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RESEARCH ARTICLE

Synthesis and biological studies of complexes of 2-amino-*N*(2-aminobenzoyl) benzohydrazide with Co(II), Ni(II), and Cu(II)

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The present work is concerned with the synthesis and coordination compounds of 2-amino-*N*(2-aminobezoyl) benzohydrazide (ABH). The ligand was synthesized by the reaction of methylanthranilate and hydrazine in 2:1 molar ratio. It can be viewed as a modified form of hydrazide. The ligand was characterized by ^{1}H-NMR, ^{13}C-NMR, mass spectrometry, elemental analysis, and infrared studies. The ligand has got $-NH_2$ moeity, the site for chelation. The complexes of Co(II), Ni(II), and Cu(II) chlorides and bromides were prepared. These complexes were characterized by elemental analysis, infrared, conductance, and magnetic susceptibility studies. Infrared spectra studies confirmed the formation of complexes, while elemental studies suggested the complexation of $[M(ABH)X_2]$ (where X = Cl^- or Br^-) composition.

Knowing about the importance of –N–N– linkage in the biologically active compounds, the synthesized complexes were studied for their biological activity, and were found to be potentially strong in inhibition activity as compared to the neat ligand.

Keywords 2-amino-*N*(2-aminobezoyl)benzohydrazide, coordination compounds, bioassay studies

1 Introduction

Hydrazides are used in various medicines, for example, the antituberculosis drug, isonicotinic acid hydrazide (isoniazid) [1], and the antihypertensive and peripheral vasodilator drug, hydralazine [2]. Isoniazid is shown to produce lung tumors in mice [3], and induce chromosome aberrations and sister chromatid exchanges in cultured rodent cells [4]. Hydrazides are also components in various complex drugs, such as nitrofurans and oxazolidone [5,6].

Furazolidone [*N*-(5-nitro-2-furfurylidine)-3-amino-2-oxazolidone] contains two chemical rings: a nitrofuran-ring, responsible for the antibacterial and antiprotozoal activity, and an oxazolidone-ring (AOZ), which is a hydrazide [6]. They are used as antibacterial drugs in veterinary medicine. One of them, known as hydrazide, is used by itself as an ion exchange resin since it can react with carbonyl compounds [6]. It has been found that the complex of metals, like copper, zinc, cobalt, and iron, bounding to ligand containing oxygen, nitrogen, or sulfur show enhanced property of antihypertensive drugs, antimalarial, antimicrobial, electron transfer, or any type of oxygen transport reaction [7–30]. On the industrial scale, metal complexes of copper, nickel, cobalt, and chromium have wide range of applications, such as dyes and pigments [31–39].

In the context of our research on complexation of diammine derived ligands [40–43], we thought to synthesize a modified diammine by replacing the methoxy moiety of methyl anthranilate with hydrazine in order to add to our previous research [40–43]. The structure of the synthesized ligand is given in Figure 1.

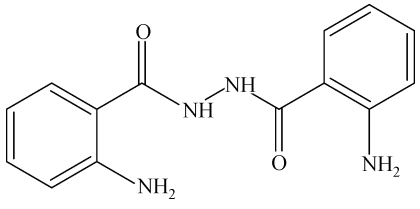

Figure 1 The structure of 2-aminobenzohydrazide (ABH) ligand.

2 Experimental

2.1 Materials and methods

All chemicals and solvents used were of Analar grade. Metal (II) salts of Co, Ni, and Cu were used as chlorides obtained from Riedel-de-Haen, Germany, and were used as such without further purification. The partial dehydration of the salts was carried out by drying the hydrated salts in a vacuum oven for several hours at 80°C–100°C. Methyl anthranilate was obtained from Acros Organics, USA, and hydrazine monohydrate from PANREAC quimica SA, Barcelona, Espania. Solvents were distilled at least twice before use. Elemental analysis was obtained from Vario Elemntar II, Germany. Melting points were recorded on Gallenkamp apparatus and reported as such. Biologic activities were determined by the standard procedure.

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2.2 Preparation of ligand

According to the procedure adopted by Galal et al. [44], 0.060 mol of methyl anthranilate was mixed with 0.022 mol of hydrazine monohydrate in a round bottom flask, and the resulting reaction mixture was refluxed at 80°C–90°C for 1 h with constant stirring. Needle-type crystals of the prepared ligand appeared by keeping the reaction mixture for about two hours in a refrigerator. Crystals were washed with *n*-hexane and recrystallized with dry ethanol. The yield was 48%.

2.3 General preparation of solid complexes

All complexes of 2-aminobenzohydrazide (ABH) were prepared using the same general procedure. The required amount of partially dehydrated salts was dissolved in a minimum amount of anhydrous ethanol or methanol. Dehydration of the metal salts was carried out by reacting with the calculated amount of 2,2-dimethoxy propane as dehydrating agent. The solution was stirred up for about 0.5 h in order to ensure complete dehydration. Dissolved ligand was added slowly to the metal salt solution with constant stirring. The solid complex was formed immediately on mixing the two solutions, or in either case, the complex was obtained by reducing the volume of the solution on a rotary evaporator. The products were filtered through sintered glass crucible, washed several times with *n*-hexane or dried ethanol, and dried under vacuum. The reaction is shown in Figure 2.

