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Research Article

A novel nicotinoyl thiourea manganese complex: synthesis, characterization, and biological activity studies

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ABSTRACT

In this study, nicotinoyl thiourea synthesized by starting from nicotinic acid and 3,5-dimethoxy aniline according to the literature. The resulting product was reacted with Manganese (II) acetate tetrahydrate and nicotinoyl thiourea manganese complex was synthesized with a metal-ligand ratio of 1: 1. The chemical structure of newly synthesized metal complex was characterized by FTIR, HRMS, XRD, and elemental analysis. In the second part of the study, the antibacterial and antioxidant activities of the synthesized metal complex were investigated. According to the obtained results, metal complex did not show any antibacterial activity. However, metal complex exhibited strong or equipotent antioxidant properties compared to standard antioxidants in DPPH, ABTS, and Cuprac methods. For this reason, metal complex can be evaluated as an antioxidant agent in food protection and the treatment of many diseases related oxidative stress.

Keywords: Thiourea, manganese, metal complex, antibacterial, antioxidant.

Yeni bir nikotinoyil tiyoüre mangan kompleksi: sentez, karakterizasyon ve biyolojik aktivite çalışmaları

ÖZ

Bu çalışmada nikotinoil tiyoüre, nikotinik asit ve 3,5-dimetoksi anilinden başlanarak literatüre göre sentezlenmiştir. Elde edilen ürün Mangan (II) asetat tetrahidrat ile tepkimeye sokularak 1:1 metal-ligand oranıyla nikotinoyil tiyoüre mangan kompleksi sentezlenmiştir. Sentezlenen yeni metal kompleksinin kimyasal yapısı FTIR, HRMS, XRD ve elementel analiz ile karakterize edilmiştir. Çalışmanın ikinci bölümünde sentezlenen metal kompleksin antibakteriyel ve antioksidan aktiviteleri araştırılmıştır. Elde edilen sonuçlara göre metal kompleksi herhangi bir antibakteriyel aktivite göstermemiştir. Bununla birlikte metal kompleksi DPPH, ABTS ve kuprak metotlarında standart antioksidanlara göre güçlü veya eşit potansiyelli antioksidan özellikler sergilemiştir. Bu nedenle, metal kompleksi gıdanın korunması ve oksidatif stres ile ilişkili birçok hastalığın tedavisinde bir antioksidan ajan olarak değerlendirilebilir.

Anahtar Kelimeler: Tiyoüre, mangan, metal kompleks, antibakteriyel, antioksidan.

1. INTRODUCTION

Thiourea with general formula of $(R_1R_2N)(R_3R_4N)C=S$ is an important group having a sulphur atom. If the carbonyl group is attached to thiourea, it is called 1-(acyl or aroyl) substituent thiourea.[1] Thioureas are important substances for the synthesis of heterocyclics.[2] They can coordinate with transition metals because of using both oxygen and sulphur atoms.[3] To the best of our knowledge, thiourea derivatives have also a wide spread of usability in the synthetic organic chemistry, agrochemical industrys, building blocks in the synthesis of low molecular weight compounds, and pharmaceutical industry because of their activities such as antithyroid, antihaemolytic, and antioxidant.[4] The literature includes various derivatives associated with aroyl thioureas

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having many biological activities such as anti-intestinal nematode[4], antibacterial and antifungal[5], hepatitis C virus inhibitor[6], urease inhibitor[7], and histamine H3, H4 receptors.[8]

It is known that benzoyl thioureas form complexes with various transition metals such as Ni, Co, Ag and Mn due to carbonyl, thiocarbonyl, and amine groups.[9] Previous studies demonstrate that many metal complexes of benzoyl thioureas have been reported.[10-12] Although benzoyl thioureas and metal complexes are well-known in the literature, there is no experimental data about metal complexes of nicotinoyl thioureas. Nicotinoyl thioureas including a pyridine ring instead of a benzene ring were synthesized in our previously study due to have many biological activity, especially such as antibacterial activity.[13] Therefore, it was aimed to synthesize novel manganese complex of synthesized nicotinoyl thiourea. Antioxidants are important substances for the human body. Free radicals are harmful materials produced by cells. Oxidative stress may occur as a result of the body's inability to effectively remove these free radicals that damage cell and body functions.[13] The principal aim of this study was to synthesize the metal complex and compare the ligand and metal complex in terms of their biological activities. Therefore, we also aimed to comparison of their antibacterial, and antioxidant properties.

