

## Synthesis, Structural, and Antibacterial Studies of Some Mixed Ligand Complexes of Zn(II), Cd(II), and Hg(II) Derived From Citral Thiosemicarbazone and N-Phthaloyl Amino Acids

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*A series of new mixed ligand complexes of Zn(II), Cd(II), and Hg(II) with cis-3,7-dimethyl-2,6-octadienthiosemicarbazone (CDOTSC; LH) and N-phthaloyl amino acids (AH) have been synthesized by the reaction of metal dichloride with ligands CDOTSC and N-phthaloyl derivative of DL-glycine (A<sub>1</sub>H), L-alanine (A<sub>2</sub>H), or L-valine (A<sub>3</sub>H) in a 1:1:1 molar ratio in dry refluxing ethanol. All the isolated complexes have the general composition [M(L)(A)]. The plausible structure of these newly synthesized complexes has been proposed on the basis of elemental analyses, molar conductances, molecular weight measurement, and various spectral (IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR) studies, and four coordinated geometries have been assigned to these complexes. All the complexes and ligands have been screened for their antibacterial activity.*

**Keywords** Mixed ligand complexes; thiosemicarbazone; N-phthaloyl amino acids; antibacterial activity

### INTRODUCTION

During the last few decades, there are numerous reports on transition metal complexes derived from various ligands, such as amino acids,<sup>1,2</sup> Schiff bases of amino acids,<sup>3,4</sup> N-protected amino acids,<sup>5</sup> semicarbazone, thiosemicarbazone,<sup>6–14</sup> and oximes.<sup>15–19</sup> N-protected amino acids and thiosemicarbazones are potential ligands that have aroused

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much interest because of their interesting bonding pattern and potential biological applications of their metal complexes. The triorganotin (IV) compounds of N-protected amino acids exhibit some insecticidal effects on Bean Weevils (*Sitophilus graneria*) and also show fungicidal activity on *Aspergillus niger* and *Helminthosponum taulosum*.<sup>20</sup> The study of semi- and thiosemicarbazone compounds has received great impetus in recent years due perhaps to their remarkable activity against bacteria<sup>21</sup> and fungi;<sup>22</sup> these compounds also have been shown to possess antitubercular,<sup>23</sup> antimalarial,<sup>24</sup> and antitumor<sup>25</sup> activities. The biological activities of thiosemicarbazone ligands have been attributed to their trace metal complexing abilities, and the metal compounds have been generally found to possess enhanced therapeutic properties.<sup>26</sup> Recently, a publication reported on the synthesis and characterization of mixed ligand complexes of titanocene dichloride derived from heterocyclic  $\beta$ -diketonates and N-protected amino acids.<sup>27</sup> However, there are no literature reports on the synthesis of mixed ligand complexes derived from thiosemicarbazone of citral and N-phthaloyl amino acids. As an extension of work described in our previous communications,<sup>28,29</sup> in the present communication we report the synthesis, structural, and antibacterial studies of some mixed ligand complexes of transition metals derived from these potential organic ligands.

## EXPERIMENTAL

All reactants and solvents were of analytical grade. The tri-ethylamine was distilled over KOH pellets. Solvents were purified by the literature method.<sup>30</sup> Metal contents of complexes were measured by complexometric titration with EDTA.<sup>31</sup> Sulfur was estimated gravimetrically as BaSO<sub>4</sub>. The ligands *cis*-3,7-dimethyl-2,6-octadienthiosemicarbazone (CDOTSC)<sup>28</sup> and N-phthaloyl derivative of amino acids<sup>32</sup> used were synthesized by a reported method. Elemental analyses were performed at the Regional Sophisticated Instrumentation Centre, Central Drug Research Institute, Lucknow. Molar conductances were measured in 10<sup>-4</sup> M DMF solution on a  $\mu$ p-based conductivity meter model 1601/E. Melting points were determined in sealed capillaries. IR absorption spectra were recorded in the 4000–200 cm<sup>-1</sup> region (KBr disc) on a Shimadzu FT-IR 8400/8900 spectrometer, and <sup>1</sup>H NMR spectra were recorded on a Jeol 300 MHz FT-NMR system. Chemical shift are reported in  $\delta$  (ppm) versus SiMe<sub>4</sub> with CDCl<sub>3</sub> and DMSO-d<sub>6</sub> solvents proton residuals as the internal standard. Molecular weights of these complexes were determined by the cryoscopic method using Backmann's thermometer and were found to be in agreement with calculated value (Table I).

