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Antimicrobial Activity Studies of Metal Complexes of 2-Aminobenzothiazole Derivatives

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Research Article

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Abstract

2-Aminobenzothiazole and its derivatives generally have applications in drug discovery, development of diabetes treatments, epilepsy, amyotrophic lateral sclerosis, analgesia, tuberculosis treatment, and viral infections. In this study, Fe(III) (**2**, **7**, **12**, **17**), Co(II) (**3**, **8**, **13**, **18**), Ni(II) (**4**, **9**, **14**, **19**), and Cu(II) (**5**, **10**, **15**, **20**) complexes of 2-aminobenzothiazole (**1**), 2-amino-6-chlorobenzothiazole (**6**), 2-amino-6-methylbenzothiazole (**11**), and 2-amino-6-methoxybenzothiazole (**16**), respectively, were synthesized by the method found in the literature. The architectures of the synthesized complex compounds (**1-20**) were postulated through the application of Atomic Absorption Spectroscopy (AAS). Furthermore, the antimicrobial activities of compounds 1–20 were tested against *Candida albicans* (antifungal activity) and *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus*, *Listeria monocytogenes*, and *Enterococcus faecalis* (antibacterial activity). The results were compared with those obtained using the control compounds Fluconazole and Ketoconazole (antifungal activity) and Vancomycin, Levofloxacin, Cefepime, and Chloramphenicol (antibacterial activity). As a result of activity studies, synthesized compounds show activity against bacteria and yeasts. The best activity results were observed compounds **6** and **10** in *C. albicans* yeast, compound **20** in *S. aureus* bacteria, compound **13** in *E. faecalis* bacteria, compounds **12**, **13**, **17**, and **20** in *B. subtilis* bacteria, compounds **5** and **19** in *P. aeruginosa* bacteria, compounds **1**, **4**, **6**, **9**, **17**, and **20** in *E. coli* bacteria, and compounds **5**, **6**, **8**, **17**, and **19** in in *L. monocytogenes* bacteria. In particular, compound **4** for *E. Coli*, **6,** and **10** for *C. albicans* showed better activity than the control compounds.

Keywords: 2-Aminobenzothiazole, metal complex, antibacterial activity, antifungal activity

2-Aminobenzotiyazol Türevlerinin Metal Komplekslerinin Antimikrobiyal Aktivite Çalışmaları

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Özet

2-Aminobenzotiyazol ve türevlerinin genel olarak, ilaç keşfi uygulamaları, diyabet tedavilerin geliştirilmesi, epilepsi, amyotrofik lateral skleroz, analjezi, tüberküloz tedavisi ve virüs enfeksiyon uygulamaları vardır. Bu çalışmada, 2-aminobenzotiyazol (**1**), 2-amino-6-klorobenzotiyazol (**6**), 2-amino-6-metilbenzotiyazol (**11**) ve 2-amino-6-metoksibenzotiyazolün (**16**) Fe(III) (**2**, **7**, **12**, **17**), Co(II) (**3**, **8**, **13**, **18**),

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Ni(II) (**4**, **9**, **14**, **19**) ve Cu(II) (**5**, **10**, **15**, **20**) kompleksleri, literatürde bulunan yöntemle sentezlenmiştir. Sentezlenen kompleks bileşiklerin (**1-20**) yapıları, Atomik Absorpsiyon Spektroskopisi (AAS) uygulanarak önerilmiştir. Ayrıca, **1-20'**nin antimikrobiyal özellikleri *Candida albicans*'a (antifungal aktivite) ve *Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Staphylococcus aureus, Listeria monocytogenes*, and *Enterococcus faecalis*'e (antibakteriyel aktivite) karşı da test edilmiştir. Sonuçlar, kontrol bileşikleri Flukonazol ve Ketokonazol (antifungal aktivite) ve Vankomisin, Levofloksasin, Sefepim ve Kloramfenikol (antibakteriyel aktivite) kullanılarak elde edilen sonuçlarla karşılaştırılmıştır. Aktivite çalışmaları sonucunda, sentezlenen bileşikler bakteri ve mayalara karşı aktivite göstermiştir. En iyi aktivite sonuçları *C. albicans* mayasında **6** ve **10** nolu bileşiklerde, *S. aureus* bakterisinde **20** nolu bileşikte, *E. faecalis* bakterisinde **13** nolu bileşikte, B. subtilis bakterisinde **12**, **13**, **17** ve **20** nolu bileşiklerde, *P. aeruginosa* bakterisinde **5** ve **19** nolu bileşiklerde, *E. coli* bakterisinde **1**, **4**, **6**, **9**, **17** ve **20** nolu bileşiklerde ve *L. monocytogenes* bakterisinde **5**, **6**, **8**, **17** ve **19** nolu bileşiklerde gözlemlenmiştir. Özellikle *E. coli* için **4** numaralı, *C. albicans* için **6** numaralı ve **10** numaralı bileşikler kontrol bileşiklerinden daha iyi aktivite göstermiştir.