2. MATERIALS AND METHODS

2.1. Chemicals

Nicotinic acid, thionyl chloride ($SOCl_2$), potassium thiocyanate (KSCN), Manganese (II) acetate tetrahydrate [$Mn(CH_3COO)_2.4H_2O$], 3,5-dimethoxyaniline, dmso-d_6 and all solvents were bought commercially and it was used just like that. TLC was carried out on silica gel plates with F-254 indicator and compounds were monitored with UV lamp. ^1H and ^{13}C NMR were recorded on a Bruker 400 MHz instrument and reported in DMSO-d_6. Chemical shifts are reported in ppm by using TMS as an internal standard. The melting points were recorded on an electrothermal melting point apparatus (Electrothermal IA9100) in sealed capillaries and are uncorrected. HRMS were performed on Agilent 6530 Accurate-Mass instrument. FT-IR (Fourier transform) spectra were obtained on a Shimadzu IRTracer-100 spectrometer with GladiATR 10. Elemental analysis (C, H, N) was obtained on a Leco CHNS 932 instrument. XRD spectrum was obtained from GNR Explorer XRD Instrument.

2.2. Synthesis of nicotinoyl chloride (2)

This compound **(2)** was synthesized from nicotinic acid (**1**) and $SOCl_2$ as describes previously.[14]

2.3. Synthesis of 3-isothiocyanatopyridine (nicotinoyl isothiocyanate) (3)

Compound (**3**) was synthesized from nicotinoyl chloride (**2**) and KSCN as describes previously.[15]

2.4. Synthesis of N-Nicotinoyl-N'-(3,5-dimethoxyphenyl) thiourea (Ligand) (5)

N-Nicotinoyl-N'-(3,5-dimethoxyphenyl) thiourea (ligand) (**5**) was synthesized according to the literature.[13] All spectral data are in accordance with the literature.

2.5. Synthesis of complex $[Mn(L)CH_3COO].2H_2O$ (6)

Nicotinoyl thiourea (**5**) (2 eqv.) was dissolved in 15 ml DMF to which a solution of Manganese (II) acetate tetrahydrate ($Mn(CH_3COO)_2.4H_2O$) (1 eqv.), dissolved in H_2O (20 ml), was added drop by drop while stirring powerfully, at room temperature. The mixture was refluxed for additional 3 hours, followed by addition of distilled H_2O (100 ml). After cooling in a refrigerator to 4°C for 24 hours, the dark solid residual was collected by centrifugation and washed three times with distilled water (3 ml). As a result of this procedure, the product was obtained as a deep brown-black powder. Yield; 81%, Mp; >400°C. FT-IR spectrum, ν, cm^{-1}: 1683 (s) (C=O), 1558 (s) (C=N). Analysis Calculated for $C_{17}H_{22}MnN_3O_7S$ %: C 43.69; H 4.74; N 8.99; S 6.86. Found, %: C 43.72; H 4.72; N 8.96; S 6.88. HR-MS (ES+), m/z (calc./found): 467.0559/467.2182.

2.6. Antibacterial activity studies

To determine antibacterial activity, agar well diffusion method was applied as described previously.[16] In this context, Mueller Hinton Agar (MHA) were standardized to a cell density of $1.5x10^8$/mL (McFarland No. 0.5), the turbidity of the bacteria was qualified at 600 nm. Wells (6 mm diameter) were burrowed in the plates and these were filled with the samples (100 µl). Netilmicin (NET30), Ofloxacin (OFX) and Cefsulodin (CFS) were drew on as positive standard antibiotics, and negative control was 10% (v/v) DMSO solution. The three different concentrations of previously synthesized compound and newly synthesized manganese complex were evaluated against five different bacterial strains. Incubation of the bacterial strains was carried out at 37°C during 24-72 hours. At the end of this period, the diameters of the zones were measured in millimeters. All experiments were done three times according to the described procedure.[16]

2.7. Bacterial Strains

As clinical pathogenic bacteria were used *Acinetobacter baumannii* (ATCC 1609), *Enterococcus faecalis* (ATCC 49462), *Escherichia coli* (ATCC 2523), *Methicillin-*

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resistant Staphylococcus aureus (MRSA) (ATCC 67106), and *Pseudomonas aeruginosa* (ATCC 9027).