**TABLE I Analytical Data for CDOTSC (LH) and N-Phthaloyl Amino Acids (AH) and Their Metal Complexes**

Compound	Empirical formula	Yield (%)	M.P. (°C)	Analysis found (Calcd.) %				Molar Cond. <sup>a</sup> ( $\Omega^{-1}\text{cm}^2\text{mole}^{-1}$ )	Mol. Wt. found (Calcd.)
				C	H	N	S		
LH	$\text{C}_{11}\text{H}_{19}\text{N}_3\text{S}$	82	92	58.65 (58.62)	8.53 (8.49)	18.61 (18.64)	14.20 (14.23)	—	232 (225)
A <sub>1</sub> H	$\text{C}_{10}\text{H}_7\text{NO}_4$	85	192	58.61 (58.55)	3.46 (3.44)	6.80 (6.83)	—	—	201 (205)
A <sub>2</sub> H	$\text{C}_{11}\text{H}_9\text{NO}_4$	79	151	60.30 (60.28)	4.17 (4.14)	6.34 (6.39)	—	—	224 (219)
A <sub>3</sub> H	$\text{C}_{13}\text{H}_{13}\text{NO}_4$	73	102	63.21 (63.16)	5.29 (5.30)	5.60 (5.66)	—	—	250 (247)
[Zn(L)(A <sub>1</sub> )]	[Zn(C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>4</sub> S)]	72	280 <sup>b</sup>	51.12 (51.07)	4.95 (4.89)	11.23 (11.34)	6.37 (6.49)	13.31 (13.24)	486 (494)
[Cd(L)(A <sub>1</sub> )]	[Cd(C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>4</sub> S)]	67	298	46.58 (46.63)	4.53 (4.47)	10.32 (10.36)	5.85 (5.92)	20.81 (20.78)	535 (541)
[Hg(L)(A <sub>1</sub> )]	[Hg(C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>4</sub> S)]	70	278 <sup>b</sup>	40.13 (40.09)	3.89 (3.84)	8.82 (8.90)	5.02 (5.09)	31.73 (31.88)	633 (629)
[Zn(L)(A <sub>2</sub> )]	[Zn(C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>4</sub> S)]	68	301	52.11 (52.02)	5.11 (5.16)	11.08 (11.03)	6.28 (6.31)	12.80 (12.87)	502 (508)
[Cd(L)(A <sub>2</sub> )]	[Cd(C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>4</sub> S)]	71	299 <sup>b</sup>	47.56 (47.62)	4.78 (4.72)	10.12 (10.09)	5.81 (5.77)	20.30 (20.26)	548 (555)
[Hg(L)(A <sub>2</sub> )]	[Hg(C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>4</sub> S)]	76	305	41.05 (41.09)	4.12 (4.07)	8.73 (8.71)	5.02 (4.98)	31.15 (31.19)	650 (643)
[Zn(L)(A <sub>3</sub> )]	[Zn(C <sub>24</sub> H <sub>30</sub> N <sub>4</sub> O <sub>4</sub> S)]	65	308 <sup>b</sup>	53.81 (53.78)	5.58 (5.64)	10.48 (10.45)	5.92 (5.98)	12.25 (12.20)	532 (536)
[Cd(L)(A <sub>3</sub> )]	[Cd(C <sub>24</sub> H <sub>30</sub> N <sub>4</sub> O <sub>4</sub> S)]	70	302	49.48 (49.45)	5.13 (5.19)	9.65 (9.61)	5.51 (5.49)	19.20 (19.28)	578 (583)
[Hg(L)(A <sub>3</sub> )]	[Hg(C <sub>24</sub> H <sub>30</sub> N <sub>4</sub> O <sub>4</sub> S)]	73	318 <sup>b</sup>	42.98 (42.95)	4.47 (4.50)	8.38 (8.35)	4.70 (4.78)	29.92 (29.89)	667 (671)

<sup>a</sup>Molar conductance determined at 298 K in  $10^{-4}$  M DMF solution.

