Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. 77 (2) 229–240 (2012)
JSCS–4411
UDC 547.496/.497+546.302+
542.913:615.27:543.4
Original scientific paper

Synthesis, characterization of thiosemicarbazone metal complexes and their antioxidant activity in different *in vitro* model systems

DESIREDDY HARIKISHORE KUMAR REDDY[1], SEUNG-MOK LEE[1]*, KALLURU SESHAIAH[2] and K. RAMESH BABU[3]

[1]*Department of Environmental Engineering, Kwandong University, Gangneung, Republic of Korea,* [2] *Inorganic and Analytical Chemistry Division, Department of Chemistry, Sri Venkateswara University, Tirupati – 517 502, India and* [3] *Department of Biochemistry, Sri Venkateswara University, Tirupati – 517 502, India*

(Received 25 March, revised 12 September 2012)

Abstract: The synthesis of bimetallic Cu(II), Co(II), Ni(II), Zn(II) and U(VI) complexes with general stoichiometry $[H_2L\ M(X_2)(H_2O)_2]$ (where H_2L is the di-deprotanated ligand and X is chloride/sulphate) were obtained with the ligand terephthaladehyde bis(thiosemicarbazone) (H_2L) and are discussed. The ligand and its binuclear complexes were characterized by micro analysis (CHNS), ^{1}H-NMR, FT-IR, UV-vis, TG-DTA and conductance measurements. The thermal behaviour of these complexes showed that the hydrated complexes loose water molecules of hydration in the first step, followed immediately by decomposition of the anions and ligand molecules in the subsequent steps. The molar conductance measurements of the complexes in DMF correspond to the non-electrolytic nature of the complexes. Furthermore, the antioxidant activity of the ligand and its complexes were determined *in vitro* by the hydroxyl radical scavenging, DPPH, NO and reducing power methods. The obtained IC_{50} value of the DPPH activity for complex **2** (IC_{50} = 0.254 M) was shown to be the best.

Keywords: thiosemicarbazone; transition metal complexes; spectral analysis; bimetallic complexes; antioxidant activity

INTRODUCTION

Thiosemicarbazones (TSCs) have become the subject of intense research interest with coordination chemists as they are simple to prepare, have excellent complexation ability with both transition and non-transition elements and the complexes have interesting structural characteristics and possible analytical applications. This interest and wide range of applications resulted in a large number

* Corresponding author. E-mail: leesm@kwandong.ac.kr
doi: 10.2298/JSC120325099K

of papers and several reviews on TSCs.[1–4] In addition, TSCs have received considerable attention due to their broad profile of pharmacological activity, as they afford a diverse variety of compounds with different activities.[5,6] The mechanism of action of TSCs is due to their ability to inhibit DNA biosynthesis, possibly by blocking the enzyme ribonucleotide diphosphate reductase; binding to the nitrogen bases of DNA, hindering or blocking base replication, or creating lesions in the DNA strands by oxidative rupture.[7,8] The remarkable biological activities of TSCs have provided real impetus to drive developments in their coordination chemistry, which subsequently showed that the biological activity of TSCs is related to their metal complexing ability. In some cases, the highest activity of TSCs is associated with a metal atom, and the biological properties of TSCs are often related to their metal ion coordination. The lipophilicity, which controls the rate of entry of TSCs into the cell, is modified by coordination. Additionally, the metal complexes can be more active than the free ligands, and some of the side effects associated with free ligands may decrease upon complexation. In addition, the complexes may exhibit bioactivities which are not exerted by free ligands.[9] Studies related to new developments in metal-based drugs are both promising and of great interest in the development of therapeutic agents.[10,12]

Atherosclerosis and its associated complications are currently the major causes of cardiovascular morbidity and mortality worldwide. Elevated levels of cholesterol, especially low-density lipoprotein (LDL) and triglycerides, along with free radical oxidative stress are recognized as the leading causes of atherosclerosis and coronary heart disease. Hydroxyl radicals ($OH^{\bullet}$) are generated by the metal ions present in serum, and changes in their oxidation states result in oxidative damage of LDL and other lipoproteins in plasma, which is responsible for the initiation and progression of atherosclerosis in hyperlipidemic subjects.