2.4 Instrumentation

Infrared spectra (IR) were taken in the range of 4000–600 cm on PYE UNICAM Infrared Spectrophotometer in KBr disc. The far IR spectra were examined in KBr discs in the region of 400–20 cm^{-1} on a FT-IR SHIMADZU spectrometer. The absorption spectra of solution of complexes in the range of 200–900 nm using different solvents were obtained on Jasco DEC-1 Spectrophotometer with 1 cm matched quartz cells. Molar conductance of the solution of the metal complexes was determined using a conductivity meter type HI-8333. All measurements were carried out at room temperature using freshly prepared solution. Magnetic susceptibilities were measured by Gouy method at room temperature using Hg $[Co(SCN)_4]$ as a standard [45]. Magnetic moments were thus calculated. The cations and anions were estimated by using typical analytical procedure.

Bioactivities were investigated using agar-well diffusion method [46]. Bacterial strains of 2–8 h old in column containing approximately 104–106 colony forming units (CFU) per mL were used in these assays. The wells were dug in the media with the help of a sterile metallic borer with centers at least 24 mm. Recommended concentration (100 μL) of the test sample 1 $mg \cdot mL^{-1}$ in DMSO were introduced in the respective wells. For other wells supplemented with DMSO and reference antibacterial drug, gentamycin served as negative and positive controls, respectively. The plates were incubated immediately at 37°C for 20 h. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). Growth inhibition was compared with the standard drug gentamycin. To clarify any participating role of DMSO in the biologic screening, separate studies were carried out with the solutions alone of DMSO, and they showed no activity against any bacterial strains. All these complexes were found to be potentially active against these bacterial strains.

3 Results and discussions

The ABH is characterized by elemental analyses, mass spectrum, and NMR spectroscopy (proton and ^{13}C).

3.1 Elemental and mass spectra analysis

Elemental analytical data of ABH and its complexes are very close to the theoretical values, as shown in Table 1. Elemental analysis show that the metal to ligand ratio is 1∶1, and the composition of metal complex is $M(ABH)X_2$ (where X is Cl^-, Br^-, and NO_3^-). The mass spectrum of ABH shows a peak at *m*/*z* of 270, which is due to the ABH^+ ion.

3.2 Conductance, melting points, and magnetic moments measurements

Conductance and melting points of the complexes are given in Table 2; conductance data show that the metal complexes are nonelectrolyte in nature, indicating that the chloride or

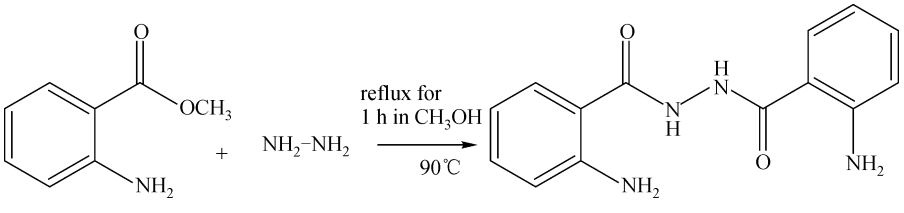

Figure 2 Methyl anthranilate hydrazine 2-amino-*N*(2-aminobezoyl)benzohydrazide.

Table 1 Analytical data of ABH and its complexes

complexes	color	C / %	H / %	N / %	cation / %	anion / %
$C_{14}H_{14}N_4O_2$	white	62.62 (62.21)	6.08 (5.22)	20.81 (20.73)	—	—
$[NiCl_2\ (C_{14}H_{14}N_4O_2)]$	light green	42.80 (42.05)	4.30 (3.53)	14.90 (14.01)	14.02 (14.68)	17.20 (17.73)
$[NiBr_2(C_{14}H_{14}N_4O_2)]$	grayish green	33.20 (34.40)	3.21 (2.89)	12.95 (11.46)	11.88 (12.01)	32.67 (32.69)
$[CoCl_2(C_{14}H_{14}N_4O_2)]$	blackish violet	42.45 (42.02)	2.42 (3.53)	15.97 (14.00)	16.97 (14.73)	16.67 (17.72)
$[CoBr_2(C_{14}H_{14}N_4O_2)]$	dark green	33.22 (34.38)	3.15 (2.89)	12.61 (11.46)	12.00 (12.05)	32.60 (32.68)
$[CuCl_2(C_{14}H_{14}N_4O_2)]$	yellowish green	42.50 (41.55)	2.40 (3.49)	13.20 (13.84)	15.00 (15.70)	16.49 (17.52)
$[CuBr_2(C_{14}H_{14}N_4O_2)]$	yellowish green	34.40 (34.06)	3.17 (2.86)	11.70 (11.35)	12.90 (12.87)	31.24 (32.37)

Calculated values are given in parenthesis

Table 2 Conductance, melting points, and magnetic moments data

complex	solvent	m.p. / °C	molar conductance / ($S \cdot cm^{-1}$)	Cor × M × 10^{-6} / (c.g.s)	μ_{eff} at 298K / (B.M)
$C_{14}H_{14}N_4O_2$	—	108–110	—	—	—
$[NiCl_2\ (C_{14}H_{14}N_4O_2)]$	pyridine	152–154	0.245	3547.04	2.889
$[NiBr_2(C_{14}H_{14}N_4O_2)]$	DMF	122	4.135	3034.16	2.70
$[CoCl_2(C_{14}H_{14}N_4O_2)]$	pyridine	67–71	1.446	9948.66	4.89
$[CoBr_2(C_{14}H_{14}N_4O_2)]$	DMF	163	8.501	8127.91	4.42
$[CuCl_2(C_{14}H_{14}N_4O_2)]$	pyridine	206–208	1.239	1941.129	2.159
$[CuBr_2(C_{14}H_{14}N_4O_2)]$	pyridine	168–170	1.012	1977.24	2.180

bromide ions are located inside the coordination sphere. All the complexes show magnetic susceptibilities, as shown in Table 2.

