(2-chloro-6-nitroquinolin-3-yl)-1H-

benzo[d]imidazole (3g): Yield: 79 %, m.p.: >300 °C. IR (KBr) ν cm⁻¹: 3471, 3354, 3352 and 3136 (N-H), 3009 and 2833 (C-H of Ar), 1591 and 1539 (C=N of benzimidazole), 1498 and 1454 (C=N of quinoline), 1415, 1379 and 1282 (C-N), 835 and 798 (C-Cl). ¹H NMR (400 MHz, DMSO-*d*₆) δ in ppm: 7.38-7.42 (t, 1H, Ar-H of benzimidazole ring), 7.55-7.59 (t, 1H, Ar-H of benzimidazole ring), 7.76 (s, 1H, Ar-H of quinoline ring), 7.90-7.92 (d, 1H, Ar-H of benzimidazole ring; *J* = 7.6 Hz), 7.96-7.98 (d, 1H, Ar-H of benzimidazole ring; *J* = 8.8 Hz), 8.25 (s, 1H, Ar-H of quinoline ring), 8.33-8.35 (d, 2H, Ar-H of quinoline ring; *J* = 8.4 Hz), 11.34 (s, 1H, H of imidazole ring). ¹³C NMR (100 MHz, DMSO-*d*₆) δ in ppm: 114.11, 116.90, 118.36, 123.82, 124.48, 126.77, 127.50, 129.40, 129.58, 135.16, 139.03, 149.55, 151.20, 159.54. Mass *m/z*: 324 (M). Mol. Wt.: 324. Anal.Ca. for C₁₆H₉ClN₄O₂; Ca. for C, 59.18; H, 2.79; N, 17.25; Found: C, 59.01; H, 2.63; N, 17.06 %.

Synthesis of Co(II) complexes 3'a-g: 2-(2-chloro-6,7-substituted quinolin-3-yl)-1H-benzo[d]imidazole ligands **3a-g** (1.0 mmol) was dissolved in hot ethanol (20 mL) and the resulting solution was treated with hydrated cobalt chloride salt (0.5 mmol) dissolved in ethanol (10 mL) with continuous stirring at room temperature. Then, the reaction mixture was stirred at 40 °C to separate out the product **3'a-g** from the reaction mixture within 7-15 days. The obtained solid product then collected through whatmann 42 filter paper and wash with ethanol.



Scheme 2. Reaction scheme for the synthesis of complexes **3'a-g**.

Biological activity

Microbial strains

Total seven microorganisms were used for *in vitro* antimicrobial activity including four bacterial strains, two Gram negative *Escherichia coli* (MTCC 442), *Pseudomonas aeruginosa* (MTCC 441) and two Gram positive *Staphylococcus aureus* (MTCC 96), *Streptococcus pyogenes* (MTCC 443) and three fungus strain *Candida albicans* (MTCC 227), *Aspergillus niger* (MTCC 282) and *Aspergillus clavatus* (MTCC 1323).

Assay for *in vitro* antimicrobial activity

Each of the test compounds and standards ciprofloxacin and ampicillin for antibacterial activity and griseofulvin and nystatin for antifungal activity were dissolved in DMSO initially at 2000 $\mu\text{g mL}^{-1}$ and then were serially diluted in two series for culture medium as: 1000, 500, 250 $\mu\text{g mL}^{-1}$ and 100, 50, 25, 12.5, 6.25 $\mu\text{g mL}^{-1}$ concentrations. The bacteria were subcultured on Nutrient agar and fungi were subcultured on Sabouraud's dextrose agar (SDA) and incubated aerobically at 37 °C. The minimum inhibitory concentrations (MICs) were defined as the lowest concentrations of the compounds that prevented visible growth. The used solvent was tested against all microbial strains and confirmed that it had no any kind of activity against microorganisms.

Agar disc diffusion method

This test was evaluated for each compound was performed in the petri plates. In subsequent studies, the selected standard drugs for antibacterial and antifungal activity were also tested for the comparative study between new compounds and standards. The culture of bacterial and fungal strains was prepared in 4 mL of Muller Hinton broth at 37 °C for 24 hours in incubator. The turbidity of culture suspension was adjusted with sterile Muller Hinton broth in order to obtain turbidity comparable to a No. 1 McFarland turbidity standard. One mL of this suspension was pipetted into the Muller Hinton agar plate and distributed evenly over the surface of the medium by gently stirring the plate. The surface of the medium was allowed to dry for 15 minutes at room temperature and was pierced with 7 mm diameter holes. The serial twofold diluted series of synthesized compounds from 2000-6.25 $\mu\text{g mL}^{-1}$

concentrations were impregnated in the pierced holes (7 mm) of the discs (88 mm) and applied to the surface of inoculated plates. The Petri plates were placed in an incubator at 37 °C. After 24 hours of incubation the Petri plates was examined by considering 22 mm ZOI as the susceptible [11].

Determination of MIC

The minimum inhibitory concentration (MIC) of the compounds was determined by the micro broth dilution technique using Muller Hinton broth. Serial twofold dilutions ranged from 1000, 500, 250 $\mu\text{g mL}^{-1}$ and 100, 50, 25, 12.5, 6.25 $\mu\text{g mL}^{-1}$ concentrations for compounds. The inoculum was prepared in broth which had been kept overnight at 37 °C and which had been diluted with Muller Hinton broth to give a final concentration of 10^8 cfu mL^{-1} (where cfu = Colony forming unit) in the test tray. The micro plates were covered and placed in plastic bags to prevent drying. After incubation at 37 °C for 24 hours, the MIC value was defined as the lowest concentration of the compound giving complete inhibition of visible growth and the zone of inhibition (ZOI) was measured in millimeter diameter [12].

Antitubercular activity

The ligands **3a-g** and their Co(II) complexes **3'a-g** have been tested in the primary test against the standard strain of *Mycobacterium tuberculosis* H₃₇Rv (ATCC 27294) in BACTEC 12B medium using a broth micro dilution assay, the Micro plate Alamar Blue Assay (MABA) susceptibility test [13] by using rifampin and isoniazid as a reference drugs. Compounds exhibiting fluorescence were tested in the BACTEC 460 radiometric system. The final concentration (>6.25 $\mu\text{g/mL}$) of ligands **3a-g** and their Co(II) complexes **3'a-g** were added in LJ medium after inspissation and the chemical containing medium was distributed in 7 mL amounts in screw capped tubes. After that the tubes were inspissated in the sloping position at 80 °C for 45 minutes. The medium was inoculated according to the recommendation of W.H.O. [14]. The inoculum for the susceptibility test was prepared by adding approximately 2 mg of growth from the primary culture on a loop to a 5 mL sterile distilled water in 7 mL screw capped tubes together with six 3 mm glass leads. The tubes were shaken mechanically for 1 minute and a full 3 mm loopful of the suspension

inoculated to each slope. Duplicate slopes for each ligands **3a-g** and their Co(II) complexes **3'a-g** were inoculated. A drug free control slopes were set up with each test and tubes incubated at 37 °C. The results of the tests were read after 4 weeks incubation.

