

Synthesis and characterization of metal complexes of 2, 4-Dichloro-5-sulfamoylbenzoic acid

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Abstract

Six new Mg(II) ([Mg(sba)₂]. 2H₂O, 1), Fe(II) ([Fe(sba)₂(H₂O)₄], 2), Co(II) ([Co(sba)₂(H₂O)₄], 3), Ni(II) ([Ni(sba)₂(H₂O)₄]. 5H₂O, 4), Cu(II) ([Cu(sba)₂(H₂O)₄]. 2H₂O, 5) and Cd(II) ([Cd(sba)₂(H₂O)₄]. 5H₂O, 6) complexes of 2,4-dichloro-5-sulfamoylbenzoic acid (Hsba) have been prepared. Metal compounds (1-6) characterized by AAS, elemental, FTIR, Uv-Vis., magnetic moment and molar conductivity measurements. The structures of the synthesized metal complexes were observed to be linear for 1 and octahedral for 2-6 according to analyses results. Moreover, antifungal and antibacterial activities of metal salt, Hsba and 1-6 were reviewed for their antifungal activities against *Candida Albicans* (ATCC 14053) (yeast), *Candida parapsilosis* (ATCC 22019) (yeast) and *Candida krusei* (ATCC 6258) (yeast) and antibacterial activities against *Escherichia coli* (ATCC 25922) (Gram negative), *Enterococcus faecalis* (ATCC 29212) (Gram positive), *Staphylococcus aureus* (ATCC 29213) (Gram positive). The results were checked against with the antibiotic compounds, Fluconazole as antifungal agent and Cefepime, Vancomycin, Levofloxacin as antibacterial agent. Activity against all compounds bacteria and yeasts was observed.

Keywords: 2,4-Dichloro-5-sulfamoylbenzoic acid; metal complexes; anti-microbial and anti-fungal activities

Introduction

2,4-Dichloro-5-sulfamoylbenzoic acid (Hsba) have biological activities such as fungicidal, antihypertensives (Gaidukevich *et al.* 1984)^[6], antiinflammatory (Latosinska *et al.* 2009)^[12], antihypertensive (Maeda *et al.* 1982; Ohnishi *et al.* 1982; Mochida *et al.* 1983), anticonvulsant (Lacroix *et al.* 1996), antiviral (Boissier *et al.* 1963; Hamano *et al.* 1974; Lebedev *et al.* 1985; Xia 1991; Marona and Kiec-Kononowicz 1998), saluretic, antihypertensive (Brzozowski and Pomarnacka 1980), diuretic (Arslan *et al.* 2002; Yenikaya 2011b; Latosinska *et al.* 2012; Slawinski *et al.* 2014; Matulis *et al.* 2017)^[13, 25, 18], antiglaucoma (Shett 1969; Piwinski *et al.* 1984; Cherkez *et al.* 1986; Piwinski *et al.* 1987; Yenikaya *et al.* 2011a)^[24, 22, 5, 27], antiarrhythmic and hypotensive (Brzozowski and Slawinski 1985)^[4]. A few the simple transition metal complex {NaHsba (Latosinska *et al.* 2012)^[13], Fe(III) (Ilkimen *et al.* 2020)^[10], proton transfer salts {2-aminomethylpyridine (Cherkez *et al.* 1986)^[5], 2-amino-3-methylpyridine and ethylenediamine (Piwinski *et al.* 1984)^[22] and mixed ligand metal complexes {2-amino-3-hydroxypyridine (2a3OHp) {[Cu(sba)₂(2a3OHp)₂(H₂O)₂].2H₂O}, 2-amino-3-bromo-5-nitropyridine (2a3Br5NO₂p) {[Cu(sba)₂(2a3Br5NO₂p)₂(H₂O)₂]. 2H₂O}, 2-amino-3,5-dibromopyridine (2a35DBRp) {[Cu(sba)₂(2a35DBRp)₂(H₂O)₂].2H₂O} (Ilkimen and Yenikaya 2021)^[9], 2-aminomethylpyridine (2amp) {[Zn(sba)₂(2amp)]. H₂O}, 4,4'-bipyridine (bpy) {[Mn(bpy)(sba)₂(H₂O)₂], [Co(bpy)(sba)₂(H₂O)₂], [Cu(bpy)(sba)₂], [Zn(bpy)(Hsba)].H₂O, [Ag(bpy)(sba)], [Cd(bpy)(sba)(H₂O)]} (Zhao *et al.* 2014)^[29] and 1,3-bis(4-pyridyl)propane (bpp) {[Ag₂(bpp)(sba)₂].H₂O, [Cd(bpp)(sba)₂].H₂O], and [Pb(bpp)₃(sba)₂]} (Liu *et al.* 2015)^[15] of H₂sba have been synthesized.

