

Studies on Inclusion Complexes of β -Cyclodextrin with Some Metal Complexes of Isatinylsemicarbazone and Isatinylthiosemicarbazone

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The complexes of Co(II), Ni(II), Zn(II) and Cd(II) with isatinylsemicarbazone (IstscabH) and isatinylthiosemicarbazone (IsttscabH) of composition $ML_2 \cdot 2H_2O$ [M = Co(II) or Ni(II) and LH = IstscabH or IsttscabH] and ML_2 [M = Zn(II) or Cd(II) and LH = IstscabH or IsttscabH] have been synthesized and their antibacterial activity has been investigated. Their inclusion complexes with β -cyclodextrin (β -CD) having composition $[ML_2(\beta\text{-CD}) \cdot 2H_2O]$ or $M(C_{60}H_{88}N_8O_{39}S_2)$, [M = Co(II) or Ni(II) and LH = IstscabH or IsttscabH] and $[ML_2(\beta\text{-CD})$ or $M(C_{60}H_{84}N_6O_{37}S_2)]$, [M = Zn(II) or Cd(II) and LH = IstscabH or IsttscabH] have also been isolated in solid states. All the synthesized metal complexes have been characterized by analytical data, molar conductance, magnetic susceptibility, electronic and infrared spectral studies. The tetrahedral geometry for Zn(II) and Cd(II) and octahedral geometry for Co(II) and Ni(II) have been assigned on the basis of magnetic susceptibility, UV electronic transitions and IR spectral bands assignments. The structures are retained in inclusion products. A biological activity of Schiff bases, their metal complexes and inclusion products for bacteria *Escherichia. coli*, *Bacillus subtilis* and *Staphylococcus aureus* have been screened and activity explained.

Keywords: Isatinyl derivatives, Metal complexes, Inclusion, β -Cyclodextrin.

INTRODUCTION

A number of isatin derivatives have been reported to possess antibacterial [1], antiviral [2], antihelmintic [3], herbicidal [4], fungicidal [5] and antitubercostatic [6] properties. Isatin and indole derivatives derived from natural products are known to display immense medicinal activities [7,8]. The hydrazide and hydrazine derivatives of isatin and substituted isatin possess pronounced anticonvulsant activities [9-15]. A number of Schiff bases of isatin derivatives have also been used as neurotoxic agent [11]. The epilepsy is a well known neurological disorder characterized by unprovoked seizure of convulsion and thus efforts have directed for its drug development.

Isatin semicarbazones have also been used as an excellent anticonvulsant drug [12,13]. Compound 3-(3',4'-dihydro-2-methylmarcapto-4-oxoquinazoline-3'-yl)iminoisatin has been proved to be most active anticonvulsant molecule possessing neurotoxicity [14]. A number of new *N*-methyl/*N*-acetyl-5-substituted isatin-3-semicarbazones have been reported to

possess anticonvulsant activity by Pandeya and Raja [15]. Since last decades a number of isatin derivatives have been shown to possess potential hypnotic [16], antibacterial [17,18], monoamine oxidase (MAO) inhibitory [19] and antioxidant [20] properties. However much attention has been focused on the chemistry of isatin derivatives due to its biological potentiality like anticancer, anti-protozoa, cytotoxic, their presence in hippocampus cerebellum brain and DNA cleavage [10].

Isatin derivatives have been found in some mammalian tissues where their function is as modulator of biochemical processes [20]. Isatin has been reported as "tribulin" and identified as a selective inhibitor of monoamine oxidase (MAO) [19]. A new series of 5-hydroxyisatin derivatives has been synthesized by hydroxylation of aromatic ring in isatin and these has been shown to possess anti-anxiety effect [4]. These immense medicinal activities of isatin derivatives stimulated us to synthesize some transition metal complexes of Schiff bases of isatin and to further synthesized their inclusion complexes with β -cyclodextrin (β -CD). β -Cyclodextrin is an important oligosaccharide

and capable of providing energy to physiological system and bonding capability with DNA [21]. Thus, the inclusion products with transition metal complexes of indole derivatives can possess pharmacological activity and may serve some medicinal utility. Therefore, in the present paper, the synthesis and characterization of Zn(II), Ni(II), Co(II) and Cd(II) complexes of isatinylic semicarbazone (IstscabH) and isatinylic thiosemicarbazone (IsttscabH) are reported along with their inclusion complexes with β -cyclodextrin.

EXPERIMENTAL

The required chemical and solvents were obtained from E. Merck while β -cyclodextrin and isatin were procured from Sigma-Aldrich. The C, H, N, S analysis were obtained from IIT Patna, Patna, India using Vireo MICRO V-3 Elemental Analyzer. The IR spectra were recorded on Shimadzu IR spectrophotometer in KBr disc in the range of 4000 to 600 cm^{-1} . All UV visible spectra were recorded either in ethanol or DMF in the range of 200-800 nm using a Shimadzu Spectrophotometer No. 2000 at IIT Patna. Similarly, NMR spectra were recorded in DMSO- d_6 on Bruker 400 MHz NMR spectrophotometer.