3. RESULTS AND DISCUSSION

Elemental analysis and conductance

The ligands **3a-g** were micro analyzed for C, H and N whereas, complexes **3'a-g** were micro analyzed for C, H, N and Co elements satisfactorily and results are comparatively in good agreement with their structures (Table 1). The molar conductivity values of all complexes **3'a-g** observed in the range of 6.98-18.33 $\text{cm}^2\Omega^{-1}\text{mol}^{-1}$ indicating non-electrolyte nature of all complexes.

NMR spectra

¹H NMR

The ¹H NMR spectral study of all newly synthesized ligands **3a-g** shows the characteristic broad singlet of imidazolic hydrogen of secondary amine (-NH group) at 11.69-12.69 ppm, which is the confirmation about the formation of benzimidazole ring [15]. The aromatic ring protons for all ligands were observed in the range of 6.91-8.78 ppm. The proton of methoxy and methyl substitution on quinoline ring gives single line at 3.79 ppm and 2.84 ppm for ligand **3b** and **3c** respectively.

The signals consequent to the -NH group of

benzimidazole ring in the ¹H NMR spectra of Co(II) complexes **3'a-g**, are remain unchanged with a variation of 0.05-0.09 ppm. The aromatic region of the metal complexes is considerably distorted therefore, the signals obtained cannot be identified, and this distortion is probably due to the metal ion present in the compounds. The signals corresponding to hydrogens of methoxy group (-OCH₃) and methyl group (-CH₃) are not changed or little bit shifted to down field or up field from the free ligands.

¹³C NMR

The number of carbons of the all benzimidazole ligands can be count from the number of signals obtained, which represent most of chemically non-equivalent carbons in the compounds. The chemical shift of aromatic ring carbons rather than the two carbons of imidazole ring appear in the range of 108.96-128.84 ppm whereas, the two carbons of benzene ring fused to imidazole ring observed at 129.40-141.25 ppm. The C=N carbon in all benzimidazole ligands exhibited in the range of 147.52-152.32 ppm and the carbon having chlorine substitution obtained in downfield in the range of 157.59-160.64 ppm. The methoxy and methyl group carbons of ligands **3b** and **3c** gives sharp signals at 56.40 ppm and 18.22 ppm respectively.

The ¹³C NMR spectrum of all Co(II) complexes does not show specific peaks of carbon atoms with proper values may be due to the coordination of ligands with Co(II) ion which cause distortion in the spectra.

Table 1. Analytical and physico-chemical data of complexes **3'a-g**.

Comp ^d	R ₁	R ₂	M.F.	Δ^b	Elemental analysis % Calcd. (Found)			
					C	H	N	Co
3'a	H	H	(C ₁₆ H ₁₀ ClN ₃ Cl) ₂ Co	11.14	55.76 (55.62)	2.92 (2.78)	12.19 (12.08)	8.55 (8.43)
3'b	OCH ₃	H	(C ₁₇ H ₁₂ ClN ₃ OCl) ₂ Co	13.66	54.50 (54.37)	3.23 (3.11)	11.22 (11.07)	7.86 (7.74)
3'c	CH ₃	H	(C ₁₇ H ₁₂ ClN ₃ Cl) ₂ Co	13.53	56.93 (56.77)	3.37 (3.26)	11.72 (11.58)	8.22 (8.10)
3'd	Cl	Cl	(C ₁₆ H ₈ Cl ₃ N ₃ Cl) ₂ Co	6.98	46.47 (46.32)	1.95 (1.82)	10.16 (10.12)	7.13 (7.00)
3'e	Br	H	(C ₁₆ H ₉ BrClN ₃ Cl) ₂ Co	18.43	45.37 (45.25)	2.14 (2.01)	9.92 (9.79)	6.96 (6.82)
3'f	I	H	(C ₁₆ H ₉ IClN ₃ Cl) ₂ Co	15.30	40.84 (40.69)	1.93 (1.81)	8.93 (8.79)	6.26 (6.12)
3'g	NO ₂	H	(C ₁₆ H ₉ ClN ₄ O ₂ Cl) ₂ Co	14.72	49.32 (49.17)	2.33 (2.18)	14.38 (14.23)	7.56 (7.41)

^bMolar conductance ($\text{cm}^2\Omega^{-1}\text{mol}^{-1}$) of 10⁻³ M solutions at room temperature in DMF

IR spectra

Hofmann showed that benzimidazole molecules display the strong intermolecular hydrogen

bond [16] for secondary amine in the region of 3500-2200 cm^{-1} . Precisely, the ν (N-H) stretching of secondary amine of benzimidazole ring was shows