3.3 IR evaluation

IR data given in Table 3 shows broadening of $-NH_2$ and carbonyl peak, which suggest coordination through these sites. While the peak of hydrazide–NH remains unaltered, and the peak of non coordinated carbonyl diminishes due to amide-imidic acid type tautomerism, it can be proposed that the carbonyl peak diminishes due to hydrogen bond formation with free non-coordinated amine group. Therefore, the proposed structure of the coordination compounds produced is given as shown in Figure 3.

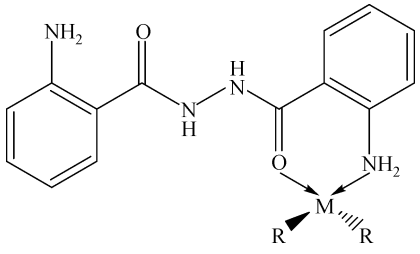

Figure 3 Proposed structures of the complexes. M = Co(II), Ni (II), and Cu(II), R = Cl^- or Br^-.

3.4 ^{1}H- and ^{13}C-NMR evaluation

The ^{1}H-NMR show doublet of doublet for protons located at 3 and 19, 4 and 18, 5 and 17, and 6 and 16, which all are

Table 3 IR spectra for ABH and its complexes (cm^{-1}) of selected region

compound	N-$H_{stretching\ frequency}$	C = $O_{stretching\ frequency}$	other bands	M–X
$C_{14}H_{14}N_4O_2$	3441.7sh,3192.9s	1720 s,w	1600, 1570	—-
$[NiCl_2\ (C_{14}H_{14}N_4O_2)]$	3400bd,3171.7	1720 s,w	1600,1570	440.7
$[NiBr_2(C_{14}H_{14}N_4O_2)]$	3400bd,3190s	1720 s,w	1600,1570	418.3
$[CoCl_2(C_{14}H_{14}N_4O_2)]$	3400.3bd,3143m	1700 s,w	1624,1540sh	400bd
$[CoBr_2(C_{14}H_{14}N_4O_2)]$	3400bd,3245	1700 s,w	1622,1549sh	521.7
$[CuCl_2(C_{14}H_{14}N_4O_2)]$	3400bd,3123.5	1714.9 s,w	1600,1570	405
$[CuBr_2(C_{14}H_{14}N_4O_2)]$	3374.2s,3143.8	1700 s,w	1609.5,1525.6	418.5

sh = sharp, m = medium, s = small, w = weak, bd = broad, M – X = metal-anion

observed at 6.7 ppm to 7.5 ppm in a very complex form, while the protons located at positions 10 and 11 are observed around 9 ppm [47], and the protons at 7 and 20 positions give a singlet at around 6.3 ppm, as shown in Figure 4.

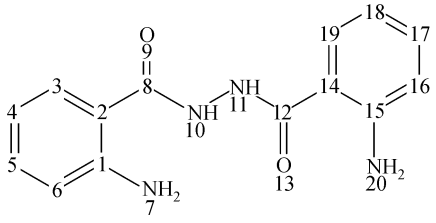

Figure 4 Labeled ligand for ^{1}H and ^{13}C-NMR studies.

^{13}C-NMR show seven peaks for all the seven identical carbons, namely, 12 and 8, 1 and 15, 2 and 14, 3 and 19, 4 and 18, 5 and 17, and 6 and 16, respectively, as shown in Figure 4.

3.5 Copper complexes

The complexes of Cu (II) show an absorption band in the region of 12000–20000 cm^{-1} (Figure 5). The envelopes of these bands are generally unsymmetrical, seeming to encompass several overlapping transitions. The magnetic moment is around 2.0 B.M [40,48–50], which is very close to the spin-only value of the unpaired electron. The conductance behavior shows that the complex is non-electrolytic.

3.6 Nickel complexes

The visible absorption spectra of Ni(II) complexes (Figure 6) show broad peak around 15500 cm^{-1}, overlapping the $^{3}T_1(F)\rightarrow{}^{3}T_1(P)$ and $^{3}T_1(F)\rightarrow{}^{3}T_2(F)$ transition probably indicating tetrahedral geometry. The magnetic moment (2.8 B.M for $[NiCl_2\ (C_{14}H_{14}N_4O_2)]$ and 2.7 B.M for $[NiBr_2(C_{14}H_{14}N_4O_2)]$) and nonelectrolytic behavior of these complexes are consistent with distorted tetrahedral symmetry of $[Ni(ABH)X_2]$ [51,52].

3.7 Cobalt complex

The magnetic moment of cobalt complex is around 5 B.M indicates three unpaired electrons. The solution spectrum of cobalt (II) complex is given in Figure 7. A set of three bands in range of 13000 to 24000 cm^{-1} are assigned to $^{4}A_2(F)\rightarrow{}^{4}T_1(P)$ transition, ν_3, in T_d symmetry. The low energy transition $^{4}A_2(F)\rightarrow{}^{4}T_1(F)$, ν_2 is not observed. The intensities and bandwidths are in accordance with T_d symmetry.