Free radicals also interact with proteins in other normal metabolic processes, which can lead to many types of pathologic changes.[13–17] To protect biomolecules against the attack of free radicals and/or to suppress the resultant damage, numerous natural and synthetic free radical scavengers and antioxidants have been developed and studied[18,19] Among them, thiosemicarabazones and their metal complexes have been evaluated for their free radical scavenger activity.[20,21]

The synthesis and characterization of copper(II), cobalt(II) and nickel(II) complexes with terephthalaldehyde bis(thiosemicarbazone) was described by Minghao *et al.*[22] In addition, the coordination polymerization (polycoordination) of terephthalaldehyde bis(thiosemicarbazone) with mercury(II) and cadmium(II) complexes was studied by Marcu *et al.*[23] However, the biological activity of terephthalaldehyde bis(thiosemicarbazone)–metal complexes has not been reported. Given the potential biological activity of thiosemicarbazone and the involvement of metal ions in cell metabolism, a systematic study was undertaken to explore this chemistry, with the development of new biologically active pharmaceuticals

as the final goal. Herein, the preparation and spectroscopic characterization of five metal complexes derived from terepthaladehyde bis(thiosemicarbazone) are reported. The ligand and metal complexes were evaluated for their antioxidant activity. It was envisaged that the thiosemicarbazone could be useful in controlling metabolic disorders by scavenging free radicals.

EXPERIMENTAL

Physical measurements

Melting points were determined by the open capillary method and are uncorrected. The metal content of the complexes was estimated using standard methods. The analysis of CHNS/O contents of ligand and metal complexes were realized on a Euro elemental analyzer. The IR spectra were recorded as KBr pellets using a Perkin–Elmer Fourier-Transform Spectrum RX1 spectrophotometer in the region 4500–450 cm^{-1}. The TG/DTA curves for the complexes were recorded on a Nietzsche thermobalance (model-STA 40g) with a P_t V_s P_t 10 % Rh thermocouple under dynamic air conditions between room temperature (≈20 °C) and 1020 °C (gradient 10 K min^{-1}).

*Synthesis of the ligand (**1**)*

The synthesis of terepthaladehyde bis(thiosemicarbazone) (**1**) was based on the following method: an ethanolic solution (50 mL) of terepthaladehyde (0.2 g) and thiosemicarbazide (0.270 g) in an ethanol–water mixture (50 mL) were mixed and refluxed for 2 h. After cooling to room temperature, the formed yellow solid was isolated and dried under vacuum.

*Synthesis of metal complexes (**2**–**6**)*

In a representative preparation, the complexes were synthesized by refluxing DMF–ethanol (1:1, 20 mL) solution of ligand (5 mmol) with an ethanolic solution (20 mL) of corresponding metal salt (10 mmol) for 12 h at 70 °C. On cooling overnight, the collared complex precipitated out. The precipitate was filtered, washed with cold DMF–ethanol and dried under vacuum. The metal salts used in this study were $CuSO_4 \cdot 5H_2O$, $CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$, $ZnSO_4 \cdot 7H_2O$ and $UO_2(CH_3COO)_2 \cdot 2H_2O$.

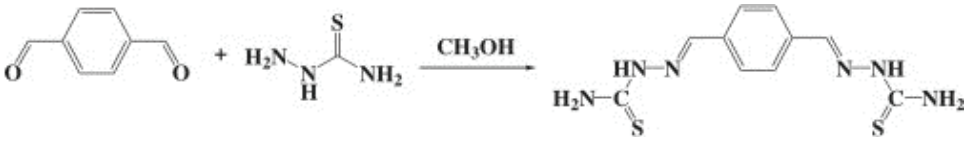
Antioxidant activity

The scavenging effects of compounds **2**–**6** on the DPPH radical were evaluated using the stable $DPPH^{\bullet}$ as the reagent.[24] In the H_2O_2 scavenging activity experiments, the hydroxyl radical ($OH^{\bullet}$) in aqueous media was generated through the Fenton Reaction.[25] For determining the nitric oxide (NO) scavenging activity, the absorbance of the chromophore formed during diazotization of nitrite with sulphanilamide and subsequent *N*-naphthylethylenediamine dihydrochloride was measured at 546 nm.[26,27] The reducing power of the synthesized compounds was determined according to the method of Oyaizu.[28]

RESULTS AND DISCUSSION

Terepthaladehyde was treated with thiosemicarbazide in refluxing methanol to afford terepthaladehyde bis(thiosemicarbazone) (H_2L). The synthetic route to the ligand is shown in Scheme 1. The synthesized ligand was confirmed by ^{1}H--NMR spectra recorded in d_6-dimethylsulphoxide (DMSO-d_6) solution using tetramethylsilane (TMS) as an internal standard. The hydrazinic proton (–N^{2}H) of the free ligand appeared as a broad single peak at 11.46 ppm.[29] The amino group