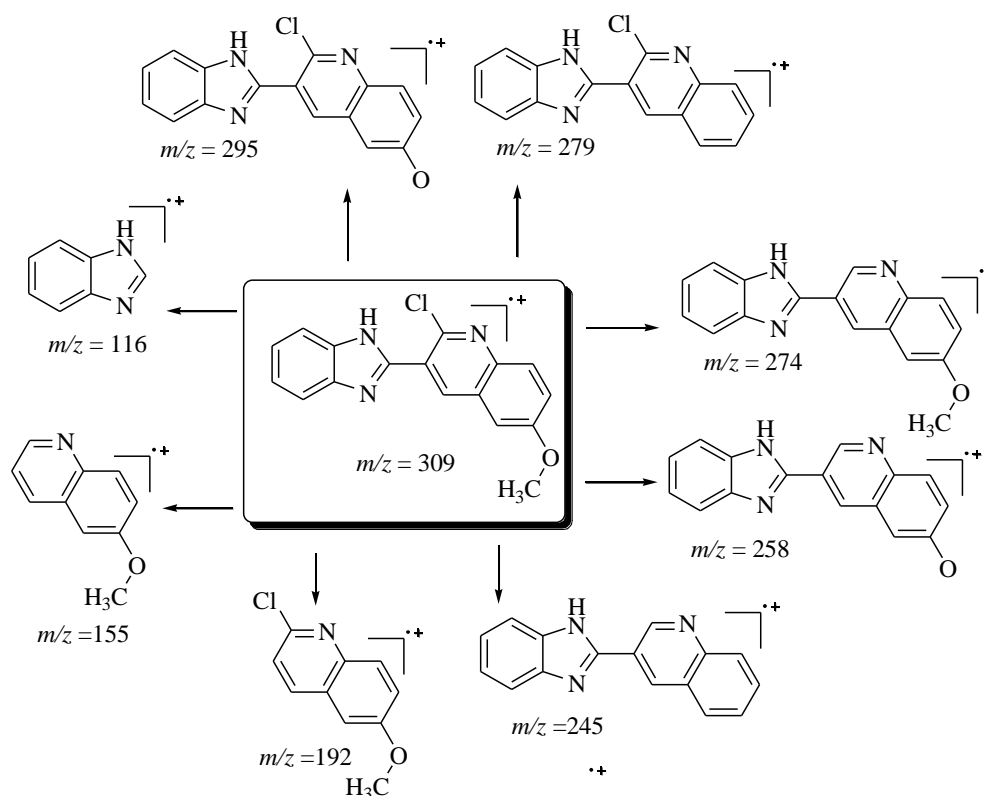
strong bands at 3471-3174 cm^{-1} for all newly synthesized ligands. The strong band observed in the range of 1691-1539 cm^{-1} were assigned to $\nu(\text{C}=\text{N})$ stretching vibrations for all ligands [17] and the aromatic ring stretching of $\nu(\text{C}-\text{H})$ were obtained in the region of 3091-3041 cm^{-1} .

The $\nu(\text{C}=\text{N})$ stretching bands were observed get shifted towards the lower frequency region in the IR spectra of Co(II) complexes, which is indicating the complex formation of benzimidazole ligands with Co(II) ions through the tertiary nitrogen of imidazole ring.

Mass spectra

GC-MS spectra of ligands

The mass spectra of all ligands show total molecular ion peaks and fragmented molecular ion peaks with respective to their molecular weight in form of cations or anions. The fragmentation in all ligands at 116-118 m/z is predictable to benzimidazole ring ion. The representative mass fragmentation prototype of ligand **3b** is portrayed in Scheme 3.



Scheme 3. Mass fragmentation prototype for ligand **3b**.

ESI-MS spectra of complexes

The ES-MS spectral analysis of complexes **3'a-g** shows the presence of the cationic as well as anionic species of $[\text{CoCl}_2\text{L}_2]^{n+/-}$, $[\text{CoClL}_2]^{n+/-}$, $[\text{CoL}_2]^{n+/-}$, $[\text{CoL}]^{n+/-}$ and $[\text{L}]^{n+/-}$ with asymmetric isotopic peak pattern where, $n = 1-9$. All complexes **3'a-g** have fragmented ion peak $[\text{L}]^{n+/-}$ of their corresponding ligands as $m/z = 274$ (M-5, 5%), 319 (M+10, 55%), 301 (M+8, 11%), 344 (M-2, 3%), 360 (M+4, 100%), 409 (M+5, 13%) and 326 (M+2, 3%) respectively.

Electronic spectra and magnetic susceptibility

The electronic spectra of benzimidazole ligands **3a-g** and their complexes **3'a-g** shows two specific bands according to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ at 230-257 nm (43478-38911 cm^{-1}) and 272-310 nm (36765-32258 cm^{-1}) with the variation of 15-20 nm in each Co(II) complexes than their corresponding ligands. The ligand to metal charge transfer transition in all Co(II) complexes demonstrated as a broad shoulder at 400-453 nm (25000-22075 cm^{-1}).

The electronic spectrums of all complexes **3'a-**

g shows bands at 565-672 nm (17699-14881 cm^{-1}) and 690-785 nm (14493-12739 cm^{-1}) which are assigned to the d-d transitions due to the ${}^4A_2 \rightarrow {}^4T_1(F)$ and ${}^4A_2 \rightarrow {}^4T_1(P)$, which are related with the proposed tetrahedral geometry to the all Co(II) complexes (18) except **3'c** complex, which have ${}^4B_{2g} \rightarrow {}^4A_{1g}$, ${}^4B_{2g} \rightarrow {}^4E_g$, ${}^4B_{2g} \rightarrow {}^4B_{1g}$ transitions

suggesting the square pyramidal geometry around the Co(II) metal ion [19]. The transition ${}^4A_2 \rightarrow {}^4T_2$ is may be merge with the ligand to metal charge transfer transition in all complexes except **3'g** complex, which, shows three bands in their UV-Visible spectrum (Figure 1). All bands observed for all complexes **3'a-g** are summarized in Table 2.

Table 2. Electronic spectral and magnetic susceptibility data of complexes **3'a-g**.

Complex	Electronic spectral bands (cm^{-1})		Assignment	μ_{eff} BM	Geometry
	LMCT	d-d bands			
3'a	23529	16393 14184	${}^4A_2 \rightarrow {}^4T_1(F)$ ${}^4A_2 \rightarrow {}^4T_1(P)$	4.59	Tetrahedral
3'b	25000	15267 13850 14881	do	4.75	Tetrahedral
3'c	22831	12987	${}^4B_{2g} \rightarrow {}^4A_{1g}$ ${}^4B_{2g} \rightarrow {}^4B_{1g}$	4.62	Square pyramidal
3'd	23202	17241 14493	${}^4A_2 \rightarrow {}^4T_1(F)$ ${}^4A_2 \rightarrow {}^4T_1(P)$	4.54	Tetrahedral
3'e	22222	16129 14388 16339	do	4.48	Tetrahedral
3'f	22075	13679	do	4.72	Tetrahedral
3'g	24876	17699 15106	${}^4A_2 \rightarrow {}^4T_2$ ${}^4A_2 \rightarrow {}^4T_1(F)$	4.67	Tetrahedral