In this study, six new Mg(II) {[Mg(sba)₂].2H₂O, 1}, Fe(II) {[Fe(sba)₂(H₂O)₄], 2}, Co(II) {[Co(sba)₂(H₂O)₄], 3}, Ni(II) {[Ni(sba)₂(H₂O)₄].5H₂O, 4}, Cu(II) {[Cu(sba)₂(H₂O)₄].2H₂O, 5} and Cd(II) {[Cd(sba)₂(H₂O)₄].5H₂O, 6} complexes of 2,4-dichloro-5-sulfamoylbenzoic acid (Hsba) were prepared and structures of powder metal complexes (1-6) have been proposed with AAS, elemental analysis, FT-IR, UV-vis, magnetic moment and molar conductivity measurements. The structures of the synthesized metal complexes were observed to be linear for 1 and octahedral for 2-6 according to results of spectroscopic analyzes. Furthermore, all compounds were screened for their antifungal activities against *Candida Albicans* (ATCC 14053), *Candida parapsilosis* (ATCC 22019) and *Candida krusei* (ATCC 6258) (yeast), and antibacterial activities against *Enterococcus faecalis* (ATCC 29212), *Staphylococcus aureus* (ATCC 29213) (Gram positive), *Escherichia coli* (ATCC 25922) (Gram negative). The results were compared with the control compounds, Cefepime, Levofloxacin and Vancomycin as antibacterial agents, and Fluconazole as antifungal agent. Activity against all compounds bacteria and yeasts was observed. Therefore, the obtained synthesis compounds can be evaluated for the synthesis of new antibacterials

Experimental section

General methods and materials

The chemicals used in this study were obtained from Sigma Aldrich and used without further purification. Elemental analysis Elementar Vario III EL, AAS studies Perkin Elmer PinAAcle 900T, FT-IR spectra Perkin Elmer Bruker Optics, Vertex 70 FT-IR spectrometer using KBr, UV-Vis spectra SHIMADZU UV-2550, Magnetic moment measurements Sherwood Scientific Magway MSB MK1 and molar conductances of the compounds WTW Cond 315i/SET were done with.

Synthesis of compounds 1-6.

A solution of 5 mmol Hsba and 2,5 mmol metal(II) acetate [Mg for 1 or Fe for 2 or Co for 3 or Ni for 4 or Cu for 5 or Cd for 6] in ethanol (50 mL) with stirring for four days to powders solids white for 1 (1.197 g, 80% yield), cream for 2 (1.2489 g, 75% yield), pink for 3 (1.004 g, 60% yield), green for 4 (1.087 g, 65% yield), blue for 5 (1.423 g, 75% yield) and white for 6 (1.084 g, 60% yield).

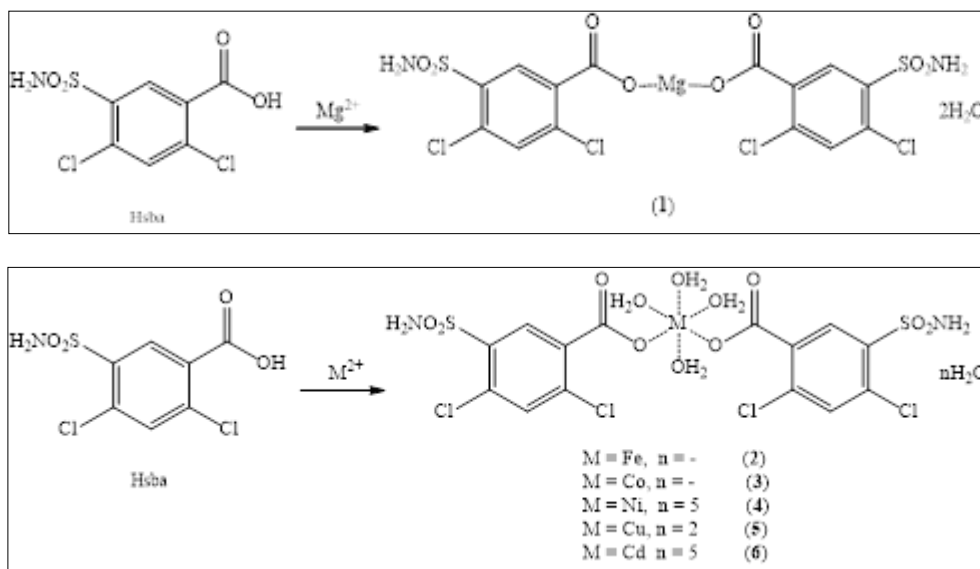


Fig 1: Syntheses of metal complexes 1-6 (a for 1, b for 2-6).

Anti-microbial Assay

In this study, microorganisms of *Escherichia coli* (ATCC 25922) (Gram negative), *Enterococcus faecalis* (ATCC 29212) (Gram positive), *Staphylococcus aureus* (ATCC 29213) (Gram positive), and *Candida Albicans* (ATCC 14053) (yeast), *Candida parapsilosis* (ATCC 22019) (yeast), and *Candida krusei* (ATCC 6258) (yeast) were used.

Determination of Anti-microbial Effect by Microdilution Method

The MICs (minimum inhibitory concentrations) of the starting materials {metal(II) acetate and Hsba} and synthesized compounds (1-6) against bacterial strains (*E. coli*, *E. Faecalis*, and *S. aureus*) and yeasts (*C. albicans*, *C. krusei* and *C. parapsilosis*) were determined. The MIC of reference antibiotics Levofloxacin, Cefepime, Vancomycin and Fluconazole were compared with the all compounds. For this purpose, U-shaped 96-well microplates were used in the microdilution method.