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Anahtar Kelimeler: 2-Aminobenzotiyazol, metal kompleksi, antibakteriyel aktivite, antifungal aktivite

Introduction

Derivatives of 2-aminobenzothiazoles are a significant class of bicyclic heterocyclic chemicals. Derivatives of 2-aminobenzothiazoles exhibit carbonic anhydrase inhibition, antimicrobial, antitumor, anti-HIV, analgesic, antifungal, anti-inflammatory, and local anesthetic properties [1]. Metal complexes of 2-aminobenzothiazole derivatives and various activity studies have been reported the literature such as Cr(I) {[Cr(NO)(CN)$_2$(**1**)$_2$(H$_2$O)]} [2], Cr(III) {[Cr(**1**)$_3$(Cl)$_3$].2H$_2$O [3], CrCl$_2$(OH)(**1**)].H$_2$O, [CrCl$_3$(**1**)$_3$].2H$_2$O, [CrCl$_3$(**1**)$_3$].MeOH, [CrBr$_3$(**1**)$_2$], [Cr$_2$(SO$_4$)$_3$(**1**)$_3$].3H$_2$O, [Cr(NO$_3$)$_3$(**1**)$_3$].3H$_2$O} [4], Fe(III) {Fe(**1**)(OH)X$_2$, Fe(**1**)X$_3$, Fe(**1**)$_3$X$_3$, Fe(**1**)(NO$_3$)$_3$.2H$_2$O, Fe$_2$(**1**)$_2$(SO$_4$).3.5H$_2$O, X = Cl, Br [5], (H**1**)$_2$[FeCl$_4$]Cl.H$_2$O, (H**1**)$_3$[Fe(ox)$_3$].2H$_2$O, ox = oxalate} [6], Co(II) {[Co(**1**)$_2$X$_2$], X = Cl, Br, I [7], Co(**1**)$_2$X$_2$, X = Cl, Br, I, NCS [8], [Co(**1**)$_2$(Ac)$_2$] [9], [CoCl$_2$(**1**)$_2$] [10], [Co(Ac)$_2$(**1**)$_2$] [11], [Co(CX$_3$CO$_2$)$_2$(**1**)$_2$], X$_3$ = F$_3$, Cl$_3$, HCl$_2$ [12], Co(**1**)$_2$X$_2$, X = Cl, Br, I, NCS [13], [CoCl$_2$(**1**)$_2$] [14]}, Ni(II) {[Ni(CX$_3$CO$_2$)$_2$(**1**)$_2$], X$_3$ = F$_3$, Cl$_3$, HCl$_2$ [12], [Ni(CH$_3$CO$_2$)$_2$(**1**)$_2$] [15], Ni(**1**)$_2$X$_2$, X = Cl, Br, I, Bu$_4$N[NiBr$_3$(**1**)], Bu = butyl [8], [Co(**1**)$_2$X$_2$], X = Cl, Br, I [7], Ni(**1**)$_2$Br$_2$ [13], [Ni(**1**)$_2$(NCS)$_2$] [16], [NiM(NCS)$_4$.n(**1**)], M = Zn, n = 6; M = Cd, n = 4; M = Hg, n = 2 [17]}, Cu(I) {(**1**)Cu$_2$I$_2$, (**1**)CuX, X = Cl, Br; (**1**)$_3$Cu$_2$(ClO$_4$)$_2$(**1**)$_2$AgX, X = NO$_3$, ClO$_4$, BF$_4$, CF$_3$COO) [18]}, Cu(II) {Cu(OAc)$_2$(**1**), Cu(Ac)$_2$(**1**)$_2$ [19], (H**1**)$_2$CuCl$_4$ [20], [Cu(CX$_3$CO$_2$)$_2$(**1**)$_2$], X$_3$ = F$_3$, Cl$_3$, HCl$_2$ [12], [(H**1**)$_2$CuCl$_4$] [21], [Cu$_2$(Ac)$_4$(**1**)$_2$] [22], [Cu(**1**)$_2$Cl$_2$] [23], Cu(**1**)$_2$X$_2$, X = Cl, Br, Cu(**1**)$_3$(ac)$_3$](ClO$_4$)$_2$, ac = aceton, Cu(**1**)$_3$](ClO$_4$)$_2$ [8], [Cu(CH$_3$CO$_2$)$_2$(**1**)$_2$] [15], [Cu$_2$(**1**)$_2$(ac)$_4$].2CH$_3$CH$_2$CH$_2$CH$_2$OH [24]}, Zn(II) {[Zn(**1**)$_2$(ac)$_2$] [25], [ZnCl$_2$(**1**)$_2$] [11], [Zn(**1**)$_2$(SCN)$_2$] [26], (H**1**)[Zn(**1**)Cl$_3$] [27], (H**1**)$_2$[ZnCl$_4$] [28], [ZnCl$_2$(**1**)$_2$].0.5CH$_3$CH$_2$OH [29], ZnX$_2$.2(**1**), X = Cl, Br, I [30], [Zn(**1**)$_2$(Ac)$_2$] [31], ZnX$_2$.2H**1**, X = Cl, Br, I, NO$_3$, Zn(ClO$_4$)$_2$; 1.5H**1**.4H$_2$O [32]}, Cd(II) {[Cd(**1**)$_2$(Ac)$_2$] [31], CdI$_2$.2H**1**, MX$_2$.H**1**, X = Cl, Br, NO$_3$, 3H$_2$O, Cd(ClO$_4$)$_2$.3H**1**.4H$_2$O [32]}, Ag(I) {(**1**)Ag$_2$X$_2$, X = Cl, I, (**1**)AgX, (**1**)$_3$Cu$_2$(ClO$_4$)$_2$(**1**)$_2$AgX, X = NO$_3$, ClO$_4$, BF$_4$, CF$_3$COO [18], [Ag(**1**)$_2$]X, X = NO$_3^-$, ClO$_4^-$, [Ag(**1**)$_2$X'], X' = NCO$^-$, SCN$^-$[33], [Ag(**1**)$_2$]NO$_3$ [34], [Ag(**1**)$_2$]NO$_3$.CH$_3$OH [35], [Ag(**1**)(NO$_3$)].aceton [36], Ag(**1**)(NO$_3$)]} [37]}, Bi(III) {BiX$_3$.(**1**) X = Cl, Br, I} [38], Sn(II) {[Sn(**1**)NO$_3$]$_n$} [39], Sn(IV) {[Bu$_2$Sn(NO$_3$)$_2$(**1**)], Bu: butyl} [40], Sn(II), Sn(IV), Sb(II) {[(M^{n+}(**1**)$_m$X$_n^-$], M = Sn, X = Cl, M = Sb, X = Cl, Br} [41], Nb(V) {NbCl$_5$.n(**1**), n = 1-3} [42], Sb(III) {SbCl$_3$.2(**1**), SbBr$_3$.1.5(**1**), SbI$_3$.(**1**)} [38], Pt(II) {[PtCl$_2$(**1**)$_2$].4DMF} [43], Tl(III) {[TlX$_3$(**1**)$_2$], X = Cl, Br [44], [TlX$_3$(**1**)$_2$], X = Cl, Br [45], Hg(II) {[Hg(**1**)Cl$_2$]$_n$, [Hg(**1**)$_2$(SCN)Cl],