(–N^1H_2) showed a signal in the region 8.05 ppm. A singlet in the region 7.99––8.01 ppm was observed which was assigned to the azomethine proton (–HC=N). In the region 7.8 ppm, the signals were assigned to chemical shifts of hydrogens on the symmetric aromatic ring of the ligand. Further the metal complexes were prepared with the ligand as described in experimental section. All the synthesized complexes were binuclear with an M:L ratio of 2:1. The molar conductance values in DMF were in the expected range (17–24 S cm^2 mol^{-1}) of non-electrolytes, indicating bonding of chloride and sulphate anions to the metal ions.[30] The complexes were analyzed for carbon, hydrogen, nitrogen, oxygen, sulphur and metals. The analytical results are given in Table I, while the physical, UV/Vis and molar conductance data are listed in Table II. The metal complexes were stable under atmospheric conditions for extended periods, and were easily soluble in dimethylsulphoxide (DMSO) and *N*,*N*-dimethylformamide (DMF); however, they were insoluble in most common solvents. The composition and coordination geometry of these complexes were established based on the following experimental observations.



Scheme. 1 Synthesis of the ligand H_2L.

TABLE I. Analytical data of the compounds

Cmpd.	Molecular formula	FW	Elemental analysis, Calcd. (found), %					
			C	H	N	S	O	M
1	$C_{10}H_{12}N_6S_2$	280.4	42.84	4.31	29.97	22.87	–	–
			(42.74)	(4.28)	(29.88)	(22.86)		
2	$Cu_2C_{10}H_{14}N_6O_4S_5$	537.54	22.34	2.63	15.63	17.90	17.86	23.64
			(22.01)	(2.34)	(15.17)	(17.24)	(17.25)	(23.25)
3	$Co_2C_{10}H_{14}Cl_2N_6O_2S_2$	503.16	23.87	2.80	16.70	12.75	6.36	23.43
			(23.56)	(2.78)	(16.64)	(12.29)	(6.33)	(23.33)
4	$Ni_2C_{10}H_{14}Cl_2N_6O_2S_2$	499.87	23.89	2.81	14.11	12.76	6.37	23.35
			(23.80)	(2.20)	(14.01)	(12.32)	(6.34)	(23.26)
5	Zn_2 $C_{10}H_{14}N_6O_4S_5$	541.27	22.19	2.61	15.53	17.77	17.74	24.17
			(22.13)	(2.36)	(15.22)	(17.32)	(17.43)	(24.02)
6	$U_2C_{10}H_{18}N_6O_8S_2$	890.47	13.49	2.04	9.44	7.20	14.37	53.46
			(13.41)	(2.01)	(9.47)	(7.56)	(14.22)	(53.54)

FT-IR spectra

The spectra of the free thiosemicarabzone ligand showed peaks of concern at 3395–3265 (two peaks), 3192 and 1593 cm^{-1}, attributed to the symmetric and asymmetric stretching of NH_2, ν(NH) and ν(C=N), respectively. Additionally, no

band due to an SH group was observed between 2600 and 2500 cm^{-1}, which is in agreement with the deprotonated thiolate form of the ligand in the complexes.[31] The strong absorption bands near 3480 and 3440 cm^{-1} in the IR spectra of both the ligand and the complexes were due to N–H stretching vibrations. The intense band at 1680 may be assigned to C=N stretching vibration in the free ligand. It showed a positive shift towards higher frequencies in the spectra of the metal complexes (an additional band was observed near 1700 cm^{-1}). The shifting of the band towards higher frequency region indicates an increase in bond order of the coordinated C=N group due to back donation of π-electrons by the metals. The spectrum of the ligand shows bands at 1358 and 1465 cm^{-1}, which were assigned to C=S and N–C–N stretching, respectively. These bands were shifted to higher values in the complexes, indicates coordination of a thiosemicarbazone to the metal centre. These bands were absent in the spectra of the complexes due to likely changes of C=S to C–S and N–C–N to N–C=N on complexation. It is evident that ligand acts as a binucleating chelating agent coordinating through the thiol sulphur and nitrogen of the (C=N) group of the Schiff base. The complexes also display bands due to coordinated water molecules. The bands in the ranges 749–849 cm^{-1} and 609–633 cm^{-1} appeared in the spectra of the complexes, which may be assigned to $\rho r(H_2O)$ and $\rho w(H_2O)$.[33]

TABLE II. Physical, UV/Vis and molar conductance data for the compounds

Cmpd.	Yield, %	Colour	M.p., °C	UV/Vis (DMF), λ / nm	Λ / S cm^2 mol^{-1}
1	92	Yellow	153–156	–	–
2	66	Dark blue	>280	224, 265, 363, 413	19
3	58	Brown	>280	242, 265, 366, 383	21
4	68	Green	>280	265, 366, 383	24
5	65	Black	>280	265, 383, 365	21
6	54	Yellow	>280	265, 382, 365	17