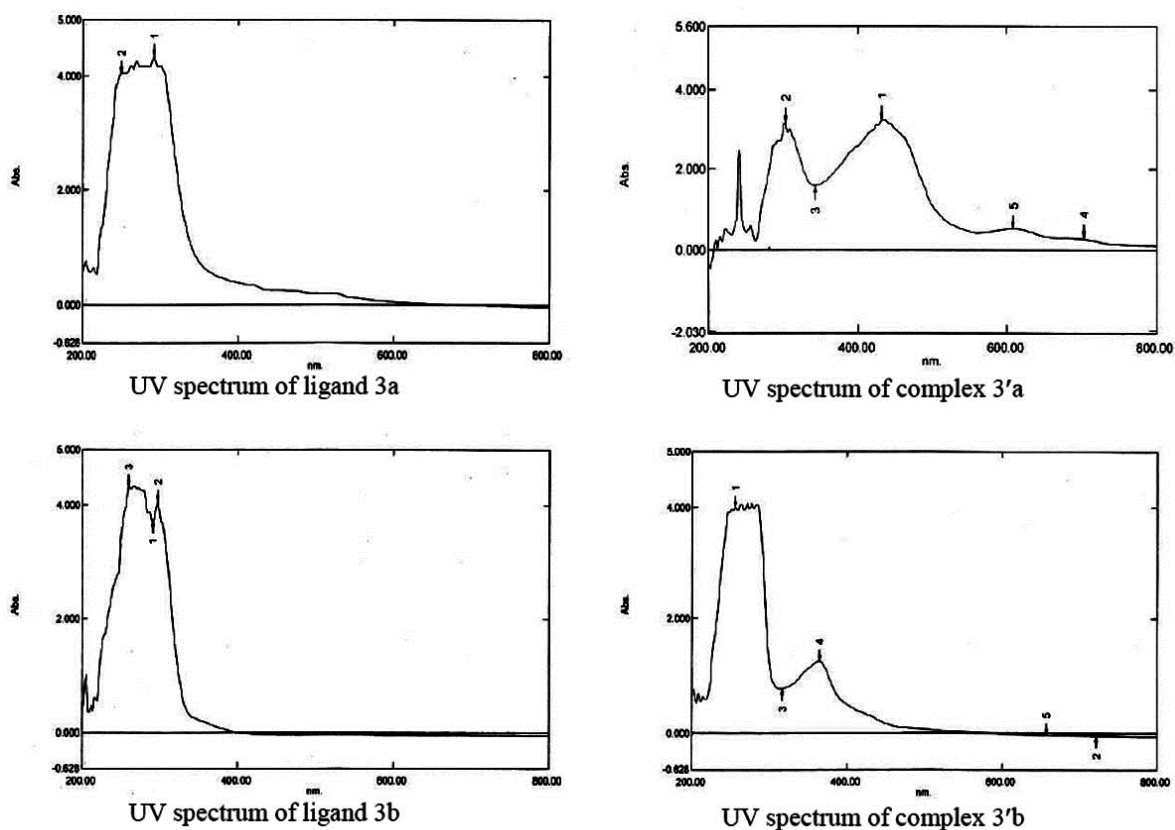
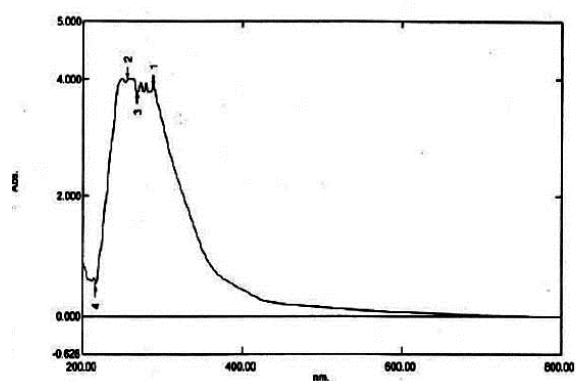
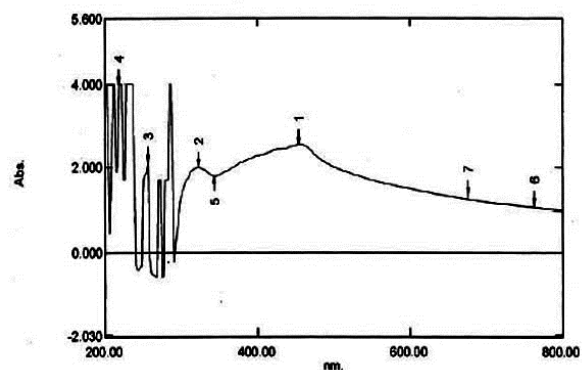


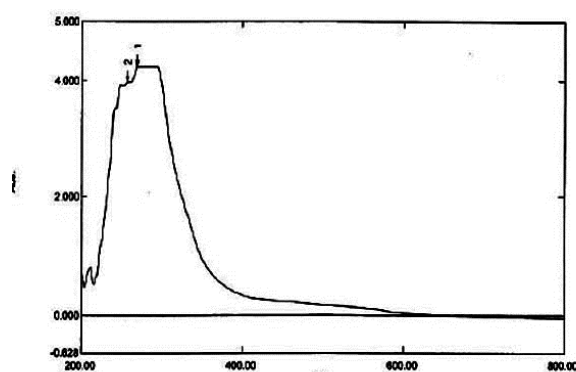
Figure 1. UV-Visible spectra of ligands **3a-g** and their complexes **3'a-g**.