$[Hg_2(\mathbf{1})_2(SCN)_4]$ [46], $HgX_2.H\mathbf{1}$, X = Cl, Br, I; $Hg(ClO_4)_2$; $HgNO_3.(\mathbf{1})$ [32]}, Re(I) {$[Re(CO)_2(PPh_3)_2(\mathbf{1})]$} [47], Ru(II) {$[RuCl_2(CO)_2(\mathbf{1})_2]$} [48], $[RuCl_2(CO)_2(\mathbf{1})_2)]$ [49]}, W(IV) {$[WO_2(NCS)_2(\mathbf{1})_2]$} [50], Pd(II) $[Pd(\mathbf{1})_2Cl_2]$ [51], $[Pd(\mathbf{1})_2Cl_2]$.DMF [52], Ru(II), Rh(III), Ag(I), Ir(VI), Os(VI), Au(III) {$[Ir(Habt)_3(H_2O)Cl_2]Cl$, $[Ru(Habt)_3(H_2O)Cl_2]$, $[Rh(Habt)_3Cl_3]$, $[OsO_2(Habt)_2(OH)_2]$, $[Ag(Habt)_2]ClO_4$ and $[Au(Habt)_3Cl]Cl_2$} [53] for 2-aminobenzothiazole (**1**), Co(II) {$[Co(\mathbf{6})_4](ClO_4)_2$, $[Co(\mathbf{6})_2X_2]$, X = Cl, Br, SCN, OAc, NO_3)} [54], Ni(II) {$[Ni(\mathbf{6})_2X_2]$ X = Cl, Br, SCN, OAc, NO_3, $[Ni(\mathbf{6})_4](ClO_4)_2$} [55], Cu(II) {$[Cu(\mathbf{6})_4](ClO_4)_2$, $[Cu(\mathbf{6})_2X_2]$, X = Cl, Br, SCN, OAc, NO_3} [54], Hg(II) {$Hg(\mathbf{6})_2X_2$, X = Br, SCN, OAc) [56] and Pd(II) $[Pd(\mathbf{6})_2Cl_2]$ [57, 58] for 2-amino-6-chlorobenzothiazole (**6**), Co(II) {$[Co(\mathbf{11})_2Cl_2]$ [59], $[Co(\mathbf{11})_2X_2]$, X = Cl, Br, SCN, OAc, NO_3)} [54], Ni(II) {$[Ni(\mathbf{11})_2X_2]$, $[Ni(\mathbf{11})_4](ClO_4)_2$} [55], Cu(II) {$Cu(\mathbf{11})_2]NO_3$} [60], $[Cu(\mathbf{11})_4](ClO_4)_2$, $[Cu(\mathbf{11})_2X_2]$, X = Cl, Br, SCN, OAc, NO_3)} [54], Hg(II) {$Hg(\mathbf{11})_2X_2$, X = Cl, Br, I, NO_3, OAc, SCN [56], Cr(I) $[Cr(NO)(CN)_2(\mathbf{11})_2(H_2O)]$ Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) {$M(\mathbf{11})X_3$, $M(\mathbf{11})_4X_2$, M = Cu, Ni, Co, Zn, Cd, Hg; X = Br, NCS, OAc, $Fe_2(\mathbf{11})_4Cl_6$}, Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) {$M(\mathbf{11})_2X_2$, $M(\mathbf{11})_4X_2$, $Fe_2(\mathbf{11})_4Cl_6$ {M = Cu, Ni, Co, Zn, Cd, Hg; X =I, NCS, OAc} [61, 62], Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) {$M(\mathbf{11})X_2$, $M(\mathbf{11})_2X_2$, $M(\mathbf{11})_4X_2$ (M = Cu, Ni, Co, Fe, Zn, Cd, Hg; X = I, NCS, OAc)} [63], Co(II) {$[Co(\mathbf{11})Cl_2]$} [64], Mo(IV) {$MoO_2(\mathbf{11})_2X_2$, X = Cl, Br} [65], Ag(I) {$Ag(\mathbf{11})_2]NO_3$} [60] and Pd(II) $[Pd(\mathbf{11})_2Cl_2]$ [57,58] for 2-amino-6-methylbenzothiazole (**11**), Cr(I) $[Cr(NO)(CN)_2(\mathbf{16})_2(H_2O)]$ [66], Co(II), Cu(II), Zn(II), Cd(II), Hg(II) {$M(\mathbf{16})_2X_2$ (M = Co, Cu, Zn; X = Cl, Br; M = Cd, Hg; X = Cl, Br, I)} [67], Mo(V) {$[H(\mathbf{16})]_2[MoOCl_5]$} [68] and Mo(IV) {$MoO_2(\mathbf{16})_2X_2$, X = Cl, Br} [65] for 2-amino-6-methylbenzothiazole (**11**).