2.8. Minimum inhibitory concentrations (MICs)

MIC values of the ligand and manganese complex were determined by using sterile 96-well plates. The compounds **5–6** were arranged ranging from 31.25 to 1000 µg/ml , inoculated at 1% (v/v) with an inoculum of 10^8 CFU/ml and at 37 °C during 24 hours were incubated. All of this experimental procedure and necessary calculations were prepared according to the manuals. To determine the minimum inhibitory concentration values, lowest concentration of compounds that inhibited visual bacterial growth was then observed.[17, 18]

2.9. Antioxidant activity studies

To determine total radical scavenging capacity of the ligand and its manganese complex, 1,1-diphenyl-2-picrylhydrazyl (DPPH$^{\bullet}$) method was used as described earlier. Radical scavenging capacity was compared with butylated hydroxytoluene, trolox, beta carotene, and ascorbic acid.[19] The solution of DPPH$^{\bullet}$ was daily prepared and kept in the dark at 4°C. 0.1mM of DPPH fresh solution was prepared in ethanol. After that, an aliquot (0.5 ml) (6.25–200 µg/ml) was added to test tubes containing 1.5 ml of ligand and its newly synthesized manganese complex in ethanol. With vigorous stirring, resulting mixtures were then incubated in the dark for half an hour. As a result, the absorbance values were measured at 517 nm by spectrophotometer.[20]

2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate) radical ($ABTS^{\bullet+}$) scavenging procedure have been improved by Re *et al*.[21] In order to form the ABTS cation radical ($ABTS^{\bullet+}$), 2 mM of ABTS solution in H_2O was reacted with oxidizing agent of 2.3 mM of potassium persulfate ($K_2S_2O_8$). Prepared ($ABTS^{\bullet+}$) was soluble in aqueous and organic solvents. To adjust desired absorbance (0.700 ± 0.025) at 734 nm, it was diluted with phosphate buffer (0.1 mM, pH 7.4). Finally, 3 ml of tested samples' solution between 6.25–200 µg/ml concentrations was treated to 1 ml of $ABTS^{\bullet+}$ and the resulting absorbance was measured at 734 nm by spectrophotometer.

By using the following equation, the capability to radical scavenge in the DPPH and $ABTS^{\bullet+}$ assays was calculated: R.S.E (%) = [(A.c-A.s) / A.c)] x 100 where R.S.E is radical scavenging efficacy, A.C is the absorbance value of the control and A.S is the absorbance value of the sample.[22] All calculations were done according to this equations.

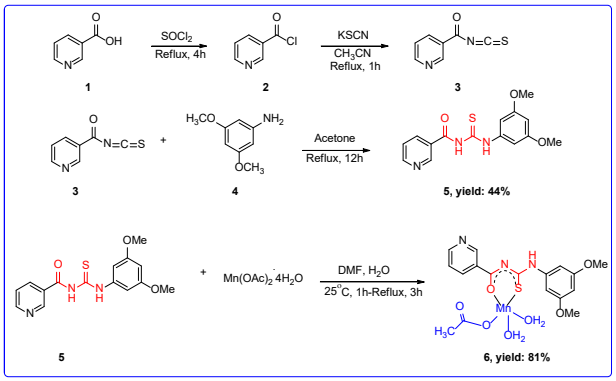
In order to determine the half maximal scavenging concentration of sample (IC_{50}), inhibition percentage against all compounds concentrations (µg/ml) was plotted.[23]

To determine antioxidant capacity, cupric ions (Cu^{2+}) reducing power assay as another method was used to earlier synthesized thiourea and its novel manganese complex. Cu^{2+} reducing capability was performed as described earlier.[24] This method is based on the reduction of Cu^{2+} to Cu^{+}. In this context, copper (II) chloride ($CuCl_2$) solution (0.01 M, 0.25 ml), ammonium acetate (CH_3COONH_4) buffer solution (1 M, 0.25 ml), and ethanolic neocuproine solution (7.5×10^{-3} M, 0.25 ml) were transferred to a test tube, which contains compounds **5–6** between 6.25–200 µg/ml concentrations. Distilled water was added to complete the final volume to 2 ml, and then shaken. After half an hour, absorbance values were measured at 450 nm.