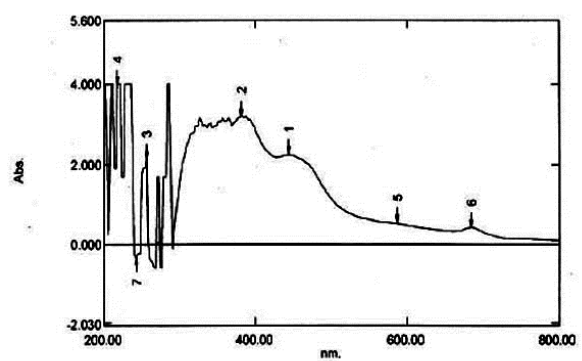
UV spectrum of ligand 3c



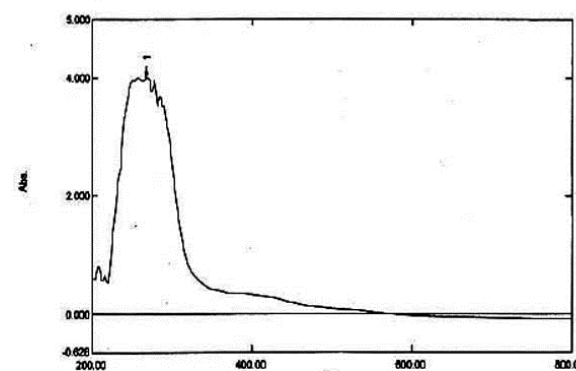
UV spectrum of complex 3'c



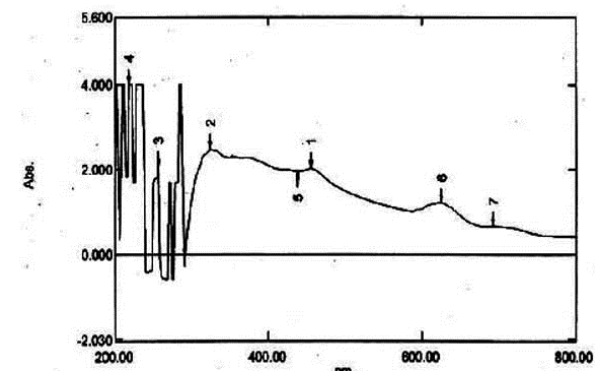
UV spectrum of ligand 3d



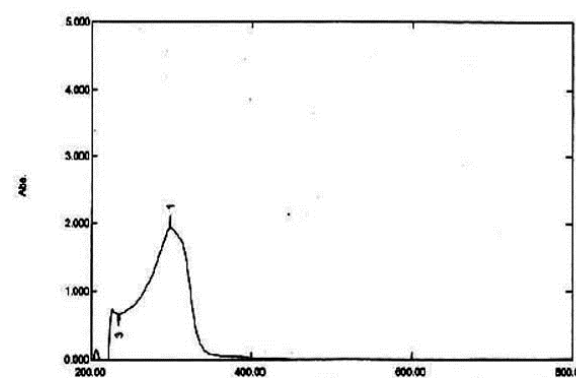
UV spectrum of complex 3'd



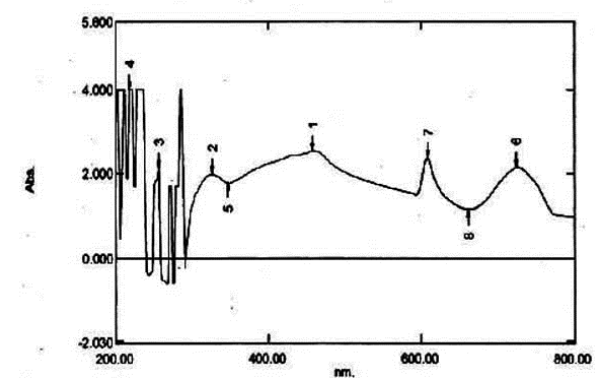
UV spectrum of ligand 3e



UV spectrum of complex 3'e

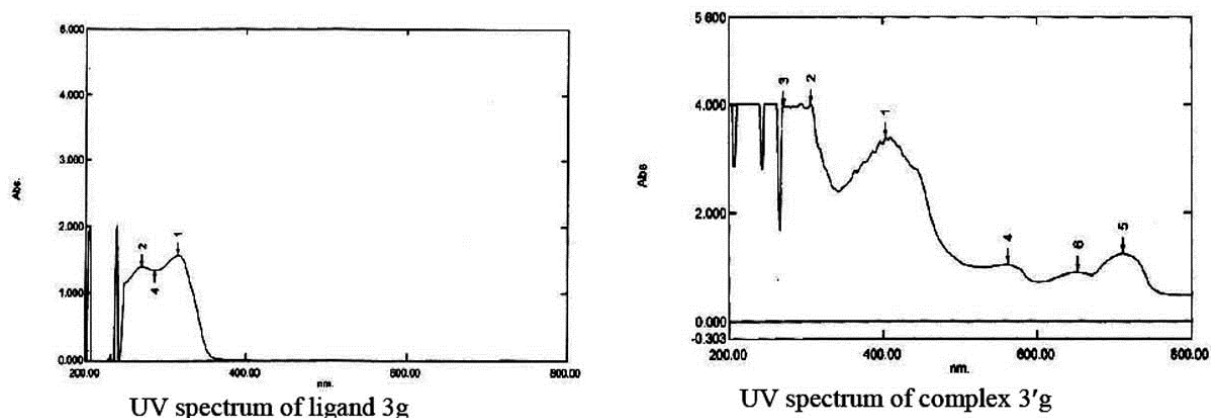


UV spectrum of ligand 3f



UV spectrum of complex 3'f

Continuation **Figure 1.** UV-Visible spectrums of ligands **3a-g** and their complexes **3'a-g**.



Continuation **Figure 1.** UV-Visible spectrums of ligands **3a-g** and their complexes **3'a-g**.

TG analysis

The thermogravimetric analysis of complexes was taken at heating rate of 20 °C per minute in nitrogen atmosphere from 30-1000 °C temperature. The complexes **3'a** and **3'e** shows 3 molecules of water, whereas, **3'b** and **3'd** complexes shows 4

molecules of water. The complexes **3'c** and **3'g** shows 1.5H₂O and 2.5H₂O molecules of water respectively in their outer sphere except **3'f** complex. All complexes decomposed in two to three steps (Figure 2) and the thermogravimetric data of all complexes are summarized in following Table 3.

Table 3. TG analysis data of complexes **3'a-g**.

Complex	TG range (°C)	Wt. loss %		Total Wt. loss		Assignment of Wt. loss	Residue
		Found	Calcd.	Found	Calcd.		
3'a	30-92	8.01	7.86			3H ₂ O	C ₆ H ₁₂ Cl ₂ CoN ₄
	92-375	43.01	43.73	65.5	65.63	C ₁₈ H ₁₀ Cl ₂ N ₂	
	375-900	14.51	14.04			C ₈ H ₈	
3'b	30-150	10.05	9.638			4H ₂ O	C ₂ H ₂ Cl ₂ CoN ₄
	150-1000	66.67	65.45	76.719	75.083	C ₃₂ H ₂₂ Cl ₂ N ₂ O ₂	
3'c	30-380	4.170	3.78			1.5H ₂ O	C ₆ H ₁₂ CoN ₄
	380-630	62.38	61.47	75.75	74.54	C ₂₈ H ₂₂ Cl ₂ N ₂	
	630-830	9.357	9.425			Cl ₂	
3'd	30-190	8.22	8.76			4H ₂ O	CoO
	190-275	21.25	23.45			6Cl	
	275-440	15.95	15.54	93.73	95.26	C ₈ H ₈ Cl	
	440-730	48.31	47.51			C ₂₄ H ₁₈ ClN ₆	
3'e	30-160	6.41	6.41			3H ₂ O	C ₆ H ₁₂ CoN ₄
	160-250	10.57	11.69	78.56	79.53	3Cl	
	250-940	61.58	61.43			C ₂₆ H ₁₈ Br ₂ ClN ₂	
3'f	30-1000	59.15	61.34	59.15	61.34	C ₁₈ H ₈ Cl ₂ I ₂ N ₂	C ₁₄ H ₁₂ Cl ₂ CoN ₄
3'g	30-190	5.91	5.81			2.5H ₂ O	Cl ₂ Co
	190-390	15.11	15.44	86.09	85.02	ClN ₂ O ₄	
	390-	65.07	63.77			C ₃₂ H ₂₁ ClN ₆	