In the contemporary context, the emergence of microbial resistance stands out as a global problem leading to increased mortality and morbidity rates. There is a need to develop the spectrum efficacy of novel compounds that can combat a wide range of resistant microorganisms. Based on this principle, we synthesized a series of metal complexes of 2-aminobenzothiazole derivatives. In this study, compounds **2** [5], **3-5** [8], **7**, **8**, **10** [54], **9** [55], **12-15** [63], and **17-20** [67] were synthesized by methods available in the literature. The architectures of the synthesized complex compounds (**1-20**) were postulated through the application of AAS. The structures of the obtained complex compounds (**1-20**) were suggested by AAS. In addition, the antimicrobial activities of all compounds (**1-20**) were investigated against bacteria and yeast. Antimicrobial results of the compounds were compared with existing antibiotics (Vancomycin, Levofloxacin, Cefepime, Chloramphenicol, Fluconazole, and Ketoconazole).

Experimental

General Techniques and Resources

All chemicals were purchased from the Abcr company. AAS analyses for Fe, Co, Ni, and Cu was detected with Perkin Elmer AAS PinAAcle 900T.

Synthesis of Metal Complexes

In this study, compounds **2** [5], **3-5** [8], **7**, **8**, **10** [54], **9** [55], **12-15** [63] and **17-20** [67] were synthesized by methods available in the literature. 1 mmol (0.1502 g) 2-aminobenzothiazole (**1**) for **2-5** or 1 mmol (0.1847 g) 2-amino-6-chlorobenzothiazole (**6**) for **7-10** or 1 mmol (0.1642 g) 2-amino-6-methylbenzothiazole (**11**) for **12-15** or 1 mmol (0.1802 g) 2-amino-6-methoxybenzothiazole (**16**) for **17-20** and 1 mmol metal(II) salt [0.1268 g $FeCl_2$ for **2**, **7**, **12**, **17** or 0.1298 g $CoCl_2$ for **3**, **8**, **13**, **18** or 0.1296 g $NiCl_2$ for **4**, **9**, **14**, **19** or 0.1345 g $CuCl_2$ for **5**, **10**, **15**, **20**] were dissolved in ethanol solution (70%) (100 mL) with stirring for 96 hours in 25 ºC. The powdered solids that settled in the reaction medium were filtered and dried (60-65% yield for **2-5**, **7-10**, **12-15**, and **17-20**, Figure 1).