Microdilution method

MHB medium was prepared as single and double force. The all compounds (4 mg) and antibiotics (4 mg) were dissolved in 2 mL of DMSO solution. The bacterial and fungal species used were incubated overnight on single-strength MHB medium and their fresh cultures were prepared. Suspensions of the cultures were prepared, and cell densities were adjusted to 0.5 Mc Farland tube turbidity (1.0×10^8 (kob)/mL).

Results and discussion

FT-IR measurements

The FT-IR spectra of the starting compound (Hsba) and compounds 1-6 (Figure 2) are given in Table 1. The broad absorption bands in the range $3552-3486 \text{ cm}^{-1}$ which are attributed to the $\nu(\text{OH})$ vibrations of coordinated water molecules for 5 and 6 and uncoordinated water molecules for 1-4. The weak bands in the range $3109-3080 \text{ cm}^{-1}$ are attributed to the stretching vibrations of aromatic of C-H. The SO_2NH_2 group of bands 3453 and 3265 cm^{-1} for Hsba are slightly shifted from those found 3450 and 3235 cm^{-1} for 1, 3393 and 3291 cm^{-1} for 2, 3362 and 3239 cm^{-1} for 3, 3416 and 3296 cm^{-1} for 4, 3377 and 3291 cm^{-1} for 5 and 3437 and 3378 cm^{-1} for 6 due to the weak intermolecular interactions. The weak bands at $527-469 \text{ cm}^{-1}$ are from the M-O vibrations of all complexes. The asymmetric/symmetric bands of $-\text{COO}^-$ groups are observed at 1684 and 1430 cm^{-1} for Hsba,

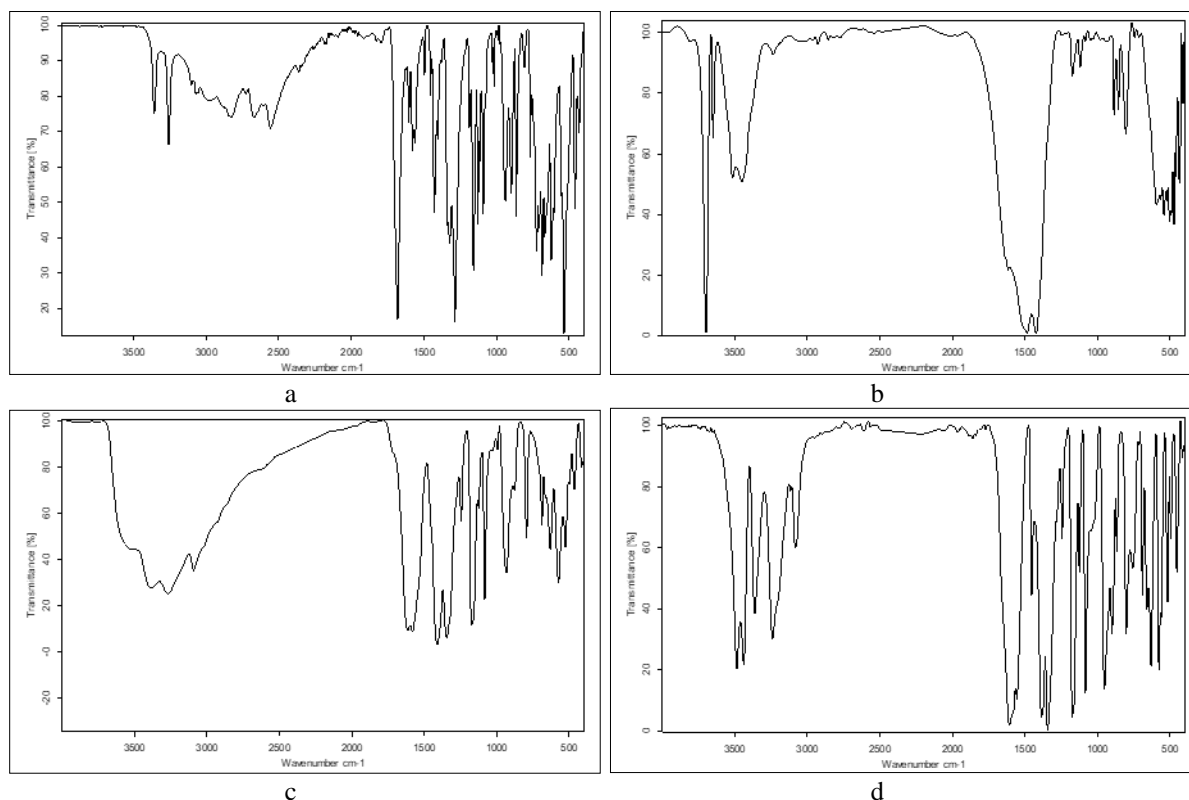
1625 and 1423 cm^{-1} for 1, 1605 and 1400 cm^{-1} for 2, 1630 and 1420 cm^{-1} for 3, 1600 and 1400 cm^{-1} for 4, 1651 and 1441 cm^{-1} for 5 and 1610 and 1400 cm^{-1} for 6. According to literature (Nothenberg *et al.* 2000), the differences ($\Delta\nu$) between asymmetric/symmetric stretches of $-\text{COO}^-$ groups higher than 200 cm^{-1} are monodentate. The values of Δ are 202 for 1, 205 for 2, 210 for 3, 200 for 4, 210 for 5 and 210 for 6. The bands at the region of 1616-1425 cm^{-1} , 1389-1040 cm^{-1} and 1215-1100 cm^{-1} are attributed to the $\nu(\text{C}=\text{C})$, $\nu(\text{C}=\text{O})$ and $\nu(\text{S}=\text{O})$ vibrations for all compounds

Table 1: FT-IR spectral data of all compounds (cm^{-1}).