3. RESULTS AND DISCUSSION

3.1. Characterization

In this study, nicotinoyl thiourea (ligand) was synthesized according to the literature.[13] Manganese complex of ligand was synthesized. The synthetic routes are given in Scheme 1. The structure of complex was eluciated by FT-IR, HRMS, elemental analysis, and XRD. Nicotinoyl chloride (**2**) was prepared from nicotinic acid (**1**) according to the literature.[14] Nicotinoyl isothiocyanate (**3**) was synthesized with KSCN[15], and then reacted with 3,5-dimethoxy aniline (**4**) in acetone at about 65°C to give nicotinoyl thiourea (**5**).[13] The ligand on interaction with $Mn(CH_3COO)_2.4H_2O$ yields manganese complex (**6**) corresponding to the 1:1 metal-ligand ratio.[9, 25] TLC (thin layer chromatography) was used to monitor the reactions. Similar to the literature, the complex is air stable, with deeply dark colored, and insoluble in both H_2O and most of commercially available the organic solvents but were sparingly soluble in DMSO and DMF.[25] In order to obtain the single crystal of the complex made many attempts but this was unsuccessful. Therefore, we do not use X-ray structure determination.



Scheme 1. Synthetic routes to the target product.

FT-IR spectrum of the ligand (**5**) (nicotinoyl thiourea) displayed the absorption band for the stretching of NH at

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3201 cm^{-1}. A strong band observed in the region of 1682 cm^{-1} in the FT-IR spectrum of the ligand (**5**) was assigned to the carbonyl group. This C=O band was shifted to the lower frequency range of 1506 cm^{-1} in the spectra of the complex (**6**), consistent with the coordination of oxygen atom to the manganese ion. Moreover, a strong band observed in the region of 1683 cm^{-1}. This band was assigned to the C=O stretching vibration of acetate attached to manganese complex. In addition, the characteristic band for C=S appeared at 1161 cm^{-1} in the spectrum of ligand was shifted to 1153 cm^{-1} on complexation, indicating relation of sulphur atom in coordination. Moreover, nitrile band formed on complex was observed in the region of 1558 cm^{-1}. IR spectra of compounds are in agreement with the literature.[26, 27] The XRD pattern of ligand (nicotinoyl thiourea) and its manganese complex exhibits sharp intense peaks throughout the spectrum showing crystalline sample. Additional peaks and shifts in the spectrum are observed when the ligand is attached to manganese (Figure 1).[28]

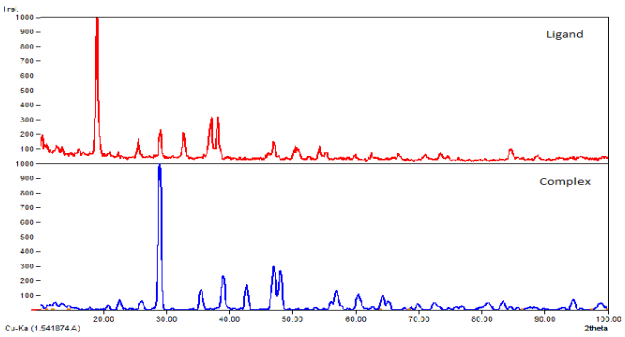

Figure 1. XRD pattern of ligand and its complexation with manganese, respectively.

Trial and error method was used to index X-ray diffraction main peaks.[28] Table 1 is shown the crystal size, hkl and 2-theta maximum.

Table 1. XRD peaks and crystal thickness calculated from Scherer's formula

Compound	2-theta maximum	hkl	Crystal size (Å)
Ligand (5)	18.99	200	5.2
[Mn(L)OAc].2H_2O (6)	28.99	85	3.08

3.2. Biological evaluations

Table 2 is shown the antibacterial activity results for ligand **5** and its manganese complex **6** against five different bacterial strains. Three Gram negative bacteria (*E. coli* ATCC 2523, *A. baumannii* ATCC 1609, and *P. aeruginosa* ATCC 9027) and two Gram positive bacteria (*S. aureus* ATCC 67106, and *E. faecalis* ATCC 49462) were used for antibacterial activity. The results revealed that ligand **5** showed highly strong antibacterial activity against tested bacterial strains[13], whereas manganese complex did not show any activity.