<sup>b</sup>Dec.

## Synthesis of CDOTSC (LH)

The ligand CDOTSC was prepared from 3,7-dimethyl-2,6-octadienal (citral) and thiosemicarbazide (1:1 molar ratio) in absolute EtOH in the presence of glacial AcOH. The mixture was refluxed for 1 h, cooled, filtered the mixture and the obtained yellow solid was recrystallized from EtOH (50%), and dried under reduced pressure.

## The Synthesis of N-Phthaloyl Amino Acids (AH)

A intimate mixture of 0.06 mole of finely ground phthalic anhydride and 0.06 mole of respective amino acids (viz., DL-glycine or L-alanine or L-valine) was heated for 30 min with stirring in an oil bath at 140–160°C. After cooling, the solid material was dissolved in 40 mL of hot MeOH; the filtered solution was diluted with H<sub>2</sub>O (40 mL), and the product was allowed to crystallize slowly. It yielded colorless needle-shape crystals of N-phthaloyl amino acid.

## The Synthesis of Complexes

A weighted amount of *cis*-3,7-dimethyl-2,6-octadienthiosemicarbazone (1.1268 g, 5 mmol) was mixed with the corresponding metal dichloride (5 mmol) solution in anhydrous EtOH (60 mL) followed by the addition of a corresponding N-phthaloyl derivative of glycine, alanine, or valine (5 mmol). After shaking the reaction mixture, triethylamine (1.0119 g, 10 mmol) was added dropwise with constant stirring. After refluxing this reaction mixture for ~9 h, the resulting solid was filtered off, washed with anhydrous Et<sub>2</sub>O to apparent dryness, and dried under reduced pressure. All the complexes were synthesized by the same method.

## RESULTS AND DISCUSSION

A systematic study of the reactions of metal dichlorides with ligands CDOTSC (LH) and a N-phthaloyl derivative of DL-glycine (A<sub>1</sub>H), L-alanine (A<sub>2</sub>H), or L-valine (A<sub>3</sub>H) (1:1:1) molar ratio in anhydrous EtOH in the presence of Et<sub>3</sub>N have been carried out. The reactions can be represented by Equation (1).



where M = Zn<sup>+2</sup>, Cd<sup>+2</sup>, and Hg<sup>+2</sup>; LH = CDOTSC



The analytical data of the complexes together with their molar conductances are given in Table I. The data are consistent with the proposed formulas for the complexes. All the complexes are insoluble in water and slightly soluble in common organic solvents but are readily soluble in DMSO and DMF. The molecular-weights measurement data of these complexes show their monomeric nature. The molar conductance data suggests the non-electrolytic nature of complexes. All the complexes are stable at r.t. and decompose on heating at  $\sim 300^\circ\text{C}$ .

### Infrared Spectra

The IR spectrum of the ligand CDOTSC shows bands in the region  $3475\text{--}3283\text{ cm}^{-1}$  due to stretching frequencies for  $\text{NH}_2$ , while the absorption for NH is present at  $3154\text{ cm}^{-1}$ . An absorption band for CN appears at  $1622\text{ cm}^{-1}$ . No band due to the SH group is observed between  $2600$  and  $2500\text{ cm}^{-1}$  in agreement with the thione form of the ligand and with the presence of a band at  $836\text{ cm}^{-1}$  for CS.

In the IR spectra of N-phthaloyl amino acids, the carboxylic OH (except for N-phthaloyl glycine) is observed at  $\sim 3400\text{ cm}^{-1}$  as a broad band while a  $\nu(\text{OH})$  deformation appeared as a sharp band at  $\sim 900\text{ cm}^{-1}$ . The band observed at  $\sim 1750\text{ cm}^{-1}$  may be assigned to a  $\nu\text{CO}_{(\text{asym})}$  (imido) vibration, and the band observed at  $\sim 1700\text{ cm}^{-1}$  is due to the mixing of  $\nu\text{CO}_{(\text{sym})}$  (imido) and  $\nu\text{COO}_{(\text{asym})}$  vibrations. The  $\nu\text{COO}_{(\text{sym})}$  band observed at  $\sim 1400\text{ cm}^{-1}$  is a weak band. The value of  $\Delta\nu = \nu\text{COO}_{(\text{asym})} - \nu\text{COO}_{(\text{sym})}$  has been found to be in the range  $300\text{--}320\text{ cm}^{-1}$  for these ligands.