	Hsba	1	2	3	4	5	6
$\nu(\text{O-H})$	2900(br)	3514(br)	3543(br)	3486(br)	3504(br)	3532(br)	3539(br)
$\nu(\text{NH}_2)$	3425(m) 3278(m)	3450(m) 3235(m)	3393(m) 3291(m)	3362(m) 3239(m)	3416(m) 3296(m)	3377(m) 3291(m)	3437(m) 3378(m)
$\nu(\text{C-H})_{\text{Ar}}$	3090(w)	3027(w)	3080(w)	3082(w)	3093(w)	3109(w)	3088(w)
$\nu(\text{C}=\text{O})$	1684(s) 1430(s)	1625(s) 1423(s)	1605(s) 1400(s)	1630(s) 1420(s)	1600(s) 1400(s)	1651(s) 1441(s)	1610(s) 1400(s)
$\nu(\text{C}=\text{C})$	1430(s) 1401(s)	1616(s) 1485(s)	1540(s) 1459(s)	1580(s) 1556(s) 1454(s)	1574(s) 1536(s) 1442(s)	1590(s) 1556(s) 1425(s)	1571(s) 1546(s) 1446(s)
$\nu(\text{C-O})$	1352(s) 1250(s) 1169(s)	1246(s) 1082(s)	1370(s) 1247(s) 1040(s)	1386(s) 1244(s) 1083(s)	1339(s) 1241(s) 1080(s)	1385(s) 1297(s) 1043(s)	1348(s) 1274(s) 1076(s)
$\nu(\text{S}=\text{O})$	1073(s) 1160(s)	1173(s) 1119(s)	1171(s) 1148(s) 1114(s)	1173(s) 1160(s) 1124(s)	1172(s) 1151(s) 1121(s)	1151(s) 1100(s)	1173(s) 1121(s)
$\nu(\text{M-O})$	-	459(w)	527(w)	518(w)	522(w)	469(w)	491(w)

UV/Vis measurements

The electronic spectra (1×10^{-3} M concentrations in DMSO) of Hsba and compounds 1-6 (Figure 3) were registered. Characteristic $\pi-\pi^*$ transitions are observed at 257 ($35120 \text{ Lmol}^{-1}\text{cm}^{-1}$) and 285 ($11230 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for Hsba, 286 ($26190 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 1, 285 ($30580 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 2, 290 ($28120 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 3, 296 ($36700 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 4, 290 ($29250 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 5 and 288 ($23230 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 6. The d-d transitions bands are seen at 776 ($100 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 2, 549 ($90 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 3, 766 ($150 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 4 and 779 ($190 \text{ Lmol}^{-1}\text{cm}^{-1}$) nm for 5. The d-d transition bands were not observed for 1 and 6 due to d^0 for 1 {Mg(II)} and d^{10} for 6 {Cd(II)} electronic structure of metal ion.