Electronic spectra

With aim to obtain information about the type of the electronic transition and interaction liable to exist in solutions, the electronic spectra of ligand and their complexes were measured in DMF solvent. The recorded spectra of ligand displayed two main absorption bands. The first band was observed in the 260−265 nm range as a broad and/or a shoulder band. This band could be ascribed to π–π* transitions of the benzenoid system of the compounds strongly overlapped with n–π* electronic transitions involving the nonbonding electrons of the azomethine nitrogen atom. The longer wavelength band(s) in the recorded spectra of the ligands observed in the range 316–355 nm can be ascribed to the transition within the whole molecule, essentially as intramolecular charge transfer (CT) interactions. The CT bands seem to originate from the aryl moiety, whereas the positive charged azomethine carbon atom was the acceptor centre. This behaviour sug-

gests an instantaneous complex formation in solution from the reaction of the ligand with each of the employed metal ions. Bands due to the n–π* transition of the C=N chromophores occurred between 260−265 nm as the ligand shifts to lower energy upon complexation.[33] In the ultraviolet region, the bands observed in the range 267–299 nm in spectra of metal complexes can be ascribed to an intraligand electronic transition, because bands in these regions were sensitive enough to the type of metal ion used.

The longer wavelength band(s) of the free ligand at 363–366 nm acquired a red shift on complex formation with a metal ion. A new band was observed at longer wavelengths (in the range of 382–413 nm) in case of the complex solutions. This behaviour can be explained as follows. The longer wavelength band observed in the spectrum of the free ligands can be assigned to an intramolecular CT transition liable to take place within the solute molecule. Thus the red shift observed in the λ_{max} of this band on complex formation with the divalent transition metal ions Mn(II), Co(II), Cu(II) and Zn(II) can be interpreted based on the principle of an expected easier CT transition within the complexed Schiff bases rather than within the free ligand. This is due to the positive charge of the coordinating metal ions. On the other hand, these bands strongly overlap with an intermolecular transition from the ligand molecule to the vacant orbitals localized on the coordinated metal ions, *i.e.*, LMCT.

Thermogravimetric analysis

Thermogravimetric (TG) and differential thermal (DTA) analyses were employed to describe the thermal behaviour of the prepared complexes **2**–**6.** The TG curve of complex **2** showed three mass loss steps. The first mass loss step occurred in the temperature range 160–300 °C, the second one in the temperature range 300–620 °C and the third step between 620–770 °C. The DTA curve showed two exothermic peaks, one at 290 °C and the other at 620 °C. The TG curve of complex **3** showed four mass loss steps. The first step occurred in the temperature range between 260–300 °C. In this temperature range, one small endo effect was observed at 280 °C. The second mass loss step occurred in the temperature range 300–580 °C. In this temperature range, two exothermic peaks were observed at 370 and 520 °C. The third mass loss step occurred in the temperature range 580––750 °C. The fourth decomposition step occurred between 750–880 °C. This range was accompanied by one small endo effect at 870 °C. The TG and DTA study for complex **4** presented two regions of decomposition. In the TG study, the first mass loss step occurred in the temperature range between 260 and 320 °C. In this temp range (260–320 °C), one endothermic peak at 270 °C was observed. The second mass loss step occurred in the temperature range 320–710 °C. In this temperature range, two exothermic peaks were observed, one at 360 °C and the other at 700 °C. The TG and DTA study for complex **5** showed a two-

-step decomposition. The first mass loss step occurred in the temperature range 270–530 °C, while the second decomposition step occurred between 530–650 °C. In the temperature range of the first stage of mass loss, one small endo and one small exo effect can be seen on the DTA curve at 280 and 370 °C, respectively. The second mass loss step was accompanied by two exo effects with maxima at 530 and 630 °C, respectively.

The thermal behaviour of these complexes showed that the hydrated complexes lost water molecules of hydration in the first step followed immediately by decomposition of the anions and ligand molecules in the subsequent steps. The final decomposition steps of the complexes are attributed to complete decomposition of the complexes leaving M residues (M = Cu, Co, Ni, Zn and U).

Antioxidant activities of the ligand and complexes

The antioxidant activities of terepthaladehyde bis(thiosemicarabzone) (**1**) and its metal complexes **2**–**6** were evaluated by several *in vitro* methods in order to compare the results and to establish some structure–antioxidant–activity relationships for each method. The evaluation study was performed at various concentrations and comparative studies were realised with standard antioxidants.