3.8 Bio-assay investigations

The complexes of ABH were investigated for their bioactivity against various available microorganisms. These microorganisms include gram positive and gram negative bacteria along with a selected species of fungi. Gram Negative bacteria include *E. coli*, *Salmonella typhi*, *Enterobacter aerogenes*, *Proteus vulgaris*, and *Pseudomonas aeruginosa*; the selected gram Positive bacterial strain is *Staph aureus* and fungus like *Candida albican.*

These studies show that the metal complexes become more biologically active as compared to neat organic moiety. The results are reported in Table 4.

All these complexes were found to be potentially active against these bacterial strains. It is evident that the overall potency of the ligand was enhanced on coordination, as shown in comparative graphs in Figures 8–16.

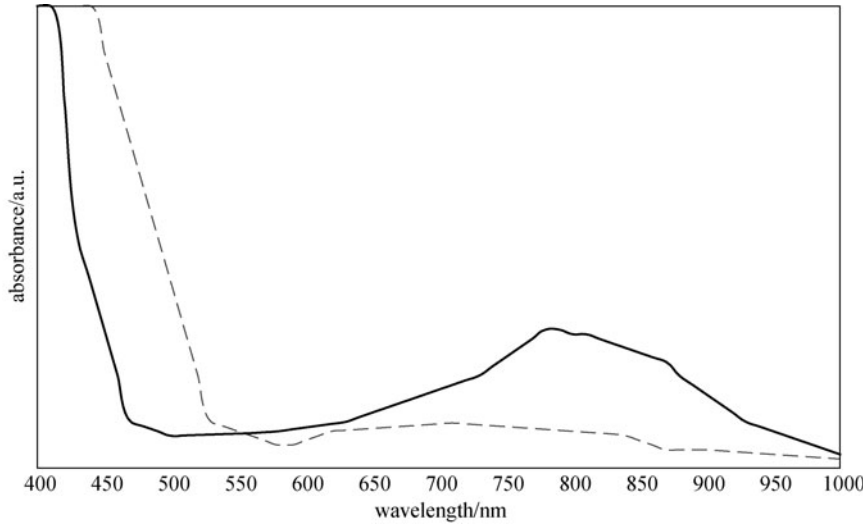

Figure 5 Visible spectrum of copper ABH complexes. The solid line represents $[CuCl_2(C_{14}H_{14}N_4O_2)]$, while the dash line marks $[CuBr_2(C_{14}H_{14}N_4O_2)]$.

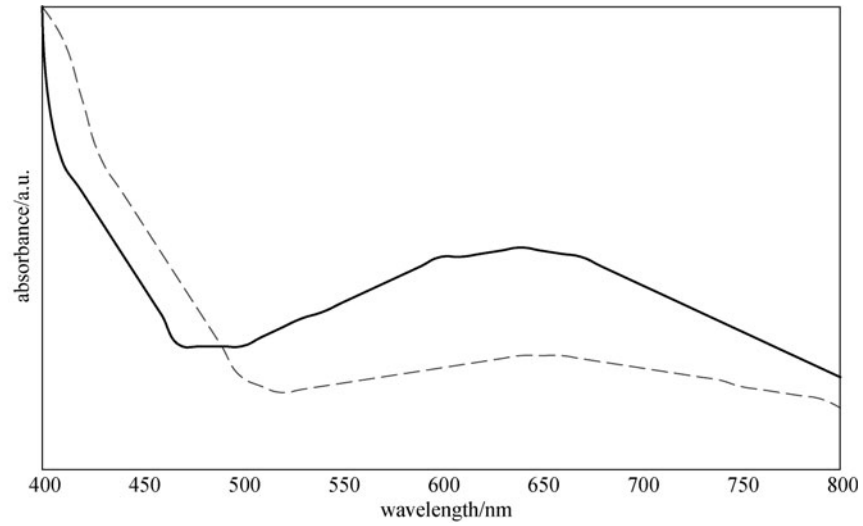

Figure 6 Visible spectrum of nickel ABH complexes. The solid line represents $[NiCl_2(C_{14}H_{14}N_4O_2)]$, while the dash line marks $[NiBr_2(C_{14}H_{14}N_4O_2)]$.