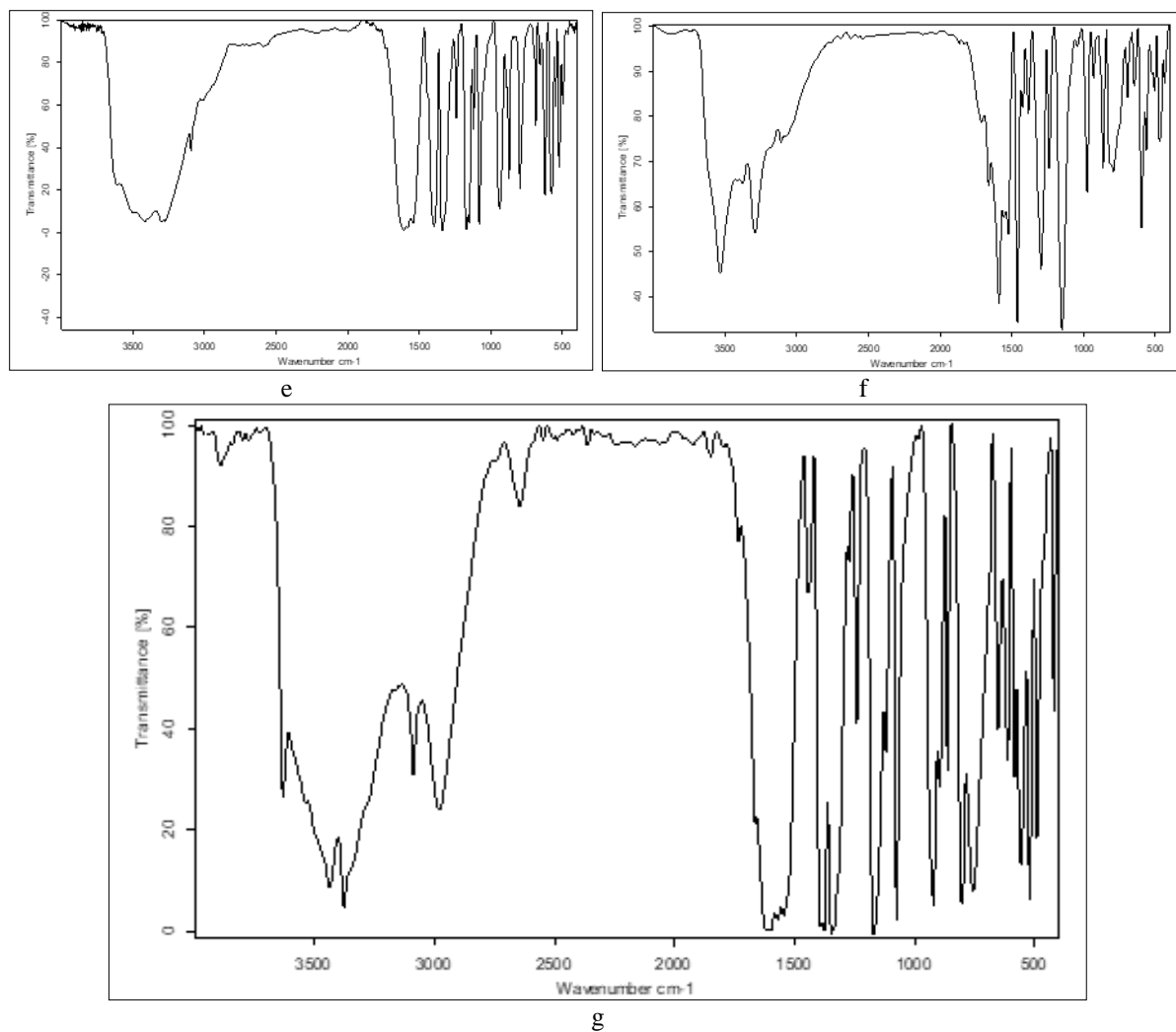
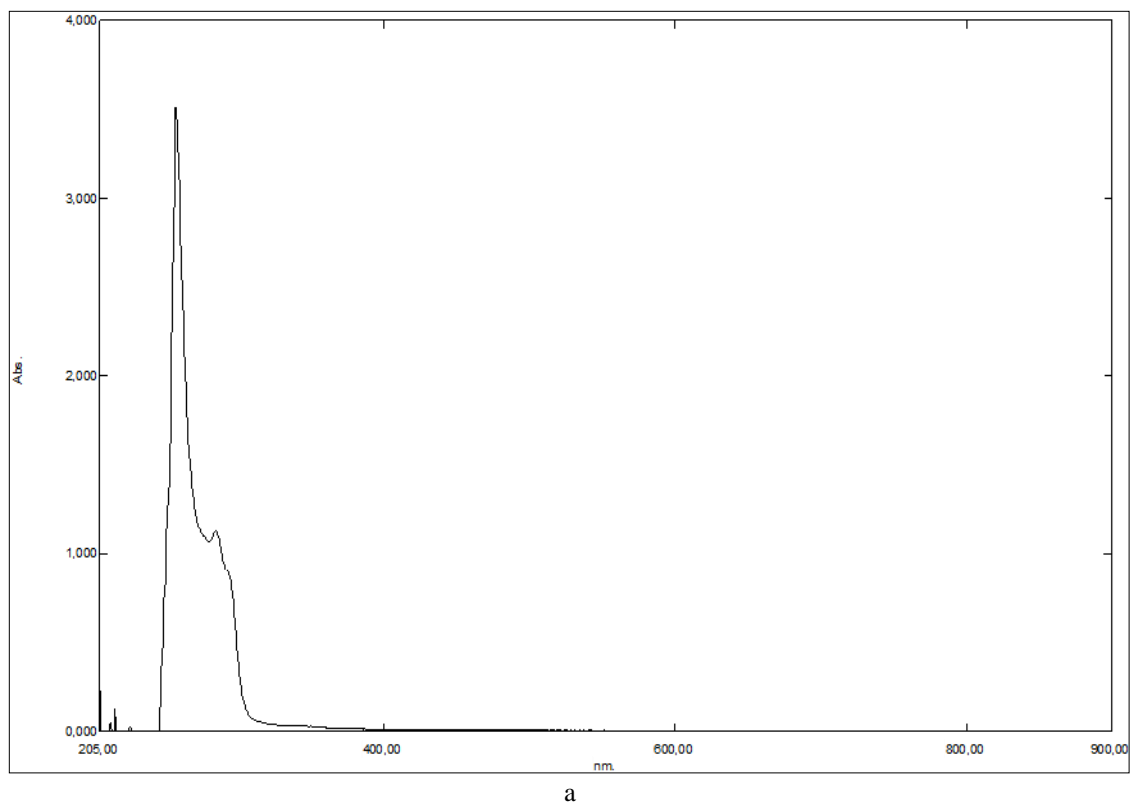