DPPH radical scavenging activity. The percentage activity of DMF solutions of compounds **1**–**6** were examined and compared. The activities of the complexes as a function of concentration are shown in Fig. 1. All the complexes **2**–**5**

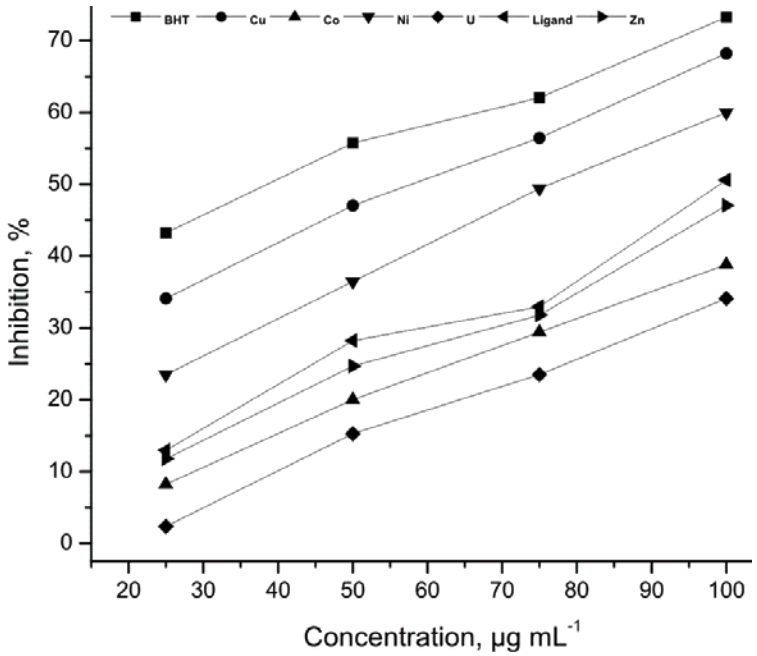


Fig. 1. Scavenging activity of compounds **1**–**6** for DPPH.

showed comparable or slightly lower activity than the standard, butylated hydroxytoluene (BHT). The copper complex **2**, containing an electron donating group showed the dominate DPPH scavenging activity. Nickel complex **3** exhibited slightly lower activity than that of compound **2**. At low concentrations, compound **6** showed negligible DPPH activity The IC_{50} values for all the compounds were calculated.

Reducing power. The reducing power of compounds **2**–**6** as a function of their concentration are shown in Fig. 2. The reducing power of the standard BHT at various concentrations showed a higher absorbance value to those of the newly synthesized compounds. The reducing power of newly synthesized compound solutions in DMF increased with increasing concentration. All the analogues **2**–**6** showed high absorbance values which were comparable or slightly lower than those of the standards. The presence of the lone pair electron in complex **2** resulted in a higher reducing power. The absorbance values for compound **6** were very low, showing the low reducing power of this complex, while compounds **2**–**5** showed higher values indicating their higher reducing power but lower than that of the standards.

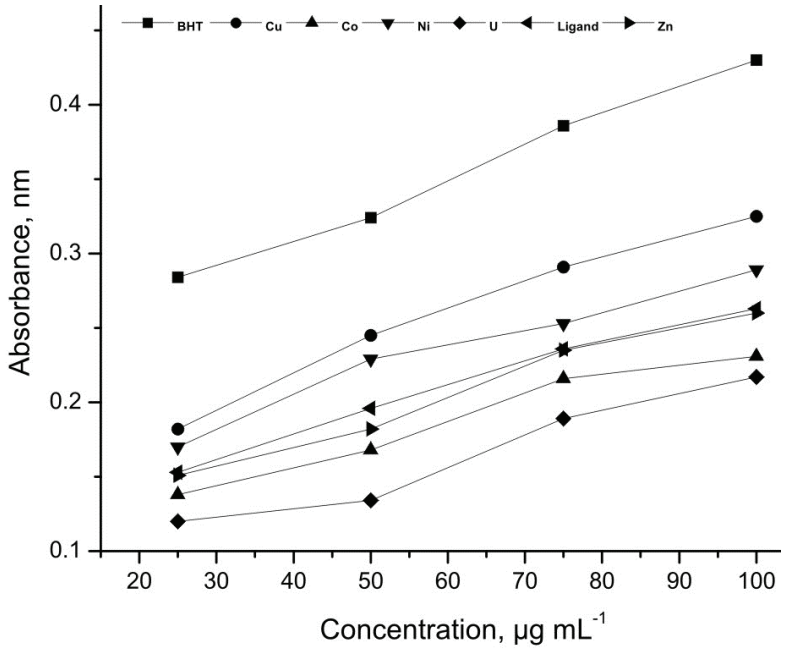


Fig. 2. Reducing power scavenging activity of compounds **1**–**6**.