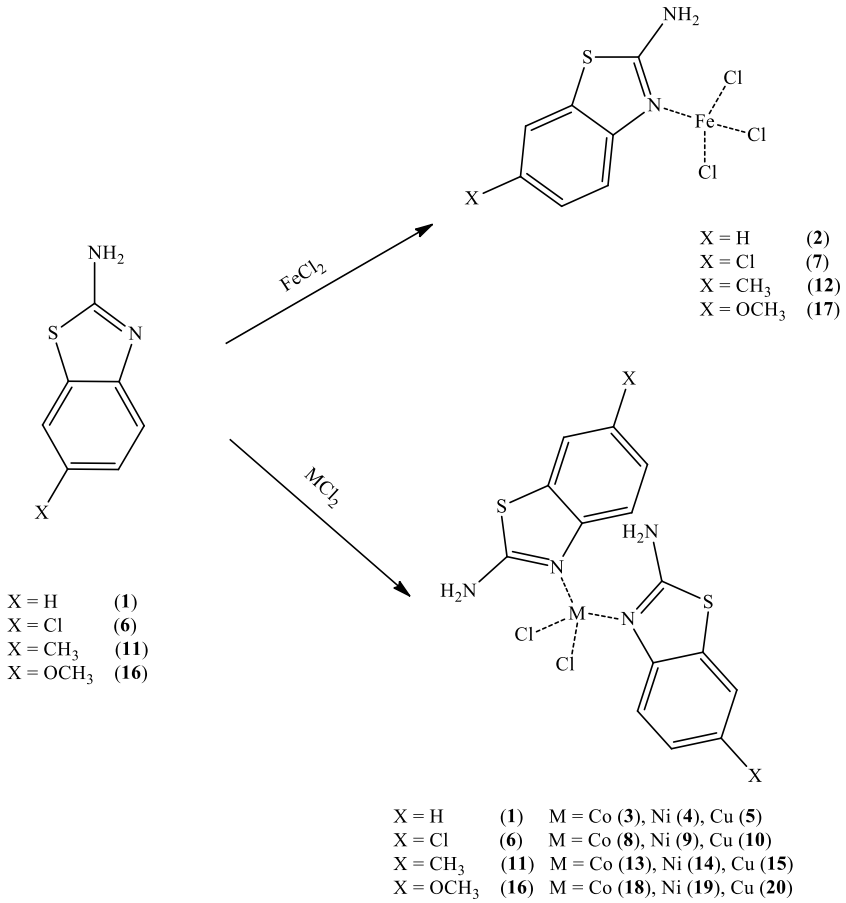


Figure 1. *Syntheses of* ***1-20***

Antimicrobial Study

The compounds' antibacterial qualities were determined using the microdilution susceptibility test, and the necessary *Escherichia coli* (ATCC 25922) and *Enterococcus faecalis* (ATCC 29212) bacteria were provided by Eskişehir Osmangazi University, and *Candida albicans* (F89) yeast and *Bacillus subtilis*, *Listeria monocytogenes* (ATCC 7644), *Staphylococcus aureus* (NRRL B-767), and *Pseudomonas aeruginosa* (ATCC 27853) bacteria were provided by Eskişehir Technical University. Chloramphenicol, Vancomycin, Cefepime and Levofloxacin were used as control compounds for the indicated bacteria. Fluconazole and Ketoconazole were used as control compounds for the antifungal activity of the compounds. In determining the antimicrobial activities of all compounds and reference drugs, the micro-tube dilution technique was applied to determine the lowest concentration value (MIC) that inhibits the growth of microorganisms [69, 70]. The compounds' antibacterial efficacy was assessed using the Microbroth Dilution Susceptibility Assay. The samples were produced as stock solutions in dimethylsulfoxide. In 2 milliliters of DMSO solution, 4 milligrams of synthesized chemicals and 4 milligrams of antibiotics were dissolved. Using McFarland No. 0.5 standard solution, overnight-grown bacterial and yeast suspensions in double-strength Mueller-Hinton broth were standardized to 10^8 Colony Forming Units/mL. Next, 100 milligrams of each suspension of microorganisms was put into each well. As a negative control, the last well in the chain devoid of any microorganism was employed. Sterile distilled water and the medium served as a positive growth control. The MIC was established by determining the first well that remained turbidity-free after incubation at 37 °C for 18–24 hours. All data presented were verified in three independent experiments, and the same results were obtained.

Results and Discussion

Results of AAS

AAS analysis was performed to compare the metal ratios of the obtained complexes with those found in the literature {**2** [5], **3-5** [8], **7**, **8**, **10** [54], **9** [55], **12-15** [63], and **17-20** [67]}. AAS results for metal complexes (**2-5**, **7-10**, **12-15**, and **17-20**) are given in Table 1. The obtained results indicated the metal:(**1**/**6**/**11**/**16**) ratios were observed to be 1:1 for **2**, **7**, **12**, and **17** and 1:2 for **3-5**, **8-10**, **13-15**, and **18-20** (Table 1).