A study and comparison of infrared spectra of thiosemicarbazone (CDOTSC), N-phthaloyl amino acids, and their mixed ligand complexes (Table II) imply that both ligands behave as a monobasic bidentate ligand. The  $\nu(\text{C}=\text{N})$  shift of the CDOTSC from  $1622\text{ cm}^{-1}$  to a lower frequency in the spectra of the metal complexes indicated a coordination of the azomethine nitrogen atom.<sup>33</sup> The appearance of a new band in the  $408\text{--}467\text{ cm}^{-1}$  region are assigned to  $\nu(\text{M-N})$  and support the coordination of a nitrogen of the azomethine group.<sup>34</sup> The band having considerable  $\nu(\text{C}=\text{S})$  character, a shift from  $836\text{ cm}^{-1}$  in the uncomplexed CDOTSC to  $725\text{--}768\text{ cm}^{-1}$  from spectra of the complexes, indicates coordination of a thione/thiolato sulfur atom.<sup>35</sup> The  $\nu(\text{M-S})$  bands have been assigned in the  $352\text{--}385\text{ cm}^{-1}$  range and support the coordination of the thione/thiolato sulfur atom<sup>36</sup> on a loss of the N(3) hydrogen from the thiosemicarbazone moiety in the complex; an additional carbon-nitrogen double bond  $\text{N}(3) = \text{C}(2)$  is formed. This new  $\nu(\text{C}=\text{N})$  vibration band is observed in  $1565\text{--}1580\text{ cm}^{-1}$  region.<sup>34</sup>

**TABLE II Infrared Absorption Frequencies (cm<sup>-1</sup>) of CDOTSC and N-Phthaloyl Amino Acids and Their Mixed Ligand Complexes**

Compound	CDOTSC (LH)		C(O)C <sub>6</sub> H <sub>4</sub> C(O)NCHRCOOH (AH)				Nonligand band			
	$\nu(\text{NH}_2)$	$\nu(\text{NH})$	$\nu(\text{C}\equiv\text{N})$	$\nu(\text{CS})$	$\nu(\text{OH})$	$\nu(\text{CO})$	$\nu(\text{COO})$	$\nu(\text{M-N})$	$\nu(\text{M-S})$	$\nu(\text{M-O})$
LH	3475 as 3283 s	3154	1622	836	—	—	—	—	—	—
A <sub>1</sub> H	—	—	—	—	*	1750	1700 as 1410 s	—	—	—
A <sub>2</sub> H	—	—	—	—	3424	1744	1715 as 1395 s	—	—	—
A <sub>3</sub> H	—	—	—	—	3450	1748	1705 as 1390 s	—	—	—
[Zn(L)(A <sub>1</sub> )]	3460 as 3285 s	—	1603	740	—	1752 as 1710 s	1580 as 1415 s	434	352	402
[Cd(L)(A <sub>1</sub> )]	3442 as 3282 s	—	1588	743	—	1748 as 1705 s	1570 as 1425 s	456	365	410
[Hg(L)(A <sub>1</sub> )]	3454 as 3286 s	—	1595	768	—	1750 as 1715 s	1580 as 1405 s	440	370	408
[Zn(L)(A <sub>2</sub> )]	3458 as 3295 s	—	1579	757	—	1742 as 1703 s	1600 as 1425 s	464	348	415
[Cd(L)(A <sub>2</sub> )]	3457 as 3280 s	—	1585	735	—	1743 as 1708 s	1592 as 1418 s	425	360	407
[Hg(L)(A <sub>2</sub> )]	3480 as 3292 s	—	1599	741	—	1746 as 1705 s	1560 as 1420 s	447	375	398
[Zn(L)(A <sub>3</sub> )]	3463 as 3287 s	—	1602	732	—	1747 as 1706 s	1570 as 1428 s	408	385	405
[Cd(L)(A <sub>3</sub> )]	3473 as 3281 s	—	1607	745	—	1740 as 1710 s	1575 as 1438 s	467	381	418
[Hg(L)(A <sub>3</sub> )]	3465 as 3288 s	—	1596	725	—	1750 as 1707 s	1564 as 1417 s	449	377	423

as = asymmetric; s = symmetric; \*NH — stretching vibration occur at 3163 cm<sup>-1</sup>.