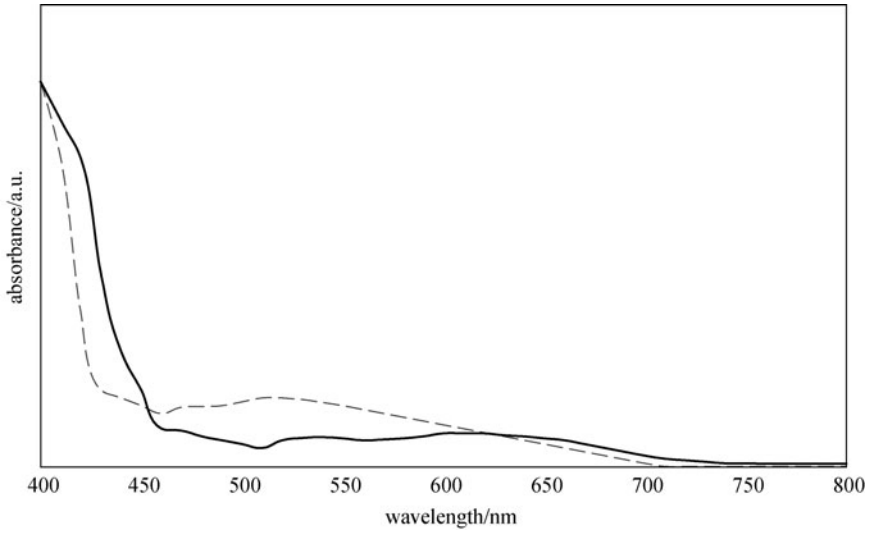

Figure 7 Visible spectrum of cobalt ABH complexes. The solid line represents $[CoCl_2(C_{14}H_{14}N_4O_2)]$, while the dash line marks $[CoBr_2(C_{14}H_{14}N_4O_2)]$.

Table 4 Biologic activities of complexes against gram negative, gram positive, and fungus

Compound	*E.coli*	*Staphylococcus aureus*	*Salmonella typhi*	*Enterobacter aerogenes*	*Proteus vulgaris*	*Pseudomonas aeruginosa*	*Candida albican*
Gentamycin	21	38	35	31	39	28	22
ABH	1	1	2	1	1	0	0
$[NiCl_2\ (C_{14}H_{14}N_4O_2)]$	16	21	38	30	20	19	32
$[NiBr_2(C_{14}H_{14}N_4O_2)]$	17	26	22	22	17	23	35
$[CoCl_2(C_{14}H_{14}N_4O_2)]$	24	29	40	25	19	25	34
$[CoBr_2(C_{14}H_{14}N_4O_2)]$	24	31	40	30	23	24	35
$[CuCl_2(C_{14}H_{14}N_4O_2)]$	14	28	18	20	14	26	32
$[CuBr_2(C_{14}H_{14}N_4O_2)]$	17	26	16	17	19	19	19

Gram Negative: *E.coli, Salmonella typhi, Enterobacter aerogenes, Proteus vulgaris,* and *Pseudomonas aeruginosa*
Gram Positive: *Staphylococcus aureus*
Fungus: *Candida albican*

Figures 8–13 show the comparison between the inhibitory activities of metal complexes with the ligand from which they are derived and with the antimicrobial drug. It becomes clear that ABH on complexation show pronounced inhibitory activity.

Figures 14 and 15 show that the metal complexes of the same anion are comparable to each other and to the standard drug. We can conclude from this comparison that cobalt (II) complexes of the same ligand are more potent than the [Ni(II) and Cu(II) ABH] complexes. Similar conclusion can be drawn for the $[Co(ABH)Br_2]$ complex by locating Figure 15.

The effect of bromide and chloride on the inhibitory activity can be concluded in Figure 16, which shows that the chloride complexes of these metal with ABH ligand are potentially stronger than the bromide complexes.

The series that we can conclude from these graphs is shown as follows:

Co(II) > Ni(II) > Cu(II) and $Co(ABH)Cl_2 > Co(ABH)Br_2$, $Ni(ABH)Cl_2 > Ni(ABH)Cl_2$, $Cu(ABH)Cl_2 > Cu(ABH)Br_2$.

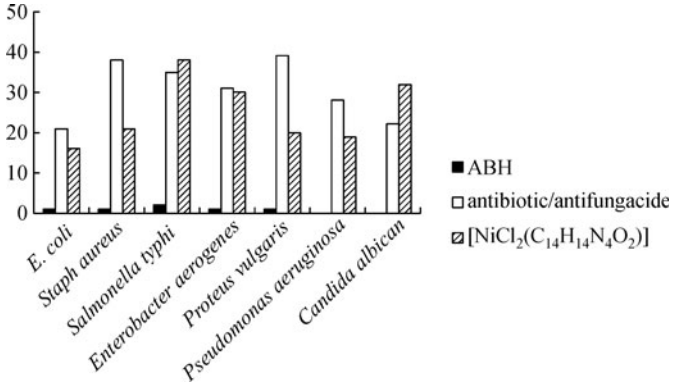

Figure 8 Comparsion of $[NiCl_2 (C_{14}H_{14}N_4O_2)]$ with antibiotic/antifungacide and ABH.

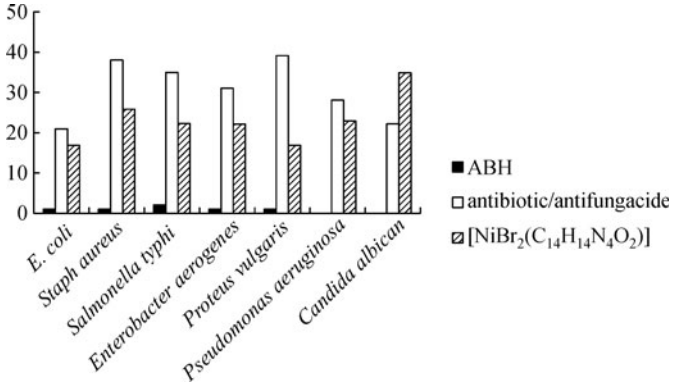

Figure 9 Comparsion of $[NiBr_2(C_{14}H_{14}N_4O_2)]$ with antibiotic/antifungacide and ABH.