Table 1. *AAS results of metal complexes*

Compound	Formula	Molecular Mass	Found% Anal. Cald.%
2	$C_7H_6Cl_3FeN_2S$	321.40	17.90(17.88)
3	$C_{14}H_{12}Cl_2CoN_4S_2$	430.24	13.70(13.70)
4	$C_{14}H_{12}Cl_2N_4NiS_2$	430.00	13.70(13.70)
5	$C_{14}H_{12}Cl_2CuN_4S_2$	434.85	14.60(14.61)
7	$C_7H_5Cl_4FeN_2S$	346.85	16.10(16.10)
8	$C_{14}H_{10}Cl_4CoN_4S_2$	499.13	11.80(11.81)
9	$C_{14}H_{10}Cl_4N_4NiS_2$	498.89	11.80(11.76)
10	$C_{14}H_{10}Cl_4CuN_4S_2$	503.75	12.60(12.61)
12	$C_8H_8Cl_3FeN_2S$	326.43	17.10(17.11)
13	$C_{16}H_{16}Cl_2CoN_4S_2$	458.29	12.86(12.90)
14	$C_{16}H_{16}Cl_2N_4NiS_2$	458.02	12.80(12.81)
15	$C_{16}H_{16}Cl_2CuN_4S_2$	462.91	13.70(13.73)
17	$C_8H_8Cl_3FeN_2OS$	342.43	16.30(16.31)
18	$C_{16}H_{16}Cl_2CoN_4O_2S_2$	490.29	12.00(12.02)
19	$C_{16}H_{16}Cl_2N_4NiO_2S_2$	490.05	12.00(11.98)
20	$C_{16}H_{16}Cl_2CuN_4O_2S_2$	494.91	12.80(12.84)

Antimicrobial Results of Compounds

In this study, the antimicrobial efficacies of **1-20** were evaluated utilizing the microdilution methodology. The minimum inhibitory concentration (MIC) values for all tested compounds are presented in Table 2. Analysis of the MIC values indicates that all tested compounds possess antibacterial and antifungal properties. Antibacterial and antifungal activity values obtained from metal complexes of aminobenzothiazole derivatives are consistent with similar studies in the literature [39, 71-75]. Against the *C. albicans* yeast, compounds **6** and **10** exhibited a higher effect than the control drugs. Compounds **1-4**, **7**, **9**, **11**, **12**, **14-16**, and **20** exhibited less effect than Fluconazole and Ketoconazole, while the other compounds had similar effects to Fluconazole and Ketoconazole. Against *S. aureus* bacteria, all compounds (except compound **20**) showed less effect than with Cefepime and Vancomycin, while compound **20** was determined to have equal effects with Cefepime and Vancomycin. The all compounds (except **1**, **11**, **12**, and **15**) showed less effect than Levofloxacin and Chloramphenicol, while compounds **1**, **11**, **12**, and **15** were determined to have equal effects with Levofloxacin and Chloramphenicol. Against *E. faecalis* bacteria, compound **13** was found to have similar effects to Vancomycin and Levofloxacin, while the other compounds showed less effect than with Vancomycin and Levofloxacin. Compounds **4**, **6-8**, **10**, **12**, and **16** were found to have similar effects to Chloramphenicol and Cefepime, while the other compounds (except compound **13**) exhibited less effect than Chloramphenicol and Cefepime. Compound **13** was more effective than Chloramphenicol and Cefepime. Against *B. subtilis* bacteria, Compounds **12, 13, 17** and **20** had similar effects to Levofloxacin and Vancomycin, while the other compounds (except compounds **7** and **14**) had similar effects to Cefepime and Chloramphenicol. Compounds **7** and **14** exhibited less effect than all control compounds. Against *P. aeruginosa* bacteria, compounds **5** and **19** for Levofloxacin and

Cefepime, compounds **3**, **6-8**, **12**, **16**,**17**, and **20** for Vancomycin, and compounds **1**, **2**, **4**, **9-11**, **13-15**, and **18** for Chloramphenicol had similar effects.