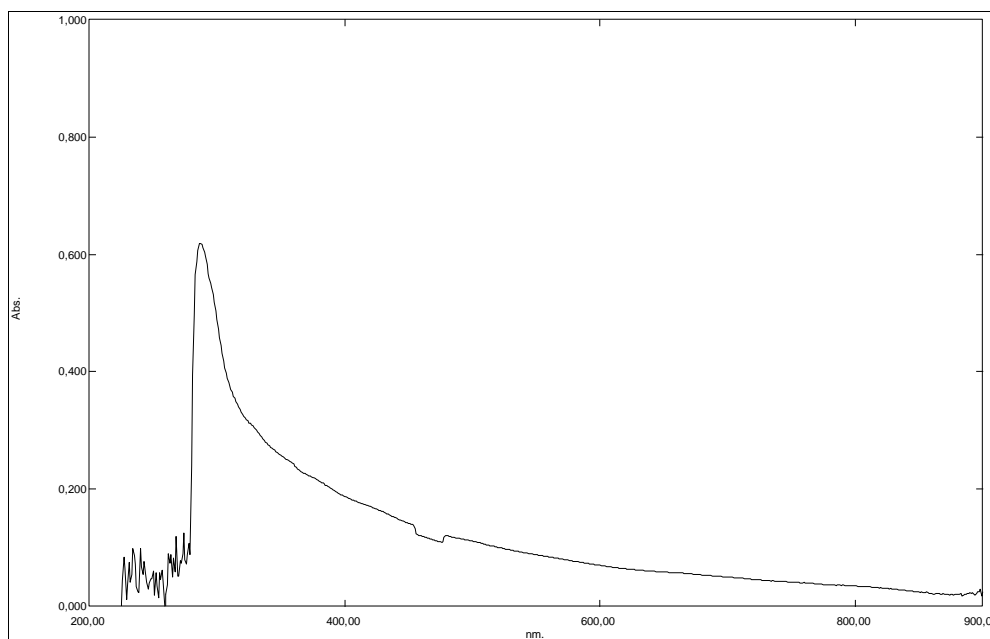
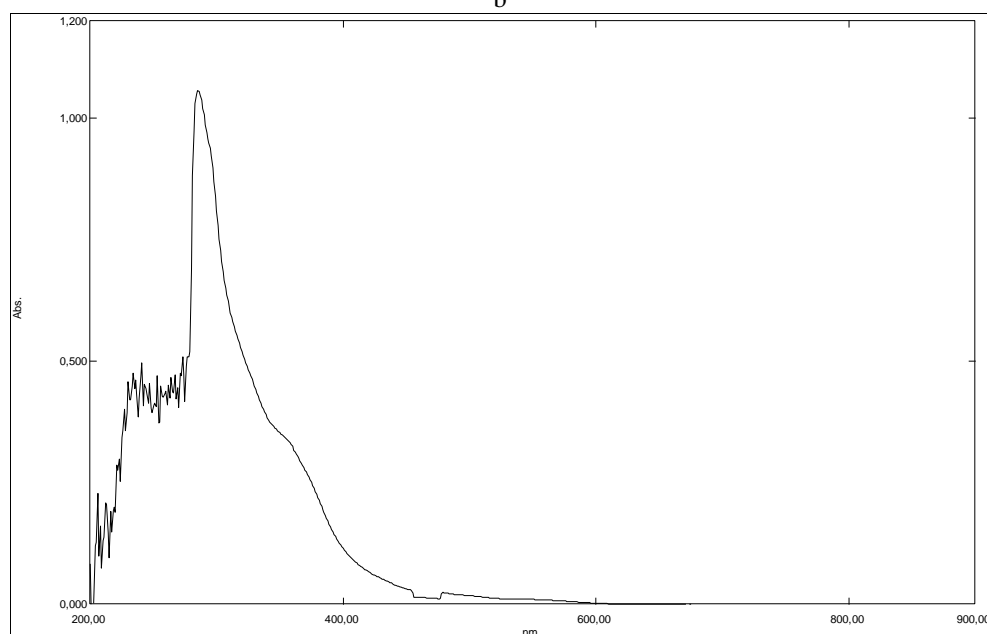