The MICs of ligand **5** were evaluated at concentration 31.25 µg/ml. The previously synthesized compound **5** inhibited the growth of bacteria with an inhibition zone varying between 25–29 mm, 18–23 mm, and 10–20 mm for concentrations of 1000, 500 and 250 µg / ml, respectively.[13] A study have shown that the presence of methoxy substituent on benzene reduces the activity due to electron donating group. They have also reported that a pair of electrons that does not participate in bonding are resonating on benzene ring.[29] In another study have determined that the presence of the 4-methoxy group in benzoyl thiourea compounds with aniline groups reduces antibacterial activity (MIC: generally >1000 µg/ml).[30] Conversely, our compound contains a pyridine ring instead of a benzene ring. Commercially available large number of drugs with antimicrobial, and antioxidant activity in the market contain a pyridine ring.[31]

Table 2. Antibacterial activity of compounds **5-6.**

Bacteria	Compound	Concentrations (µg/mL)[a]			MIC[b]	Negative Control[c]	Positive Control[d]		
		1000	500	250			OFX	NET 30	CFS
Acinetobacter baumannii	5	25	20	18	31.25	-	9	7	8
	6	-	-	-	-				
Enterococcus faecalis	5	28	19	10	31.25	-	11	10	9.5
	6	-	-	-	-				
Escherichia coli	5	29	23	20	31.25	-	9.8	7	7.7
Pseudomonas	5	27	21	17	31.25	-	10	10	9
Staphylococcus aureus	5	25	18	15	31.25	-	11	18	9
	6	-	-	-	-				

Evidenced by our previously studies that nicotinoyl thioureas comprising aniline ring having methoxy group at different positions have stronger activity than benzoyl thioureas.[13, 32] It has been determined that compounds containing thiocarbonyl, carbonyl and amine groups have antibacterial properties especially against gram-negative bacteria[33] because they react with nucleophilic and electrophilic centers of bacterial surface[34] and induce antibacterial activity. Thus, we think that this may be the reason why our ligand shows antibacterial activity. On

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the other hand, its manganese complex did not any show antibacterial activity. Notably a report demonstrate that the ligand may be more reactive with the microelements present in the environment or the formed complexes may have an extraordinary coordination that may be inert to cell components. They also concluded that the ligand prepared may be more reactive with microelements essential for bacterial nutrition.[9] Therefore, our manganese complex may not have shown any antibacterial activity because the thiocarbonyl, carbonyl, and amine groups are participated on complexation. This knowledge supports our conclusion why while our ligand has antibacterial activity, our complex does not have antibacterial activity.