H_2O_2 scavenging activity. The data of the suppression ratio for $OH^{\bullet}$ are shown in Fig. 3. The inhibitory effect of the compounds tested on $OH^{\bullet}$ were concentrate dependent and the suppression ratio increased with increasing sample

concentrations in the range tested. The average suppression ratio of the uranium complex (IC_{50} = 144.09 μM) for $OH^{\bullet}$ was the lowest of all the compounds. The copper(II) complex (IC_{50} = 66.72 μM) was the most effective among all the tested complexes. The order of the suppression ratio of the tested compounds for $OH^{\bullet}$ was **2** > **4** > **1** > **5** > **3** > **6**.

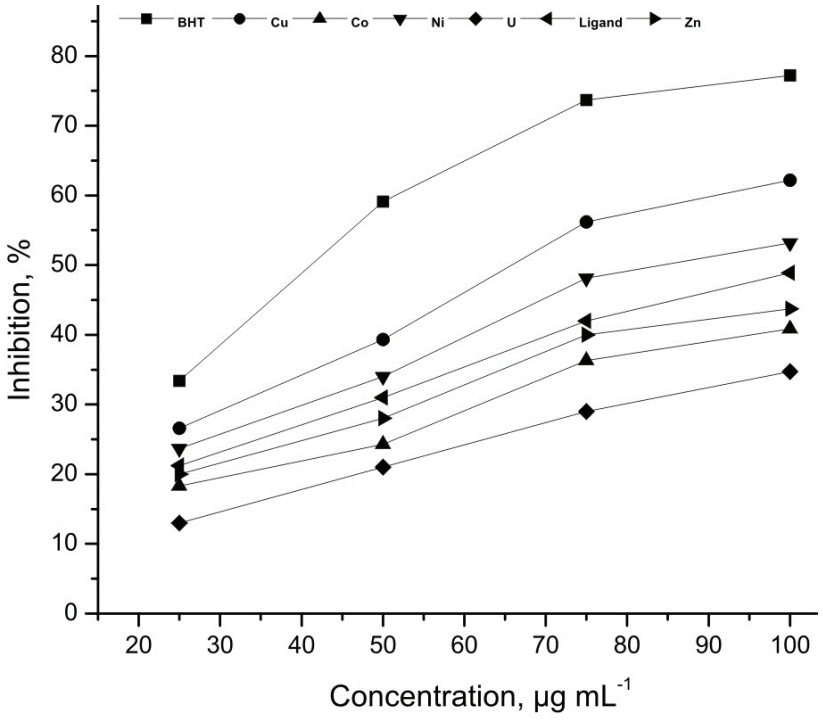


Fig. 3. Scavenging activity of compounds **1**–**6** for H_2O_2.

Nitric oxide (NO) scavenging activity. Nitric oxide undergoes a facile radical–radical reaction with $O_2^{\bullet-}$ to yield $ONOO^-$, a reaction that is three times faster than the SOD-catalyzed dismutation of $O_2^{\bullet-}$. This diversion of $O_2^{\bullet-}$ through $ONOO^-$ oxidation and decomposition pathways would also limit H_2O_2 accumulation and subsequent reactions of H_2O_2 by decreasing the amount of $O_2^{\bullet-}$ available for spontaneous or SOD-catalyzed dismutation. It was find that the inhibitory effects of the compounds tested on $NO^{\bullet}$ were concentration dependent and the suppression ratio increased with increasing sample concentrations in the range tested (Fig. 4). The average suppression ratio of the uranium complex (IC_{50} = 233.64 μM) for $NO^{\bullet}$ was the lowest of all the tested compounds. The copper(II) complex (IC_{50} = 134.87 μM) was the most effective among all the complexes. The order of the suppression ratio of the tested compounds for $NO^{\bullet}$ is **2** > **4** > **1** >**5** > **3** > **6**.