Fig 2: FT-IR spectrum of a for Hsba, b for 1, c for 2, d for 3, e for 4, f for 5 and g for 6.

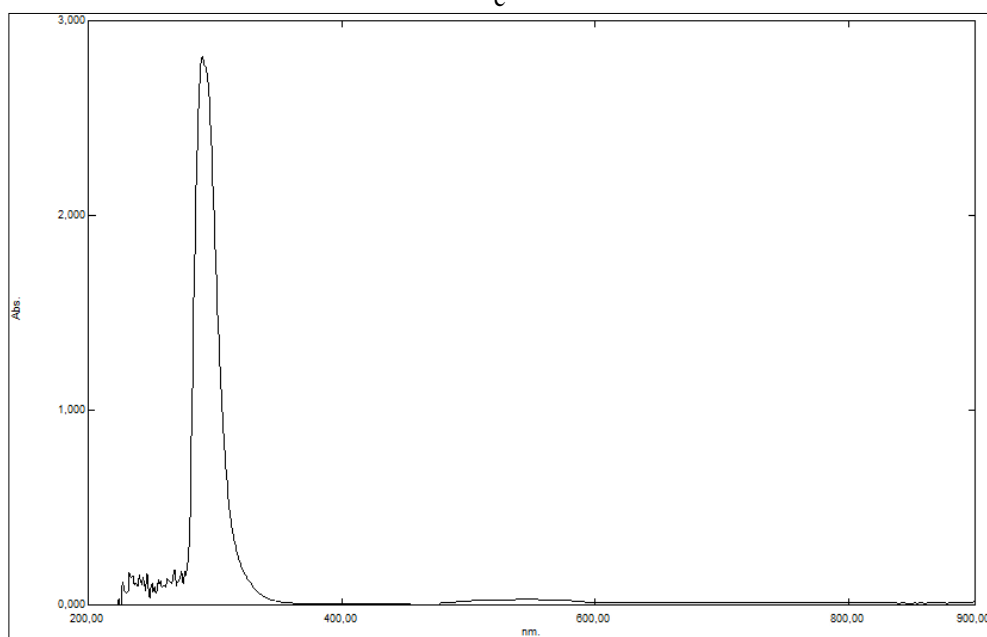




b



c



d

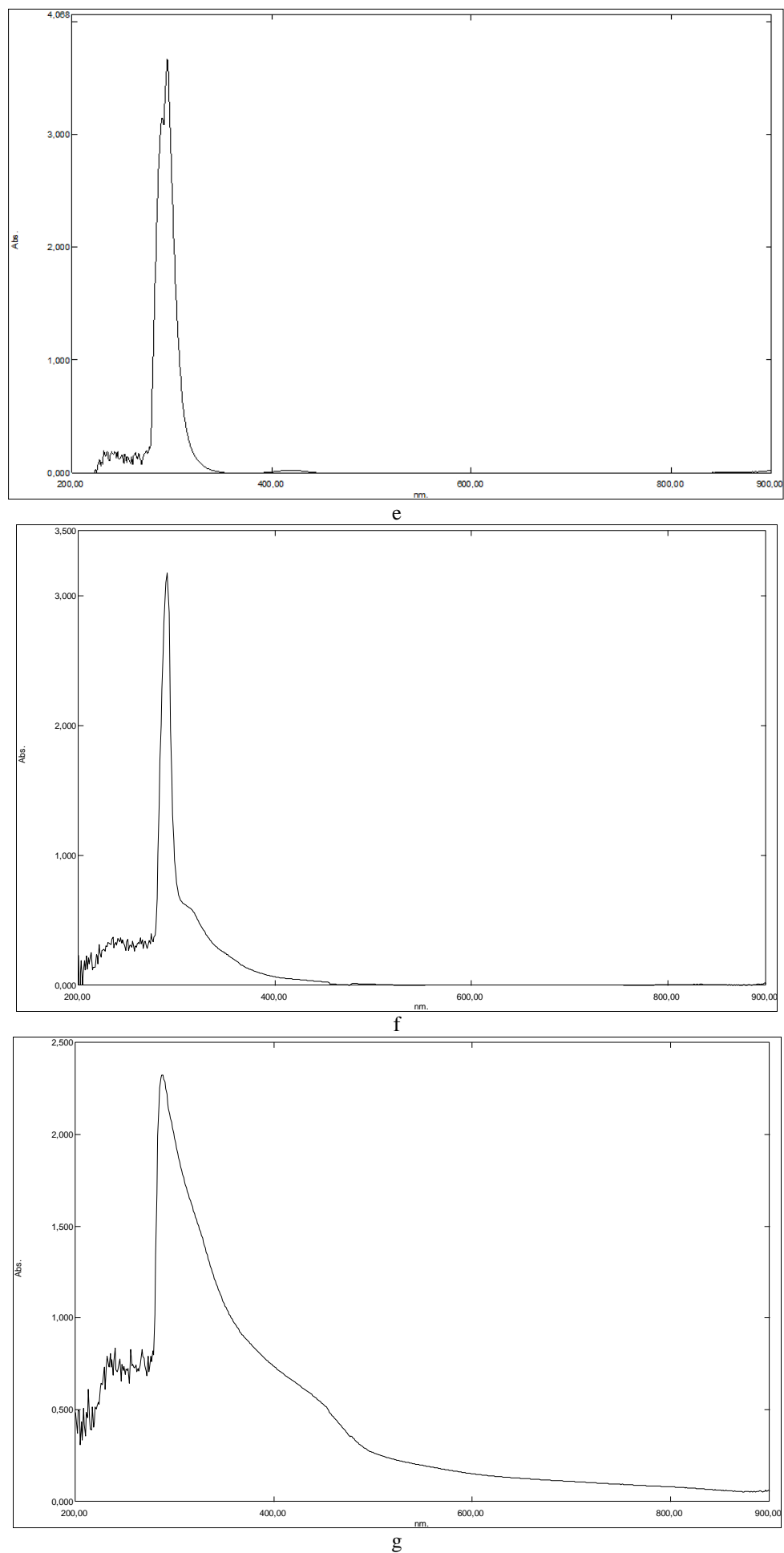


Fig 3: FT-IR spectrum of for Hsba, b for 1, c for 2, d for 3, e for 4, f for 5 and g for 6.

Magnetic moment and molar conductivity measurements

Magnetic susceptibilities of metal complexes 1–6 were found experimentally as 0 for 1, 4.90 for 2, 3.85 for 3, 2.80 for 4, 1.70 BM 5 and 0 BM for 6. These magnetic moment values of 1-6, indicate the presence of zero (d^0), four (d^6), three (d^7), two (d^8), one (d^9) and zero (d^{10}) unpaired electron, respectively.

The result of molar conductivity data in DMSO of all complexes (2.4 for 1, 2.4 for 2, 3.1 for 3, 5.4 for 4, 1.2 for 5 and $3.4 \Omega^{-1}\text{cm}^2 \text{mol}^{-1}$ for 6) are non-ionic (Geary 1971)^[7].