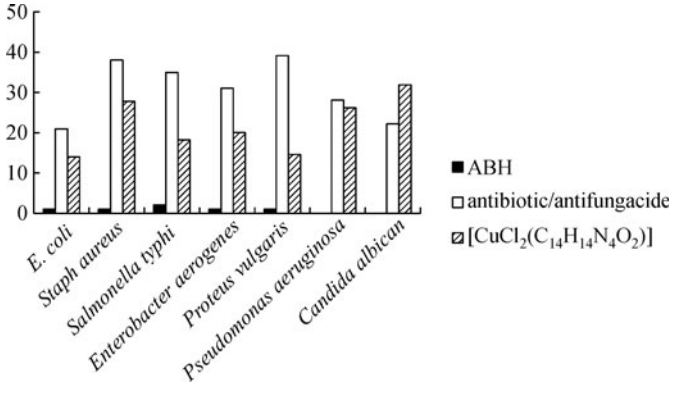

Figure 10 Comparsion of $[CuCl_2(C_{14}H_{14}N_4O_2)]$ with antibiotic/antifungacide and ABH.

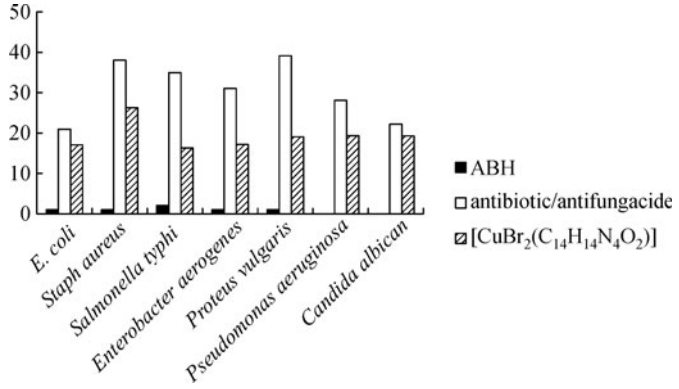

Figure 11 Comparsion of $[CuBr_2(C_{14}H_{14}N_4O_2)]$ with antibiotic/antifungacide and ABH.

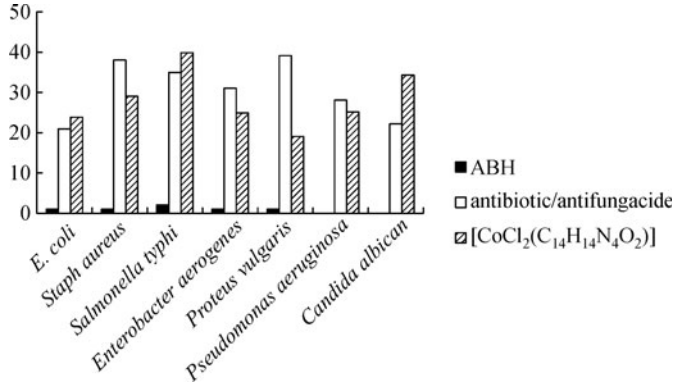

Figure 12 Comparsion of $[CoCl_2(C_{14}H_{14}N_4O_2)]$ with antibiotic/antifungacide and ABH.

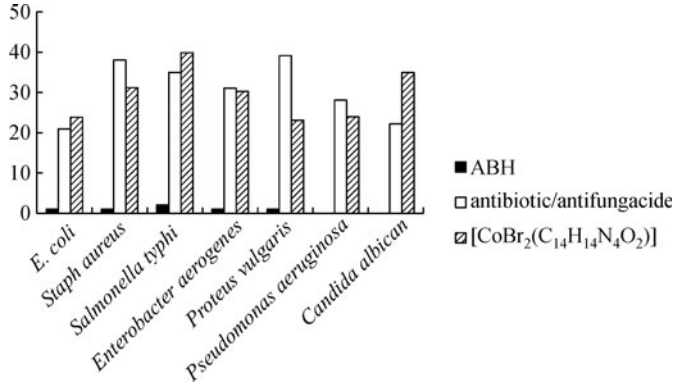

Figure 13 Comparsion of $[CoBr_2(C_{14}H_{14}N_4O_2)]$ with antibiotic/antifungacide and ABH.

4 Conclusion

The synthesized complexes of ABH ligand show tetrahedral geometries. Magnetic moment studies prove the assigned geometries. The synthesized hydrazine derived ligand showed antibacterial/antifungal properties. In comparison, the copper (II), nickel (II), and cobalt (II) metal complexes of this compound showed more activity against one or more bacterial/fungal strains, thus introducing a novel class of metal-based bactericidal and fungicidal agents. The series for the inhibitory activities is shown as follows:

$Co(II) > Ni(II) > Cu(II)$ and $Co(ABH)Cl_2 > Co(ABH)Br_2$, $Ni(ABH)Cl_2 > Ni(ABH)Cl_2$, $Cu(ABH)Cl_2 > Cu(ABH)Br_2$.