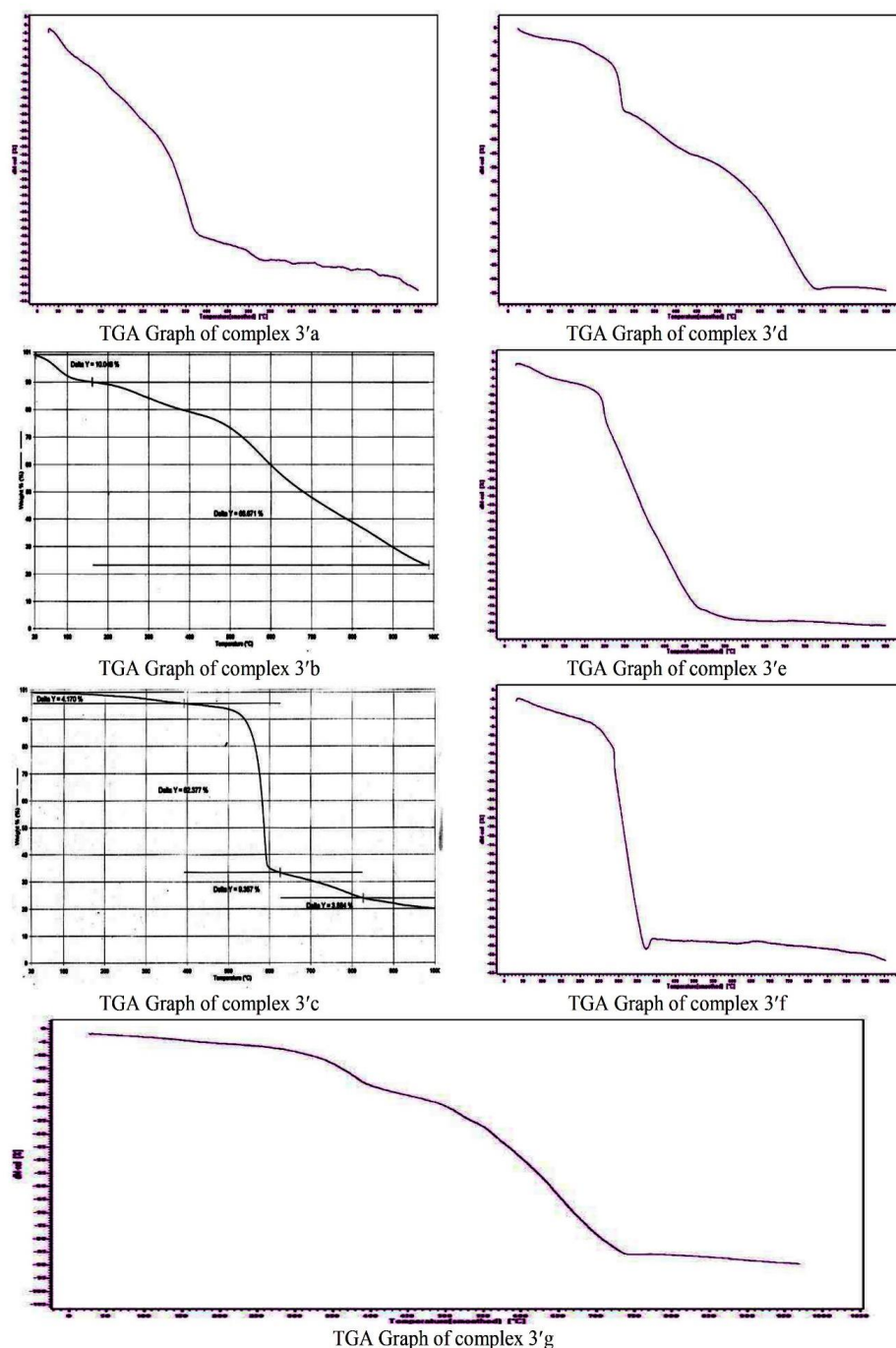


Figure 2. TGA graphs of complexes 3'a-g.

Biological activity

The antimicrobial activity data of all ligands **3a-g** and their Co(II) complexes **3'a-g** are summarized in Table 4.

Antibacterial data collected for the above synthesized complexes **3'a-g** display good activity comparable with reference drugs in some of the cases, whereas moderate antibacterial activity was found for

others against all bacterial strains by means of MIC values ranging from 6.25 to 1000 $\mu\text{g mL}^{-1}$. A few of these **3'a-g** complexes are more active than their parent ligand as well as the Reference drugs used for the study. The compounds, microorganism and minimum inhibition concentration (MIC) are as follows.

Only ligands **3e** (12.5 $\mu\text{g mL}^{-1}$ MIC) and **3g**

(100 $\mu\text{g mL}^{-1}$ MIC) shows activity against *Escherichia coli* having 25 mm and 13 mm zones of inhibition (ZOI) respectively. Ligand **3e** is four and eight times more active than the standard drugs ciprofloxacin and ampicillin respectively whereas, ligand **3g** is activity wise similar to that ampicillin with 11 mm ZOI. The

complex **3f** (25 $\mu\text{g mL}^{-1}$ MIC and 18 mm ZOI) is more active than its ligand **3f** (1000 $\mu\text{g mL}^{-1}$ MIC and 8 mm ZOI) and displays two and fourfold excess activity with ciprofloxacin and ampicillin respectively against *Escherichia coli*.

Table 4. Antimicrobial activity of ligands **3a-g** and their complexes **3'a-g** through agar disc diffusion method (Minimum Inhibition Concentration in $\mu\text{g mL}^{-1}$).