Antioxidant properties are very important because of remove harmful effects of free radicals. To determine the free radical scavenging efficacy of various antioxidant materials, DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ assays have been widely used and these assays are important to screen of antioxidant properties of plant extractions, organic compounds etc. Antioxidant activity of previously synthesized compound **5**[13], novel manganase complex **6,** and standard antioxidants such as butylated hydroxytoluene, beta carotene, trolox, and ascorbic acid were specified with DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ assays. Samples were analysed for their antioxidant activity ranging from 6.25–200 µg/ml concentrations. Figure 2 shows a significant decreasing (p<0.05) in the concentration of 1,1-diphenyl-2-picrylhydrazyl (DPPH$^{\bullet}$) radical because of the scavenging ability of previously synthesized thiourea compound by our group, newly synthesized manganese complex, and standards. The scavenging efficacy of samples **5–6** and standards on the 1,1-diphenyl-2-picrylhydrazyl (DPPH$^{\bullet}$) radical reduced in the order of Ascorbic acid > trolox > 6 > 5 > butylated hydroxytoluene > beta carotene, which were 94.95%, 94.41%, 85.36%, 76.69%, 66.03%, 65% at the concentration of 200 µg/ml, respectively. Absorbance values of samples also decreased with an increasing concentration. Figure 2 shows the radical scavenging activity according to the DPPH$^{\bullet}$ method. IC_{50} values in DPPH$^{\bullet}$ method were determined as 4.49 µg/ml (r^2: 0.9985) for 5, 4.77 µg/ml (r^2: 0.9785) for 6, 4.65 µg/ml (r^2: 0.9765) for ascorbic acid, 4.69 µg/ml (r^2: 0.9962) for trolox, 4.59 µg/ml (r^2: 0.9912) for butylated hydroxytoluene, and 4.65 µg/ml (r^2: 0.9796) for beta carotene. Radical scavenging efficacy of samples **5–6** and standards in the DPPH$^{\bullet}$ method decreased in the following order: 5 > butylated hydroxytoluene > beta carotene > ascorbic acid > trolox > 6. A lower the IC_{50} value indicates a higher the antioxidant activity of samples (Table 3). These results have demonstrated that previously synthesized thiourea compound and its novel manganese complex have equipotent or weak free radical scavenging capabilities compared with standard antioxidants. Samples **5–6** were determined to show effective radical scavenging activity against 2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate) radical (ABTS$^{\bullet+}$) (p>0.001). As can be seen in Figure 2, the samples **5–6** have effective ABTS$^{\bullet+}$ radical scavenging activity depending on the concentration (6.25-200 µg/ml). The scavenging efficacy of samples **5–6** and standards on the 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate) (ABTS$^{\bullet+}$) radicals reduced in the order of butylated hydroxytoluene > beta carotene > 6 > ascorbic acid > trolox > 5 > which were 99.72%, 99.66%, 88.08%, 73.86%, 72.44%, 65.72% at the concentration of 200 µg/ml, respectively. Absorbance values of samples **5–6** also decreased with an increasing concentration. IC_{50} values for compounds **5–6** were calculated as 5.27 µg/ml (r^2: 0.9381) for 5, 4.89 µg/ml (r^2: 0.9421) for 6. Additionally, IC_{50} values were found as 3.28 µg/ml (r^2: 0.8094) for butylated hydroxytoluene, 4.94 µg/ml (r^2: 0.9841) for ascorbic acid, 4.72 µg/ml (r^2: 0.9795) for trolox, and 3.63 µg/ml (r^2: 0.9197) for beta carotene (Table 3). The 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate) (ABTS$^{\bullet+}$) scavenging efficacy of samples **5–6** and standards reduced in the following order: butylated hydroxytoluene > beta carotene > trolox > 6 > ascorbic acid > 5. A lower the IC_{50} value indicates a higher the antioxidant activity of samples. It is seen that newly synthesized manganase complex on ABTS$^{\bullet+}$ scavenging effect have more stronger than compared to ascorbic acid, while close to butylated hydroxytoluene, beta carotene, and trolox.

Table 3. Determination of half maximal concentrations (IC_{50}, µg/ml) of compounds **5–6** and standards for DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ scavenging.

Antioxidant compounds	DPPH$^{\bullet}$ scavenging		ABTS$^{\bullet+}$ scavenging	
	IC_{50}	r^2	IC_{50}	r^2
Ascorbic acid	4.65	0.9765	4.94	0.9841
Trolox	4.69	0.9962	4.72	0.9795
BHT	4.59	0.9912	3.28	0.8094
β-Carotene	4.65	0.9796	3.63	0.9197
5	4.49	0.9985	5.27	0.9381
6	4.77	0.9785	4,89	0.9421

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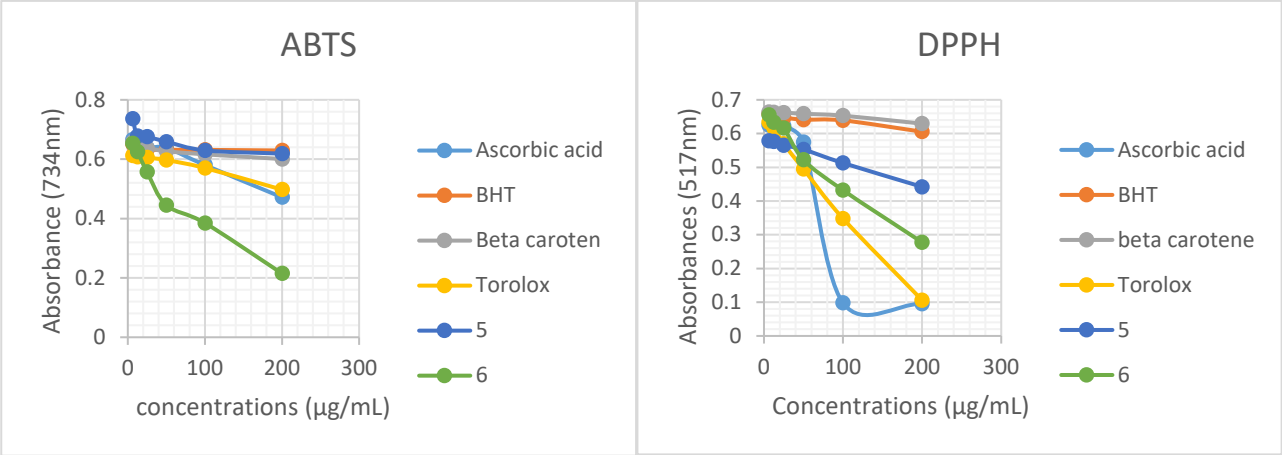