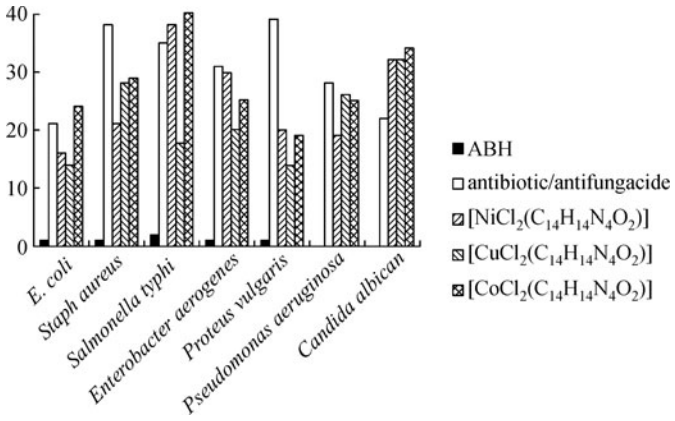

Figure 14 Comparison of chloride complexes of Ni (II), Cu (II), and Co (II) with ABH and antiobiotic/antifugacide drugs.

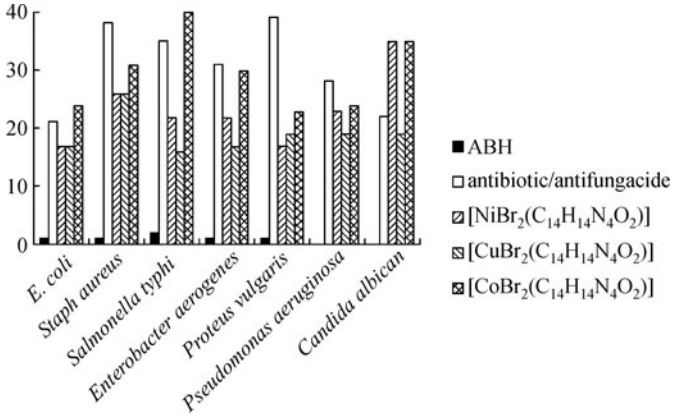

Figure 15 Comparison of bromide complexes of Ni (II), Cu (II), and Co (II) with ABH and antiobiotic/antifugacide drugs.

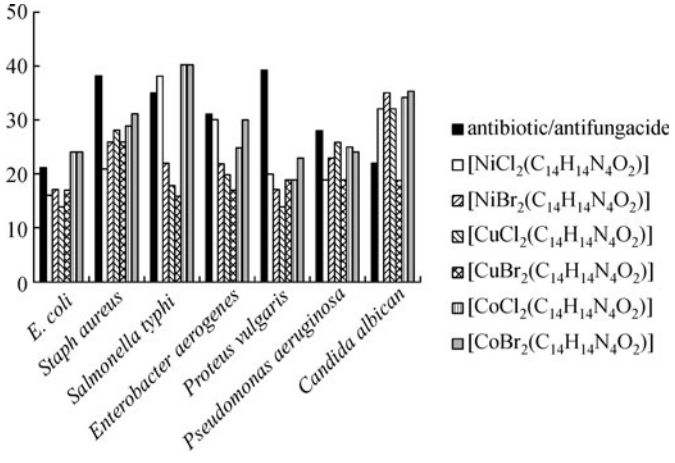

Figure 16 Comparison of synthesized coordination compounds with antibiotic/antifungacide drugs.

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References

1. Hoose, C.; Eberhardt, K.; Hartmann, W.; Wosniok, W., *Pneumologie* **1990**, *44*, 458–459
2. Vidrio, H.; Fernández, G.; Medina, M.; Alvarez, E.; Orallo, F.,