Comp ^d	Antibacterial activity				Antifungal activity		
	Gram-negative		Gram-positive		<i>C.a.</i>	<i>A.n.</i>	<i>A.c.</i>
	<i>E.c.</i>	<i>P.a.</i>	<i>S.a.</i>	<i>S.p.</i>			
3a	500	500	100	500	12.5	250	250
3b	250	1000	500	1000	500	1000	500
3c	500	>1000	250	100	1000	500	1000
3d	500	100	500	25	100	100	250
3e	12.5	500	1000	500	500	500	100
3f	1000	250	100	100	250	>1000	500
3g	100	1000	250	250	1000	100	1000
3'a	500	500	250	250	1000	100	1000
3'b	500	1000	1000	500	250	1000	500
3'c	500	12.5	12.5	100	250	500	100
3'd	1000	500	250	100	250	1000	100
3'e	500	12.5	6.25	250	1000	100	500
3'f	25	500	>1000	1000	500	500	500
3'g	500	500	250	250	1000	100	1000
Ciprofloxacin	50	50	25	25	-	-	-
Ampicillin	100	100	250	100	-	-	-
Nystatin	-	-	-	-	100	100	100
Griseofulvin	-	-	-	-	500	100	100

However only ligands **3d** and **3a,f** are active against *Pseudomonas aeruginosa* and *Staphylococcus aureus*, showing 100 $\mu\text{g mL}^{-1}$ MIC value having 17 mm, 16.5 mm and 18 mm ZOI respectively similar to reference drug ampicillin whereas for the ligands **3c** and **3g** 250 $\mu\text{g mL}^{-1}$ MIC (12 mm ZOI) value is similar to reference drug ampicillin against *Staphylococcus aureus*. Ligands **3c,f** (100 $\mu\text{g mL}^{-1}$ MIC and 15 mm ZOI) and **3d** (25 $\mu\text{g mL}^{-1}$ MIC and 22 mm ZOI) have activity similar to standard drugs ampicillin and ciprofloxacin respectively against *Streptococcus pyogenes*.

Even the lowest MIC values (12.5 $\mu\text{g mL}^{-1}$ and 25 mm ZOI) against *Pseudomonas aeruginosa* obtained for **3'c** and **3'e** complexes were also four times active than standard drug ciprofloxacin and more than their free ligands.

The complexes **3'a** and **3'g** exhibits similar activity to standard drug ampicillin (250 $\mu\text{g mL}^{-1}$ MIC and 15 mm ZOI) against *Staphylococcus aureus*. The **3'a** complex demonstrates less activity than that of the free ligand, whereas, **3'g** complex shows

comparatively similar activity to its free ligand **3g**. Contrarily the complexes **3'c** (12.5 $\mu\text{g mL}^{-1}$ MIC and 25 mm ZOI) and **3'e** (6.25 $\mu\text{g mL}^{-1}$ MIC and 30 mm ZOI) show two times and four times greater activity than reference drug ciprofloxacin and also shows more activity than those of their free ligands against *Staphylococcus aureus*. **3'c** complex shows comparatively similar activity to ampicillin reference drug and its free ligand (100 $\mu\text{g mL}^{-1}$ MIC and 17 mm ZOI), whereas, **3'd** complex shows similar MIC value with ampicillin reference drug and four times less activity than that of free ligand.

In this context **3'c** and **3'e** complexes can be considered as potentially biological active compounds better than those of free ligands as well as used reference drugs too.

It is obvious from antifungal screening data that ligands **3a,b,d,e,f** were more active against *Candida albicans* with 12.5, 500, 100, 500 and 250 $\mu\text{g mL}^{-1}$ MIC values having 27 mm, 6 mm, 14 mm, 8 mm and 19 mm ZOI respectively. The activity compared with reference drug nystatin shows ligand **3a** is eight fold more active and ligand **3d** is activity

wise similar to it. In this direction ligands **3b,e** and **3f** shows similar and two times greater activity respectively compared to reference drug griseofulvin. Only ligands **3d** and **3e** shows similar MIC values ($100 \mu\text{g mL}^{-1}$ and 17 mm ZOI) against *Aspergillus niger* and *Aspergillus clavatus* respectively to both of the used reference drugs nystatin and griseofulvin.

The complexes **3'b**, **3'c** and **3'd** have $250 \mu\text{g mL}^{-1}$ MIC value and 13 ± 3 mm ZOI, two times greater than the used reference drug griseofulvin, out of them, complexes **3'b** and **3'c** are more active than those of free ligands, whereas, **3'd** complex have less activity than that of free ligand. The complex **3'f** shows comparatively similar activity with $250 \mu\text{g mL}^{-1}$ MIC value and 14 mm ZOI to griseofulvin reference drug and less than that of free ligand. The complexes **3'a**, **3'e** and **3'g** shows similar activity to both used

reference drug nystatin and griseofulvin with $100 \mu\text{g mL}^{-1}$ MIC value and 19 mm ZOI, and potentially more active than those of their respective free ligands. The complexes **3'c** and **3'd** displays similar activity with $100 \mu\text{g mL}^{-1}$ MIC value having 20 mm ZOI to the both reference drugs nystatin and griseofulvin and they are more active than those of free ligands too.

Antimycobacterial activity is carried out by Alamar assay protocol and the obtained data is designated in Table 5. The result expressed as Minimum Inhibition Concentration in $\mu\text{g mL}^{-1}$. All ligands **3a-g** and their Co(II) complexes **3'a-g** effected <90% inhibition in primary screening (i.e., MIC < $12.5 \mu\text{g mL}^{-1}$). The ligands **3a-g** and their complexes **3'a-g** were not subjected to the further evaluation due to lack of inhibition in primary screening.

Table 5. Antimycobacterial activity of ligands **3a-g** and their complexes **3'a-g** (Minimum Inhibition Concentration in $\mu\text{g mL}^{-1}$).

Comp ^d	R ₁	R ₂	MF	MIC ($\mu\text{g mL}^{-1}$)	% Inh.	Activity
3a	H	H	C ₁₆ H ₁₀ CIN ₃ Cl	<12.5	0	-
3b	OCH ₃	H	C ₁₇ H ₁₂ CIN ₃ OCl	<12.5	0	-
3c	CH ₃	H	C ₁₇ H ₁₂ CIN ₃ Cl	<12.5	0	-
3d	Cl	Cl	C ₁₆ H ₈ Cl ₃ N ₃ Cl	<12.5	15	-
3e	Br	H	C ₁₆ H ₉ BrCIN ₃ Cl	<12.5	13	-
3f	I	H	C ₁₆ H ₉ ICIN ₃ Cl	<12.5	24	-
3g	NO ₂	H	C ₁₆ H ₉ CIN ₄ O ₂ Cl	<12.5	0	-
3'a	H	H	(C ₁₆ H ₁₀ CIN ₃ Cl) ₂ Co	<12.5	0	-
3'b	OCH ₃	H	(C ₁₇ H ₁₂ CIN ₃ OCl) ₂ Co	<12.5	1	-
3'c	CH ₃	H	(C ₁₇ H ₁₂ CIN ₃ Cl) ₂ Co	<12.5	24	-
3'd	Cl	Cl	(C ₁₆ H ₈ Cl ₃ N ₃ Cl) ₂ Co	<12.5	26	-
3'e	Br	H	(C ₁₆ H ₉ BrCIN ₃ Cl) ₂ Co	<12.5	18	-
3'f	I	H	(C ₁₆ H ₉ ICIN ₃ Cl) ₂ Co	<12.5	5	-
3'g	NO ₂	H	(C ₁₆ H ₉ CIN ₄ O ₂ Cl) ₂ Co	<12.5	0	-
Rifampicin					0.25	
Isoniazide					0.007	

4. CONCLUSION

The structure of newly synthesized benzimidazole compounds and their metal complexes were confirmed by the empirical molecular formula obtained by the elemental analysis data which was in good agreement of theoretical values of each element present in the compounds. The FT-IR, Mass, NMR and UV-Visible spectra were confirmed the formation of benzimidazole moiety in all ligands **3a-g**.