Figure 2. ABTS and DPPH free radical scavenging activity of different concentrations (6.25–200 µg/ml) of compound **5–6** and reference antioxidants; Trolox, BHT, β-Carotene and Ascorbic acid (BHT: butylated hydroxytoluene; DPPH: 1,1-diphenyl-2-picryl-hydrazyl free radical; ABTS: 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonate).

The values of the CUPRAC method are shown in Table 4. As the oxidizing agent was used the chromogenic neocuproine. Ligand **5** exhibited higher activity than beta carotene and butylated hydroxytoluene, while less active than trolox and ascorbic acid. On the other hand, novel metal complex **6** showed weaker activity than its ligand and all standards. The ascorbic acid solution had the highest CUPRAC value. The reducing power decreased in the order of ascorbic acid > trolox > 5 > butylated hydroxytoluene > beta carotene > 6 for the same concentration (200 µg/ml). The results obtained in DPPH (1,1-diphenyl-2-picrylhydrazyl), ABTS (2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate)), and CUPRAC (cupric ions (Cu^{2+}) reducing power) method revealed that previously synthesized ligand and its newly synthesized manganese complex have stronger, equipotent or weaker activity than the standards.

Table 4. Determination of reducing power of 200 µg/ml concentration of compounds **5–6** and standards by cupric ions (Cu^{2+}) reducing capacity by Cuprac method.

Antioxidants	Cu^{2+}– Cu^{+} reducing	
	λ_{450}*	r^2
Trolox	0.517 ± 0.002	0.999
BHT	0.109 ± 0.001	0.995
β-Carotene	0.102 ± 0.001	0.997
Ascorbic acid	3.613 ± 0.002	0.974
5	0.158 ± 0.004	0.907
6	0.079 ± 0.001	0.950

To the best of our knowledge from the literature, N,N'-disubstituted and benzoyl thioureas have antioxidant activities and they are an important compounds to inhibit the production of the most well-known oxygen free radicals.[35] In addition, heterocyclic compounds having a pyridine ring exhibit more antioxidant properties compared with benzene ring.[36] We demonstrated this situation in our previously reports.[13, 32] It is known that the central metal atom in metal complexes contributes positively to antioxidant activity as a result of enhancing the proton donating capacity of the ligand.[37] As with benzoyl or N, N'-disubstituted thioureas, both manganese complex **6** and our previously synthesized nicotinoyl thiourea **5** were determined to have antioxidant activities.

4. CONCLUSIONS

In this study, nicotinoyl thiourea **5,** earlier synthesized by our group, was designed as ligand. Its manganese complex **6** has been synthesized for the first time. According to the experimental evaluations, the ligand **5** coordinate to the manganese (II) ion through carbonyl and thiocarbonyl groups of nicotinoyl thiourea. The chemical structure of manganese complex was characterized by FTIR, HRMS, XRD, and elemental analysis. According to these characterizations, the metal:ligand ratio was 1:1. Antibacterial activity studies of these compounds show that earlier synthesized compund **5** have antibacterial activity against all tested bacteria, whereas its manganase complex **6** has not any antibacterial activity. Therefore, while the ligand can be considered as an agent in the treatment of bacterial infections, its manganese complex cannot. In contrast to this situation, manganese complex showed equipotent antioxidant properties compared to standard antioxidants. For this reason, compound **6** can be evaluated as an antioxidant agent in food protection and the treatment of many diseases related oxidative stress. Further research and clinical trials are required to clarify the potential of the compounds in the diseases associated with oxidative stress. Moreover, the synthesis of this complex will lead to the synthesis of more efficient new metal complexes.

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Conflict on interest

The authors declare that there is no conflict of interest with any person, institution, and company, etc.

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