The broad band appearing around  $\sim 1700\text{ cm}^{-1}$  due to  $[\nu\text{CO}_{(\text{sym})} + \nu\text{COO}_{(\text{asym})}]$  in the spectra of the N-phthaloyl amino acids splits into two after complexation.<sup>37</sup> The sharp band at  $\sim 1700\text{ cm}^{-1}$  and a medium intensity band at  $1564\text{--}1600\text{ cm}^{-1}$  may be due to  $\nu\text{CO}_{(\text{sym})}$  and  $\nu\text{COO}_{(\text{asym})}$  vibrations, respectively. The lower shift of the order of  $137\text{--}175\text{ cm}^{-1}$  in the  $\nu\text{COO}_{(\text{asym})}$  frequency  $[\Delta\nu = \nu\text{COO}_{(\text{asym})} - \nu\text{COO}_{(\text{sym})}]$  upon complexation indicates a chelating nature of the carboxylate group of N-phthaloyl amino acids. The band appearing in the region  $393\text{--}423\text{ cm}^{-1}$  may be due to M-O vibrations.

### **<sup>1</sup>H NMR Spectra**

<sup>1</sup>H NMR spectra of the  $[\text{M}(\text{L})(\text{A})]$  type complexes have been recorded in  $\text{CDCl}_3$  and  $\text{DMSO-d}_6$  (Table III). <sup>1</sup>H NMR spectra display the expected signals of a different type of proton present in complexes, but a comparison of the spectra of ligand with those of the complexes can lead to the following results:

1. The free ligand CDOTSC exhibits a signal at  $\delta 9.45$  ppm due to the N(3) proton. The absence of this signal in spectra of the complexes suggests that the proton has been lost via thioenolization and coordination of the sulfur atom.
2. The aldehyde proton ( $\text{CH}=\text{N}$ ) shifts downfield from  $\delta 7.8$  ppm in the ligand CDOTSC to  $\delta 7.82\text{--}8.01$  ppm in the spectra of complexes, which is consistent with the formation of a coordination band between the azomethine nitrogen and metal ion.
3. The free N-phthaloyl glycine ( $\text{A}_1\text{H}$ ) exhibits a signal at  $\delta 4.5$  ppm due to NH. N-phthaloyl L-alanine ( $\text{A}_1\text{H}$ ) and N-phthaloyl L-valine ( $\text{A}_3\text{H}$ ) exhibit a singlet at  $\delta 9.26$  and  $8.97$  ppm, respectively, due to a carboxylate proton ( $\text{COOH}$ ). The absence of these signals in the spectra of complexes suggests the deprotonation of a  $\text{COOH}$  group of N-phthaloyl amino acids and the coordination of a  $\text{COO}$  group to metal.

### **<sup>13</sup>C NMR Spectra**

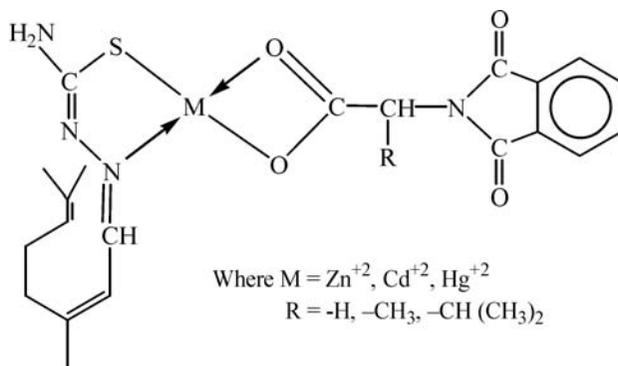
<sup>13</sup>C NMR spectra of ligands CDOTSC; N-phthaloyl glycine ( $\text{A}_1\text{H}$ ); and their Zn(II), Cd(II), and Hg(II) complexes were recorded in  $\text{CDCl}_3$  and  $\text{DMSO-d}_6$  (Table IV). The <sup>13</sup>C resonance signals are assigned according to the chemical shift theory. <sup>13</sup>C NMR spectra display the expected signals of a different type of a carbon present in complexes,