From all of the spectral, thermal and physical characterization, the proposed structures of Co(II) complexes of **3a,b,d-g** ligands are found with tetrahedral geometry, whereas, of the Co(II) complex of **3c** ligand is found with square pyramidal geometry.

The conductance data disclose that the complexes are non-electrolytes in nature. The ligands are the neutral and monodentate coordinator to the metal ions by means of imidazole-*N* ring, indicated by IR spectral characterization with observation of (C=N) stretching vibration of Co(II) complexes, which were found on ($10\text{--}45 \text{ cm}^{-1}$) lower frequency region than those of the free ligands. It is confirmed by the distorted ¹H NMR spectral signals of aromatic ring protons as well, which, indicates the presence of cobalt ion and the –NH, –OCH₃ and –CH₃ group signals remaining unchanged or quite shifted in compared to their free ligands. The thermogravimetric and elemental analysis data validate the suggested formula as well as the 1:2 stoichiometry of metal and ligand for all

complexes. The antimicrobial data exhibited that most of Co(II) complexes 3'a-g are more active than those of corresponding free ligands against bacterial and fungal strains. The 3'c, 3'e and 3'f complexes and 3a,d,e ligands display comparatively good activity more than used reference drugs against bacterial and fungal strains, which show that they are the promising leads for antimicrobial drug development. None of the compounds showed any specific inhibition towards *Mycobacterium tuberculosis* strain H₃₇Rv in primary screening

5. ACKNOWLEDGMENTS

Authors are thankful to Rajiv Gandhi National Fellowship Scheme, UGC, New Delhi for the financial support and Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF), U.S.A. for anti-mycobacterial activity.

6. REFERENCE AND NOTES

- [1] Guru, N.; Srivastava, S. D. *J. Sci. Ind. Res.* **2001**, *60*, 601.
- [2] (a) Desai, K. G.; Desai, K. R. *Bioorg. Med. Chem.* **2006**, *14*, 8271. [[CrossRef](#)] (b) Guven, O. O.; Erdogan, T.; Goeker, H.; Yildiz, S. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2233. [[CrossRef](#)]
- [3] Kus, C.; Goker, H.; Altanlar, N. *Arch. Pharmazie*, **2001**, *334*, 361. [[CrossRef](#)]
- [4] Nyati, M.; Rao, N. S.; Shrivastav, Y. K.; Verma, B. L. *Ind. J. Heterocycl. Chem.* **2006**, *15*, 295.
- [5] Angani, C. B.; Jardosh, H. H.; Patel, M. P.; Patel, R. G. *Med. Chem. Res.* **2013**, *22*, 3035. [[CrossRef](#)]
- [6] Atwell, G. J.; Baguley, B. C.; Denny, W. A. *J. Med. Chem.* **1989**, *32*, 396. [[CrossRef](#)]
- [7] Kuo, S. C.; Lee, H. Z.; Juang, J. P.; Lin, Y. T.; Wu, T. S.; Chang, J. J.; Lednicer, D.; Paull, K. D.; Lin, C. M.; Hamel, E.; Lee, K. H. *J. Med. Chem.* **1993**, *36*, 1146. [[CrossRef](#)]
- [8] Xia, Y.; Yang, Z. Y.; Xia, P.; Bastow, K. F.; Tachibana, Y.; Kuo, S. C.; Hamel, E.; Hackl, T.; Lee, K. H. *J. Med. Chem.* **1998**, *41*, 1155. [[CrossRef](#)]
- [9] Sundberg, R. J.; Martin, R. B. *Chem. Rev.* **1974**, *74*, 471. [[CrossRef](#)]
- [10] Ambika, S.; Singh, R. M. *Ind. J. Chem.* **2005**, *44B*, 1868.
- [11] Barry, A. L.; Thornsberry, C. In: *Manual and Clinical Microbiology*. Lennette, E. H.; Balows, A.; Hausler, W. J.; Shadomy, H. J., eds. ASM, Washington DC; 1985, 978.
- [12] Jones, R. N.; Barry, A. L.; Govan, T. T.; Washington, J. A. In: *Manual and Clinical Microbiology*. Lennette, E. H.; Balows, A.; Hausler, W. J.; Shadomy, H. J., eds. ASM, Washington DC: 1985, 972.
- [13] Collins, L.; Franzblau, S. G. *Antimicrob. Agents Chemother.* **1997**, *41*, 1004.
- [14] Tuberculosis in Kenya: An East African and British Medical Council Cooperative Investigation Tubercle, Land, **1970**, *51*, 1, 1-23.
- [15] Nawrocka, W.; Sztuba, B.; Kowalaka, M. W.; Liszkiewicz, H. *Farmaco* **2004**, *59*, 83. [[CrossRef](#)]
- [16] Hofmann, K. *Imidazole and Its Derivatives*. New York: Wiley Interscience Publishers, 1953.
- [17] (a) Mohan, S.; Sundaraganesan, N. *Spectrochim. Acta Part A*, **1991**, *47*, 1111. [[CrossRef](#)] (b) Sundaraganesan, N.; Ilakiamani, S.; Subramani, P.; Joshua, B. D. *Spectrochim. Acta Part A*, **2007**, *67*, 628. [[CrossRef](#)]
- [18] (a) Naresh, T. H.; Seong, I. W.; Liqiang, C.; Young-Dae, G.; Young, H. H. *J. Organomet. Chem.* **2008**, *693*, 729. [[CrossRef](#)] (b) Beaumont, R. C.; Eaton, D. R. *J. Inorg. Nucl. Chem.* **1980**, *42*, 701. [[CrossRef](#)]
- [19] Reddy, K. V. *Symmetry and Spectroscopy of Molecules*. 2nd Ed., New Delhi, India: New Age International (P) Ltd., 2009.

Supplementary data

Supplementary data associated with this article can be found at <http://www.orbital.ufms.br/index.php/Chemistry/article/downloadSupFile/530/126>