Table 2. *Antimicrobial activity values of all compounds (µg/mL)*

	C. albicans	***S. aureus***	***E. faecalis***	***B. subtilis***	***P. aeruginosa***	***E. coli***	***L. monocytogenes***
Vancomycin	-	31.25	31.25	31.25	62.50	125.00	125.00
Levofloxacin	-	62.50	31.25	31.25	31.25	31.25	62.50
Cefepime	-	31.25	62.50	62.50	31.25	31.25	62.50
Chloramphenicol		62.50	62.50	62.50	125.00	62.50	62.50
Fluconazole	62.50	-	-	-	-	-	-
Ketoconazole	62.50	-	-	-	-	-	-
1	125.00	125.00	125.00	62.50	125.00	31.25	62.50
2	125.00	62.50	125.00	62.50	125.00	62.50	62.50
3	250.00	62.50	125.00	62.50	62.50	62.50	62.50
4	250.00	62.50	62.50	62.50	125.00	15.62	62.50
5	62.50	62.50	125.00	62.50	31.25	62.50	31.25
6	15.62	62.50	62.50	62.50	62.50	31.25	31.25
7	125.00	62.50	62.50	125.00	62.50	125.00	62.50
8	62.50	62.50	62.50	62.50	62.50	62.50	31.25
9	125.00	62.50	125.00	62.50	125.00	31.25	62.50
10	31.25	62.50	62.50	62.50	125.00	125.00	125.00
11	125.00	125.00	125.00	62.50	125.00	62.50	62.50
12	125.00	62.50	62.50	31.25	62.50	62.50	125.00
13	62.50	125.00	31.25	31.25	125.00	125.00	125.00
14	125.00	62.50	125.00	125.00	125.00	62.50	62.50
15	125.00	125.00	125.00	62.50	125.00	62.50	62.50
16	125.00	62.50	62.50	62.50	62.50	62.50	62.50
17	62.50	62.50	125.00	31.25	62.50	31.25	31.25
18	62.50	62.50	125.00	62.50	125.00	125.00	125.00
19	62.50	62.50	125.00	62.50	31.25	125.00	31.25
20	125.00	31.25	125.00	31.25	62.50	31.25	62.50

***** The same results were obtained in three independent experiments.

Against *E. coli* bacteria, compounds **1**, **6**, **9**, **17**, and **20** for Levofloxacin and Cefepime, compounds **2**, **3, 5**, **8**, **11**, **12**, and **14-16** for Chloramphenicol, and compounds **7**, **10**, **13**, **18**, and **19** for Vancomycin had similar effects. Compound **4** was more effective than all control compounds. Against *L. monocytogenes* bacteria, compounds **5**, **6**, **8**, **17**, and **9** showed higher effect with all control compounds. Compounds **1-4**, **7**, **14-16**, and **20** showed similar activity to Levofloxacin, Cefepime, and Chloramphenicol. All the compounds (except **10**, **12**, **13**, and **18**) were more effective than Vancomycin, while compounds **10**, **12**, **13**, and **18** had similar effects with Vancomycin. When comparing the antimicrobial activities of the starting materials and the complexes, some metal complexes exhibited lower activity than the starting materials, while others exhibited similar or better activity. According to Table 2, it was observed that the metal complexes generally exhibited better activity. These activities may be due to factors such as the charge and number of metals, the presence of ligands, the chelating effect of the ligands, the properties of the ligands, and the number of donor atoms they contain. The difference in the activity of the complexes against bacteria and yeast is thought to be due to their ability to penetrate cell walls or membrane structures [76-78]. In conclusion, all compounds demonstrate potential applications in inhibiting bacterial and yeast growth, and derivatives of all compounds are valuable for further antibacterial and antifungal in vivo and in vitro testing.

Conclusions

In this study, Fe(III) (**2**, **7**, **12**, and **17**), Co(II) (**3**, **8**, **13**, and **18**), Ni(II) (**4**, **9**, **14**, and **19**), and Cu(II) (**5**, **10**, **15**, and **20**) complexes of 2-aminobenzothiazole (**1**), 2-amino-6-chlorobenzothiazole (**6**), 2-amino-6-methylbenzothiazole (**11**), and 2-amino-6-methoxybenzothiazole (**16**), respectively, were synthesized by the method found in the literature. The metal contents of the complexes were checked by AAS. Furthermore, the antimicrobial properties of **1-20** have also been tested against *C. albicans*, *E. coli, P. aeruginosa, B. subtilis, S. aureus, L. monocytogenes,* and *E. faecalis*. The results were compared with those obtained using the control compounds Fluconazole, Ketoconazole, Vancomycin, Levofloxacin, Cefepime, and Chloramphenicol (antibacterial activity). As a result of activity studies, synthesized compounds show activity against bacteria and yeasts. Notably, compound **4** demonstrated superior activity against *E. coli*, while complexes **6** and **10** displayed enhanced activity against *C. albicans* when compared to the control compounds. In conclusion, all compounds demonstrate potential applications in inhibiting bacterial and yeast growth, and derivatives of all compounds are valuable for further antibacterial and antifungal in vivo and in vitro testing.

Declarations

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