**TABLE III <sup>1</sup>H NMR Data of CDOTSC and N-Phthaloyl Amino Acids and Their Metal Complexes (in δ ppm)**

Compound	CDOTSC (LH)						C(O)C <sub>6</sub> H <sub>4</sub> C(O)NCHRCOOH (AH)					
	-NH <sub>2</sub>	-NH	-CH=N	=CH	-CH <sub>2</sub>	-CH <sub>3</sub>	-OH	C <sub>6</sub> H <sub>4</sub>	-CH	-CH <sub>2</sub>	-CH <sub>3</sub>	
LH	7.21 (s)	9.45 (s)	7.8 (s)	4.8 (t) 5.46 (d)	2.24 (m)	1.7 (s)						
A <sub>1</sub> H	—	—	—	—	—	—	*	7.65–8.03 (m)	—	4.49 (s)	—	
A <sub>2</sub> H	—	—	—	—	—	—	9.26 (s)	7.85 (m)	5.08 (q)	—	1.74 (d)	
A <sub>3</sub> H	—	—	—	—	—	—	8.97 (s)	7.80 (m)	4.60 (d)	—	1.12 (d)	
[Zn(L)(A <sub>1</sub> )]	7.23 (s)	—	**	4.76 (t) 5.42 (d)	2.23 (m)	1.71 (s) 1.92 (s)	—	7.60–7.98 (m)	—	4.45 (s)	—	
[Cd(L)(A <sub>1</sub> )]	7.26 (s)	—	**	4.78 (t) 5.48 (d)	2.21 (m)	1.7 (s) 1.90 (s)	—	7.69–8.01 (m)	—	4.47 (s)	—	
[Hg(L)(A <sub>1</sub> )]	7.28 (s)	—	**	4.79 (t) 5.40 (d)	2.20 (m)	1.73 (s) 1.95 (s)	—	7.72–7.96 (m)	—	4.46 (s)	—	
[Zn(L)(A <sub>2</sub> )]	7.25 (s)	—	7.95 (s)	4.8 (t) 5.39 (d)	2.24 (m)	1.68 (s) 1.93 (s)	—	7.82 (m)	5.01 (q)	—	1.67 (d)	
[Cd(L)(A <sub>2</sub> )]	7.24 (s)	—	7.99 (s)	4.81 (t) 5.42 (d)	2.22 (m)	1.69 (s) 1.90 (s)	—	7.80 (m)	4.97 (q)	—	1.71 (d)	
[Hg(L)(A <sub>2</sub> )]	7.21 (s)	—	7.97 (s)	4.79 (t) 5.40 (d)	2.26 (m)	1.71 (s) 1.93 (s)	—	7.78 (m)	4.9 (q)	—	1.69 (d)	
[Zn(L)(A <sub>3</sub> )]	7.30 (s)	—	8.01 (s)	4.82 (t) 5.46 (d)	2.24 (m)	1.67 (s) 1.95 (s)	—	7.69 (m)	4.58 (d)	—	1.09 (d)	
[Cd(L)(A <sub>3</sub> )]	7.28 (s)	—	7.99 (s)	4.83 (t) 5.42 (d)	2.23 (m)	1.65 (s) 1.88 (s)	—	7.75 (m)	2.7 (st)	—	0.95 (d)	
[Hg(L)(A <sub>3</sub> )]	7.23 (s)	—	7.82 (s)	4.82 (t) 5.41 (d)	2.24 (m)	1.72 (s) 1.9 (s)	—	7.71 (m)	2.68 (st)	—	0.90 (d)	
									4.67 (d)	—	1.1 (d)	
									2.7 (st)	—	0.95 (d)	

(s) = singlet, (d) = doublet, t = triplet, (q) quartet, (st) = septet, (m) = multiplet; \*NH<sup>+</sup> signal appeared at δ 4.5 ppm, \*\*merged with C<sub>6</sub>H<sub>4</sub> region.