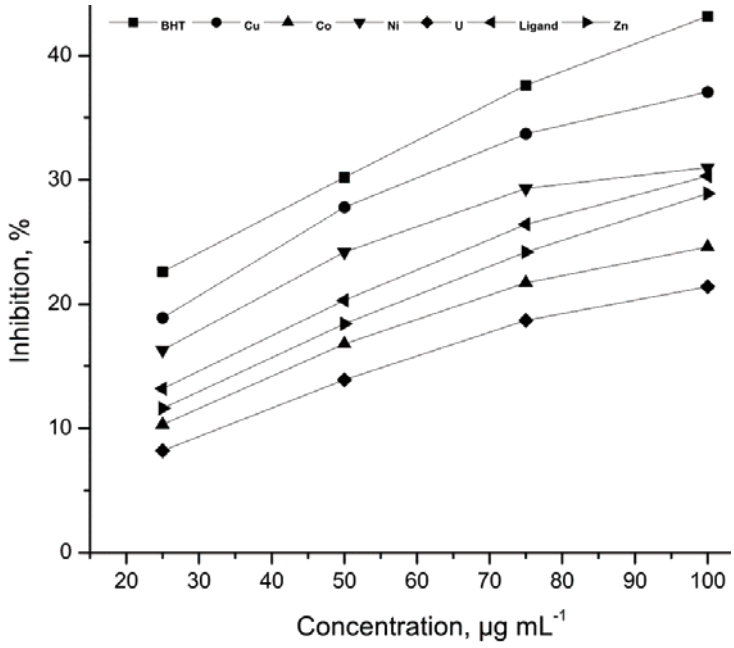
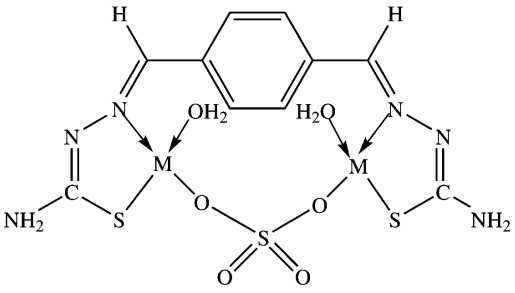


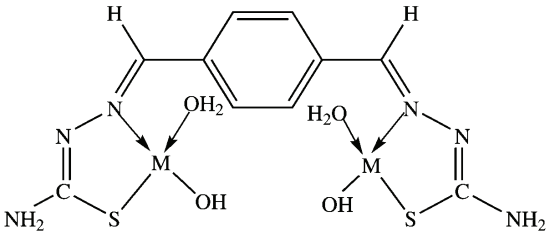
Fig. 4. Scavenging activity of compounds **1**–**6** for NO.

CONCLUSIONS

Based on the above results, the structures of metal complexes shown in Fig. 5 are proposed. The antioxidant properties of the ligand and complexes obtained were evaluated by several methods. Compounds **2**–**5** had enhanced antioxidant activities, which were comparable but slightly lower than that of the standard. The copper complex **2** revealed high DPPH scavenging, reducing power, H_2O_2 inhibition and nitrous oxide inhibition values. As a result, this study provides evidence that the chelation of different copper complexes with terepthaladehyde bis-(thiosemicarbazone) had significant influence on the antioxidant activities in different *in vitro* model systems.



Where M=Cu(II) and Zn(II)



Where M=Co(II) and Ni(II)

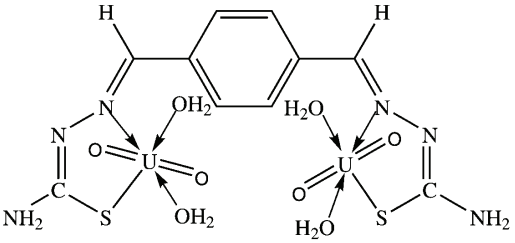


Fig. 5. The proposed structure of metal complexes with H_2L ligand.

ИЗВОД

СИНТЕЗА, КАРАКТЕРИЗАЦИЈА КОМПЛЕКСА МЕТАЛА СА ТИОСЕМИКАРБАЗОНСКИМ ЛИГАНДИМА И ЊИХОВА АНТИОКСИДАТИВНА АКТИВНОСТ У РАЗЛИЧИТИМ *IN VITRO* УСЛОВИМА

DESIREDDY HARIKISHORE KUMAR REDDY[1], SEUNG-MOK LEE[1], KALLURU SESHAIAH[2] и K. RAMESH BABU[3]

[1]Department of Environmental Engineering, Kwandong University, Gangneung, Republic of Korea, [2]Inorganic and analytical Chemistry Division, Department of Chemistry, Sri Venkateswara University, Tirupati – 517 502, India и [3]Department of Biochemistry, Sri Venkateswara University, Tirupati – 517 502, India

Полазећи од терефталалдехидbis(тиосемикарбазона) синтетисани су динуклеарни Cu(II), Co(II), Ni(II), Zn(II) и U(VI) комплекси опште формуле $[H_2LM(X_2)(H_2O)_2]$ (где је H_2L двоструко депротоновани лиганд и X је хлорид/сулфат). Лиганд (H_2L) и одговарајући комплекси су окарактерисани, поред термалне анализе и методе мерења проводљивости, применом ^{1}H-NMR, FT-IR и UV–Vis спектроскопских метода. Термална анализа ових комплекса је показала да, у првој фази, хидратисани комплекси губе молекуле воде, док у наредној фази долази до разлагања хлоридног и сулфатног анјона, као и молекула лиганда. На основу мерења моларне проводљивости у DMF растварачу закључено је да су испитивани комплекси неелектролити. Поред тога, одређена је *in vitro* антиоксидативна активност лиганда и одговарајућих комплекса.