Synthesis of Co(II), Ni(II), Zn(II) and Cd(II) complexes:

Exactly 0.01 mmol of each of the metal acetate was dissolved in aqueous ethanol (30 mL) and mixed with 0.02 mmol of ligand dissolved in hot ethanol. The resulting reaction mixtures were refluxed on a steam bath for 0.5 h when coloured product separated gradually. The contents were cooled and resulting metal complexes were collected by filtration. The metal complexes were washed with cold aqueous ethanol and dried over CaCl_2 in a desiccator. The yield of product was found in the range of 99-99.5%.

Synthesis of inclusion compound with β -cyclodextrin:

Exactly 0.01 mmol of each of the metal acetate and 0.015 mmol of β -cyclodextrin were dissolved in 50 mL hot aqueous

ethanol (1:1) and treated with 0.02 mmol of isatinylic semicarbazone (IstscabH) or isatinylic thiosemicarbazone (IsttscabH) in 100 mL hot 95% ethanol. The reaction mixture solutions were further heated on a steam bath for 1 h and left for 2 days in air. The inclusion products of the complexes of respective metals separated out slowly on evaporation. Then, the complexes were collected on a Buckner funnel and washed with cold aqueous ethanol. The yield of the complexes were found to be 80-85%. The inclusion complexes were dried in a desiccator and analyzed. The analytical results of the synthesized complexes are shown in Table-1.

Antibacterial activity: Antibacterial activity of isatin Schiff bases, IstscabH, IsttscabH and their Zn(II), Co(II) and Cd(II) complexes as well as their inclusion products complexes with β -cyclodextrin have been investigated by growth inhibition technique using petri disc method [22,23] for the bacteria viz. *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus* using streptomycin as standard. The requisite amount of metal complexes and their inclusion complexes were dissolved in DMF to get 100 $\mu\text{g mL}^{-1}$ solution. About 0.5 mL of investigated microorganism (containing 10^7 microorganism per mL) was added to a sterile nutrient agar medium just before solidification and then poured on sterile petri disc and allowed to solidify. Three holes were made in each disc using sterile cork borer (6 mm in diameter) and then 1 mL of tested complex of inclusion product dissolved in DMF was poured in these holes. Finally, the discs were incubated at 35 $^\circ\text{C}$ for 24 h and the zone of inhibition of growth were measured in mm against each bacteria. A blank containing DMF was measured and found that the inhibition was practically negligible.

RESULTS AND DISCUSSION

The reaction of ethanolic solutions of metal(II) acetate with IstscabH and IsttscabH ligands lead to formation of comp-

TABLE-1
ANALYTICAL RESULTS, ELECTRICAL CONDUCTANCE VALUES, MAGNETIC MOMENT AND MOLECULAR WEIGHT OF LIGANDS AND THEIR Ni(II), Co(II), Zn(II) AND Cd(II) COMPLEXES WITH ISATINYLIC SEMICARBAZONE AND ISATINYLIC THIOSEMICARBAZONE

Compound & Formula	Element analysis (%): Found (calcd.)					m.w. (g): Found (calcd.)	Electrical conductance ($\text{ohm}^{-1} \text{mol}^{-1} \text{cm}^2$)	μ_{eff} (BM) at 301 K
	C	H	N	S	M			
IstscabH ($\text{C}_9\text{H}_8\text{N}_4\text{O}_2$)	52.71 (52.93)	4.12 (3.95)	27.28 (27.44)	–	–	204.20	70	Dia
IsttscabH ($\text{C}_9\text{H}_8\text{N}_4\text{SO}$)	48.13 (49.06)	3.81 (3.66)	25.28 (25.44)	14.31 (14.55)	–	220.25	72	Dia
[Co(Istscab) $_2$] $\cdot 2\text{H}_2\text{O}$	43.43 (43.12)	3.72 (3.61)	22.10 (22.35)	–	11.76 (11.95)	485.2 (501.37)	12	5.06
[Ni(Istscab) $_2$] $\cdot 2\text{H}_2\text{O}$	43.12 (43.22)	3.88 (3.62)	22.37 (22.41)	–	11.41 (11.71)	481.2 (500.13)	11	3.24
[Zn(Istscab) $_2$]	45.61 (45.82)	2.97 (2.99)	23.47 (23.75)	–	13.61 (13.86)	465.2 (471.79)	13	Dia
[Cd(Istscab) $_2$]	41.39 (41.67)	3.14 (2.72)	21.46 (21.60)	–	21.13 (21.67)	475.2 (518.81)	12	Dia
[Co(Isttscab) $_2$] $\cdot 2\text{H}_2\text{O}$	40.31 (40.52)	4.23 (3.40)	21.71 (21.01)	11.87 (12.02)	10.80 (11.23)	538.13 (533.49)	15	5.11
[Ni(Isttscab) $_2$] $\cdot 2\text{H}_2\text{O}$	40.31 (40.62)	4.38 (3.40)	20.92 (21.06)	11.91 (12.05)	10.80 (10.03)	548.31 (532.25)	12	3.28
[Zn(Isttscab) $_2$]	43.31 (42.90)	3.81 (2.80)	22.12 (22.24)	12.37 (12.72)	12.61 (12.98)	523.11 (503.89)	14	Dia
[Cd(Isttscab) $_2$]	40.13 (39.24)	3.52 (2.56)	20.41 (20.34)	11.41 (11.64)	20.31 (20.40)	530.2 (550.91)	16	Dia