Vascul. Pharmacol. **2003**, *40*, 13–21
3. Delaney, J.; Timbrell, J. A., *Xenobiotica* **1995**, *25*, 1399–1410
4. MacRae, W. D.; Stich, H. F., *Mutat. Res*. **1979**, *68*, 351–365
5. Strolin-Benedetti, M.; Tipton, K. F., *J. Neural Transm. Suppl*. **1998**, *52*, 149–171
6. Saunders, S. R.; Karo, W., *Organic Functional Groups*; Academic press: New York & London, 1968, p 363–384
7. Fee, J. A.; Gaber, B. P., *J. Biol. Chem*. **1972**, *247*, 60–65
8. Cohen, H. J.; Fridovich, I., *J. Biol. Chem*. **1971**, *246*, 359–366
9. Keele, B. B. Jr; McCord, J. M.; Fridovich, I., *J. Biol. Chem*. **1970**, *245*, 6176–6181
10. Hayaishi, O.; Nozaki, M., *Science* **1969**, *164*, 389–396
11. Malkin, R.; Malmström, B. G., *Adv. Enzymol. Relat. Areas Mol. Biol*. **1970**, *33*, 177–244
12. Coleman, J. E., *Prog. Bioorg. Chem*. **1971**, *1*, 159–344
13. Tsibris, J. C. M.; Woods, R. W., *Coord. Chem. Rev*. **1970**, *5*, 417–458
14. Hodgkin, D. C. J.; Pickworth, J. H.; Robertson, R. J.; Prosen, J. G.; White, R.; Bonnett, K. N.; Trueblood, J. R.; Cannon, A. W.; et al., *Nature* **1955**, *176*, 325–328
15. Barker, H. A.; Rooze, V.; Suzuki, F.; Iodice, A. A., *J. Biol. Chem*. **1964**, *239*, 3260–3266
16. Cannata, J. J. B.; Focesi, A. Jr; Mazumder, R.; Warner, R. C.; Ochoa, S., *J. Biol. Chem*. **1965**, *240*, 3249–3257
17. Flavin, M.; Ochoa, S., *J. Biol. Chem*. **1957**, *229*, 965–979
18. Kaziro, Y.; Ochoa, S., *Adv. Enzymol. Relat. Areas Mol. Biol*. **1964**, *26*, 283–378
19. Abeles, R. H.; Lee, H. A. Jr, *J. Biol. Chem*. **1961**, *236*, 2347–2350
20. Babior, B. M., *J. Biol. Chem*. **1969**, *244*, 2927–2334 and 2917–2926
21. Abrams, R.; Duraiswami, S., *Biochem. Biophys. Res. Commun*. **1965**, *18*, 409–414
22. Burke, G. T.; Mangum, J. H.; Brodie, J. D., *Biochem*. **1970**, *9*, 4297–4302
23. Wood, J. M.; Kennedy, F. S.; Wolfe, R. S., *Biochem*. **1968**, *7*, 1707–1713
24. Ghambeer, R. K.; Wood, H. G.; Schulman, M.; Ljungdahl, L., *Arch. Biochem. Biophys*. **1971**, *143*, 471–484
25. Hauska, G. A.; McCarty, R. E.; Berzborn, R. J.; Racker, E., *J. Biol. Chem*. **1971**, *246*, 3524–3531
26. Malmstrom, B. G., *Annu. Rev. Biochem*. **1982**, *51*, 21–59
27. Coleman, J. E., *Prog. Bioorg. Chem*. **1971**, *1*, 159–344
28. Blumberg, W. E.; Peisach, J., *Biochim. Biophys. Acta* **1966**, *126*, 269–273
29. Buchanan, B. B.; Arnon, D. I., *Adv. Enzmol* **1970**, *33*, 119–176
30. Nakos, G.; Mortensen, L. E., *Biochem*. **1971**, *10*, 455–458
31. Cotton, F. A.; Wilkinson, G., *Basic inorganic chemistry 2nd Edition*; John Wiley & Sons: New York, 1987
32. Grubbs, R. H.; Trnka, T. M., *Ruthenium Catalysed Olefin Metathesis; Ruthenium in Organic Chemistry*; Wiley-VCH: Germany, 2004
33. Hong, S. H.; Grubbs, R. H., *J. Am. Chem. Soc*. **2006**, *128*, 3508–3509
34. Schawab, P.; Grubbs, R. H.; Ziller, J. W., *J. Am. Chem. Soc*. **1996**, *118*, 100–110
35. Fink, G.; Brintzinger, H. H., *Ziegler Catalysts*; Springer-verlag, 1995, p 161–164
36. Corradini, P.; Guerra, G.; Cavallo, L., *Acc. Chem. Res*. **2004**, *37*, 231–241
37. Takahashi, T., *Titanium(iv) Chloride Triethylaluminium: Encyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons, 2001
38. Elschenbroich, C.; Saizer, A., *Organomettalics, A Concise Introduction 2nd Edition*; Wiley & Sons, 1992
39. Kuil, M.; Soltner, T.; van Leeuwen, P. W.; Reek, J. N.; Reek, N. H., *J. Am. Chem. Soc*. **2006**, *128*, 11344–11345
40. Hussain, M. S.; Rehman, S. U., *Zeitschrift Fur Naturforschung* **1978**, *3*, 67–69
41. Hussain, M. S.; Rehman, S. U., *Inorg. Chim. Acta* **1982**, *60*, 231–238
42. Rehman, S. U.; Noreen, S.; Rashida, M.; Ikram, K.; Ali, I.; Ahmad, M.; Arshad; Bukhari, I. H., *Nucleus* **2009**, *46*, 501–506
43. Rehman, S.; Ali, N.; Arshad, M.; Ahmad, N.; Akhtar, G., *J. Chem. Soc. Pak*. **2009**, *31*, 391–395
44. Galal, S. A.; Hegab, K. H.; Kassab, A. S.; Rodriguez, M. L.; Kerwin, S. M.; El-Khamry, A. M. A.; El-Diwani, H. I., *Eur. J. Med. Chem*. **2009**, *44*, 1500–1508
45. Figgis, B. N.; Lewis, J.; Wilkins, R. G., *Modern Coordination Chemistry*; Interscience: New York, 1960, p 412
46. Atta-ur-Rahman; Choudhary M. I.; Thomsen W. J., *Bioassay Techniques for Drug Development*; Harwood Academic: Amsterdam, Netherlands, 2001
47. Friedman, L.; Litle, R. L.; Reichle, W. R., *Org. Synth*. **1960**, *40*, 93
48. Basee, G.; Belford, R.; Dickerson, R., *Inorg. Chem*. **1962**, *1*, 438–439
49. Sykes, A. G., *Advances in Inorganic Chemistry, Volume 39*; Academic Press, 1992, p 3
50. Yokoi, H., *Bull. Chem. Soc. Jpn*. **1974**, *47*, 3037–3040
51. Frömmel, T.; Peters, W.; Wunderlich, H.; Kuchen, W., *Angew. Chem*. **1992**, *31*, 612–613
52. Toftlund, H.; Nivorozhkin, A. L.; la Cour, A.; Adhikary, B.; Murray, K. S.; Fallon, G. D.; Nivorozhkin, L. E., *Inorg. Chim. Acta* **1995**, *228*, 237–241