(Примљено 30. априла, ревидирано 3. јула 2012)

REFERENCES

1. N. A. Mangalam, M. R. P. Kurup, *Spectrochem. Acta* **71** (2009) 2040
2. M. C. Rodríguez-Argüelles, E. C. López-Silva, J. Sanmartín, P. Pelagatti, F. Zani, *J. Inorg. Biochem.* **99** (2005) 2231

3. T. S. Lobana, R. Sharma, G. Bawa, S. Khanna, *Coord. Chem. Rev.* **253** (2009) 977
4. D. H. K. Reddy, K. Seshaiah, A. V. R. Reddy, *Orient. J. Chem.* **27** (2011) 1125
5. H. Beraldo, D. Gambino, *Mini Rev. Med. Chem.* **4** (2004) 159
6. A. G. Quiroga, C. N. Ranninger, *Coord. Chem. Rev.* **248** (2004) 119
7. K. C. Agrawal, A. C. Sartorelli, Prog. *Med. Chem.* **15** (1978) 321
8. M. C. Miller, C. N. Stineman, J. R. Vance, D. X. West, H. Hall, *Anticancer Res.* **18** (1998) 4131
9. S. Chandra, S. Raizada, T. Monika, K. S. Praveen, *Spectrochem. Acta* **69** (2008) 816
10. A. Saeed, A. A. Isab, S. Ali, A. R. Al-Arfaj, *Polyhedron* **25** (2006) 1633
11. R. J. Mauthe, E. Sideras-Haddad, K. W. Turteltaub, G. Bench, *J. Pharm. Biomed. Anal.* **17** (1998) 651
12. M. Navarro, G. Chiara, L. Messori, D. Gambino, *Drug Discov. Today* **15** (2010) 23
13. M. Valko, D. Leibfritz, J. Moncol, M. Cronin, M. Mazur, J. Telser, *Int. J. Biochem. Cell Biol.* **39** (2007) 44
14. N. Yusaku, S. Kunihiko, S. Katsumi, T. Daisuke, T. Teruhisa, N. Yoshimichi, *Biol. Chem.* **387** (2006) 373
15. S. Stohs, D. Bagchi, *Free Radical Bio. Med.* **18** (1995) 321
16. V. Marian, I. Mario, M. Milan, R. J. Christopher, T. Joshua, *Mol. Cell. Biochem.* **266** (2004) 37
17. H. Sies, *Exp. Physiol.* **82** (1997) 291
18. Y. Byun, D. Darby, K. Cooksey, P. Dawson, S. Whiteside, *Food Chem.* **124** (2011) 615
19. R. M. Wang, J. J. Mao, J. F. Song, C. X. Huo, Y. F. He, *Chin. Chem. Lett.* **18** (2007) 1416
20. D. S. Raja, N. S. P. Bhuvanesh, K. Natarajan, *Eur. J. Med. Chem.* **46** (2011) 4584
21. P. Mariana, D. Bruno, T. Jeanette, B. Lucia, G. Mercedes, C. Hugo, O. A. Claudio, N. Ester, G. Dinorah, O. Lucia, *Eur. J. Med. Chem.* **44** (2009) 4937
22. S. Minghao, W. Di, W. Jingyuan, L. Yaoxian. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **44** (2003) 751
23. M. M. Marcu, M. Dima, *Rev. Roum. Chim.* **12** (1967) 1353.
24. M. Burits, F. Bucar, *Phytother. Res.* **14** (2000) 323
25. R. J. Ruch, S. J. Cheng, J. E. Klaunig, *Carcinogenesis* **10** (1989) 1003
26. L. C. Green, D. A. Wagner, J. Glogowski, P. L. Skipper, J. S. Wishnok, S. R. Tannenbaum, *Anal. Biochem.* **126** (1982) 131
27. L. Marcocci, J. J. Maguire, M. T. Droy-Lefaix, L. Packer. *Biochem. Biophys. Res. Commun.* **201** (1994) 748
28. M. Oyaizu, *Jpn. J. Nutr.* **44** (1986) 307
29. T. S. Lobana, S. Khanna, R. J. Butcher, A. D. Hunter, M. Zeller, *Polyhedron* **25** (2006) 2755
30. G. G. Mohamed, N. A. Ibrahim, H. A. E. Attia, *Spectrochim. Acta* **72** (2009) 610
31. E. Manoj, M. R. P. Kurup, *Polyhedron* **27** (2008) 275
32. S. Chandra, J. Deeepali, K. S. Amit, *Spectrochem. Acta* **71** (2009) 1712
33. S. Rajeev, N. K. Kaushik, *Spectrochim. Acta* **72** (2009) 691.