Antimicrobial activity results

In this work, antimicrobial and antifungal activity of the free ligand (Hsba), metal(II) salts and synthesized compounds (1-6) were tested by microdilution method. Fluconazole was used as an antifungal agent while Cefepime, Levofloxacin and Vancomycin were used as antibiotic agent. MIC values of the all compounds and control drugs are given in Table 2. According to MIC values it was observed that most of the compounds have antibacterial and antifungal activity properties.

When the mic values of antibacterial agents and compounds are compared, all compounds are active against *Enterococcus faecalis*; Cd(OAc)₂.2H₂O (15.60) and 5 (31.25) showed strong activity according to Vancomycin and Levofloxacin while showed similar activity (62.50) other compounds (except Hsba). Cd(OAc)₂.2H₂O (15.60) indicated strong activity according to Cefepime while indicated similar activity 5 (31.25). The other compounds showed less activity according to Cefepime. *Staphylococcus aureus*; Cd(OAc)₂.2H₂O (15.60) and Cu(OAc)₂.2H₂O (31.25) demonstrated strong activity according to Levofloxacin while demonstrated similar activity other compounds (62.50) (except Hsba). Cd(OAc)₂.2H₂O (15.60) showed strong activity according to Vancomycin and Cefepime while showed similar activity Cu(OAc)₂.2H₂O (31.25). The other compounds showed less activity according to Vancomycin and Cefepime. *Escherichia coli*; FeSO₄.7H₂O, 1 and 3 (31.25) showed strong activity according to Levofloxacin and Cefepime while showed similar activity other compounds (62.50) (except Hsba). FeSO₄.7H₂O, 1 and 3 (31.25) observed similar activity according to Levofloxacin while observed less level of activity other compounds. Hsba (125.00) showed less activity according to standard antibacterial agents.

Table 2: MIC values of the compounds ($\mu\text{g/mL}$).

Compound	<i>E. faecalis</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>C. parapsilosis</i>	<i>C. albicans</i>	<i>C. krusei</i>
Vancomycin	62.50	31.25	62.50		-	-
Levofloxacin	62.50	62.50	31.25		-	-
Cefepime	31.25	31.25	62.50		-	-
Fluconazole	-	-	-	62.50	31.25	-
Mg(OAc) ₂ .4H ₂ O	62.50	62.50	62.50	62.50	62.50	250.00
FeSO ₄ .7H ₂ O	62.50	62.50	31.25	62.50	125	125.00
Co(OAc) ₂ .4H ₂ O	62.50	62.50	62.50	62.50	62.50	62.50
Ni(OAc) ₂ .4H ₂ O	62.50	62.50	62.50	31.25	62.50	62.50
Cu(OAc) ₂ .2H ₂ O	62.50	31.25	62.50	31.25	125	125.00
Cd(OAc) ₂ .2H ₂ O	15.60	15.60	62.50	62.50	62.50	125.00
Hsba	125.00	125.00	125.00	62.50	15.60	31.25
1	62.50	62.50	31.25	62.50	62.50	125
2	62.50	62.50	62.50	31.25	62.50	125
3	62.50	62.50	31.25	31.25	62.50	31.25
4	62.50	62.50	62.50	62.50	31.25	62.50
5	31.25	62.50	62.50	31.25	62.50	125.00
6	62.50	62.50	62.50	62.50	31.25	62.50

When the mic values of antifungal agent and compounds are compared, all compounds are active against *Candida parapsilosis*; Ni(OAc)₂.4H₂O, Cu(OAc)₂.2H₂O, 2, 3 and 5 (31.25) showed strong activity according to Fluconazole while showed similar activity (62.50) other compounds. *Candida albicans*; Hsba (15.60) indicated strong activity according to Fluconazole while indicated similar activity 4 and 6 (31.25). The other compounds demonstrated less activity according to Fluconazole. *Candida krusei*; all compounds demonstrated strong activity according to Fluconazole {Hsba = 3 (31.25) > Co(OAc)₂.4H₂O = Ni(OAc)₂.4H₂O = 4 = 6 (62.50) > FeSO₄.7H₂O = Cu(OAc)₂.2H₂O = Cd(OAc)₂.2H₂O = 1 = 2 = 5 (125.00) > Mg(OAc)₂.4H₂O (250.00)}.

Conclusions

In this present work, six novel Mg(II) {[Mg(sba)₂].2H₂O, 1}, Fe(II) {[Fe(sba)₂(H₂O)₄], 2}, Co(II) {[Co(sba)₂(H₂O)₄], 3}, Ni(II) {[Ni(sba)₂(H₂O)₄].5H₂O, 4}, Cu(II) {[Cu(sba)₂(H₂O)₄].2H₂O, 5} and Cd(II) {[Cd(sba)₂(H₂O)₄].5H₂O, 6} complexes of 2,4-dichloro-5-sulfamoylbenzoic acid have been prepared. The structures of the synthesized metal complexes were observed to be linear for 1 and octahedral for 2-6 results of analyses results. Activity against all compounds bacteria and yeasts was observed. Therefore, the obtained synthesis compounds can be evaluated for the synthesis of new antibacterials.

Acknowledgments

The authors acknowledge the support provided by Kütahya Dumlupınar University Research Fund (Grant No. 2019/12).

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