**FIGURE 1** The proposed structure formula for the complexes.

but a comparison of the spectra of ligands with those of the complexes can lead to the following conclusions:

1. A considerable upfield shift takes place in the position of  $-\text{C}-\text{S}$  (177.2 ppm, CDOTSC), and  $\text{C}=\text{N}$  (151.2 ppm, CDOTSC), indicating coordination through the azomethine nitrogen and the thiol group and consistent with earlier reports.<sup>12,38</sup>
2. The  $^{13}\text{C}$  NMR spectra of some of these complexes show a downfield shift of  $\sim 4$  ppm in the position of carboxylic carbon signal as compared to its position in the parent N-phthaloyl glycine, revealing a bidentate nature of a COO group of a the ligand, which is consistent with the assignment reported previously.<sup>20,39</sup>

On the basis of the previously discussed spectral data, the four-coordinated geometry has been suggested for these complexes (Figure 1).

### Antibacterial Activity Test

Antibacterial activity of these compounds on selected bacteria *Staphylococcus aureus*, *Bacillus subtilis* Gram (+) and *Escherichia coli* Gram (–) were carried out using the filter paper scrap diffusion method using agar nutrient as the medium. Small (8-mm, diam.) circular scraps of filter paper were prepared for the purpose of making bacteriostatic slices. Ca. 2 mg of the compound (the ligands CDOTSC, N-phthaloyl amino acids, and their metal complexes) was dissolved in 10 cm<sup>3</sup> DMSO (1%) to make a concentration of 0.2 mg/cm<sup>3</sup>. The solution (0.1 cm<sup>3</sup>) was poured into a small bottle containing 12 paper slices; it was ensured that all the solution was bottled up. The bottle was covered with a gauze and sterilized by moist heat in an autoclave at 100°C using 15 lb/in<sup>2</sup> pressure

**TABLE V Antibacterial Activity Data of CDOTSC (LH) and N-Phthaloyl Amino Acids (AH) and Their Metal Complexes**

Compound	Average value of bacteriostatic diameter (mm) <sup>a</sup>		
	<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>
LH	13	16	14
A <sub>1</sub> H	14	13	12
A <sub>2</sub> H	12	14	15
A <sub>3</sub> H	15	13	13
[Zn(L)(A <sub>1</sub> )]	16	15	16
[Cd(L)(A <sub>1</sub> )]	18	17	15
[Zn(L)(A <sub>2</sub> )]	19	16	16
[Cd(L)(A <sub>2</sub> )]	18	17	17
[Zn(L)(A <sub>3</sub> )]	17	18	15
[Cd(L)(A <sub>3</sub> )]	18	19	17

<sup>a</sup>Average values from four experiments.

for 15 min. Bacterial strains were inoculated onto the medium plate with absorbent cotton, and three previously prepared bacteriostatic slices containing the compound were put on the medium plate. One sample was inoculated in parallel on four medium plates. All plates were incubated at 35°C for 24 h and then examined. The average value of bacteriostatic diameter was calculated in mm from four experiments for each compound and are given in Table V.

It is observed from these tests that metal chelates have a higher activity than the free ligands. Such increased activity of the metal chelates can be explained on the basis of Overtone's concept and Tweedy's chelation theory.<sup>40</sup> According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid-soluble material due to liposolubility, which is an important factor that controls antibacterial activity. On chelation, the polarity of the metal ion is reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with a donor group. Further, it increases the delocalization of  $\pi$ -electrons over the whole chelates ring and enhances the penetration of the complexes into lipid membranes and blocks metal binding sites on the enzymes of the microorganism.

## CONCLUSION

The type of mixed ligand complexes isolated during the present study demonstrate that the interaction of Zn<sup>+2</sup>, Cd<sup>+2</sup>, and Hg<sup>+2</sup> salts with Citral thiosemicarbazone and N-phthaloyl amino acids leads to complexes

with 1:1:1 stoichiometry and are found to be monomeric in nature. The bidentate nature of N-phthaloyl amino acids and thiosemicarbazone has been suggested on the basis of spectral evidences. The Zn(II) and Cd(II) complexes showed enhanced antibacterial activity than the parent ligands.

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