plexes of general formula $M(\text{Istscab})_2 \cdot n\text{H}_2\text{O}$ or $M(\text{Isttscab})_2 \cdot n\text{H}_2\text{O}$. The analytical data of the complexes are presented in Table-1. From the results of elemental analysis, it is found that metal complexes has composition $[M(\text{Istscab})_2] \cdot n\text{H}_2\text{O}$ [$M = \text{Zn(II)}$, Cd(II) , Co(II) and Ni(II)] where $n = 0$ for Zn(II) or Cd(II) and 2 for Co(II) or Ni(II) and $[M(\text{Isttscab})_2] \cdot n\text{H}_2\text{O}$ [$M = \text{Zn(II)}$, Cd(II) , Co(II) and Ni(II)] where $n = 0$ for Zn(II) or Cd(II) and 2 for Co(II) or Ni(II) . The inclusion complexes of the same ligands and metal acetates with β -cyclodextrin synthesized are shown in Table-2 along with their analytical data. The composition of inclusion product correspond to composition $[M(\text{Isttscab})_2/(\text{Istscab})_2(\beta\text{-CD})] \cdot n\text{H}_2\text{O}$, [$M = \text{Zn(II)}$, Cd(II) , Co(II) and Ni(II)] where $n = 0$ for Zn(II) or Cd(II) and 2 for Co(II) or Ni(II) (Table-2). The metal complexes and inclusion products with β -cyclodextrin are generally stable at room temperature and dissolve appreciably in DMF and dioxane. The inclusion products and complexes both are quite insoluble in water. The electrical conductance values of complexes in DMF show negligible conductance value ($11\text{-}16 \text{ ohm}^{-1} \text{ mol}^{-1} \text{ cm}^2$), which qualitatively indicated non-ionic nature of the synthesized complexes [24]. However, the inclusion products show appreciable electrical conductance value ($70\text{-}85 \text{ ohm}^{-1} \text{ mol}^{-1} \text{ cm}^2$) (Table-2) indicated that hydroxyl group of β -cyclodextrin get ionized partially and therefore show appreciable high conductance value. It is found that isatinylthiosemicarbazone (IsttscabH) and isatinylsemicarbazone (IstscabH) form metal complexes as well as the 1:1 inclusion product with β -cyclodextrin.

The molecular weight of the complexes were determined by Rast camphor method [25]. It was found that molecular weight determined for the complexes correspond to the expected (calculated) value for molecular weight of metal complexes and inclusion compounds as shown in Tables 1 and 2, respectively. The magnetic susceptibility of the complexes were determined at room temperature by Gouy method [26]. As expected, it was found that Zn(II) and Cd(II) complexes as well as their inclusion products were diamagnetic. The room

temperature magnetic moment (μ_{eff}) values of Ni(II) complexes and their inclusion products occur between 3.18 and 3.32 BM whereas Co(II) complexes and their inclusion product show (μ_{eff}) values between 4.85 and 5.12 BM, respectively (Tables 1 and 2). The magnetic moment values of Co(II) and Ni(II) complexes and their inclusion products suggested octahedral environment of ligand around metal ions [27].

Electronic spectra studies: The representative electronic spectra of the ligands IstscabH, IsttscabH and $[\text{Cd}(\text{Isttscab})_2]$ complex are shown in Fig. 1. The electronic transitions with their assignment of ligand and their products are given in Table-3. The electronic absorption spectra of isatinylsemicarbazone shows absorption bands at 204, 206, 209 nm due to $\sigma \rightarrow \sigma^*$ transitions, while $\pi \rightarrow \pi^*$ transition occurs at 239, 246 and 315 nm. A weak band at 330 nm is attributed to $n \rightarrow \pi^*$ transitions [28] (Fig. 1a). The electronic bands of IsttscabH observed at 202, 206, 210, 240, 268 and 368 nm (Fig. 1b). The strong bands at 202, 206 and 210 nm are due to $\sigma \rightarrow \sigma^*$ transition and $\pi \rightarrow \pi^*$ transitions at 240 and 264 nm, respectively while a medium band appeared at 360 nm due to $n \rightarrow \pi^*$ transition [29]. In metal complexes the $\sigma \rightarrow \sigma^*$ and $\pi \rightarrow \pi^*$ transitions of ligands are mostly enveloped due to strong charge transfer transitions in complexes and they show very strong absorption below 400 nm. The Zn(II) and Cd(II) complexes display strong absorption band below 390-400 nm and no other absorptions were observed above 400 nm (Fig. 1c). In the Ni(II) complexes, a strong absorption band was found below 420 nm, which is assigned to charge transfer plus ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ transition and a weak broad band at 570-600 nm assigned to ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{F})$ transition [30]. The electronic absorption band of Co(II) complexes, $[\text{Co}(\text{IstscabH})_2] \cdot 2\text{H}_2\text{O}$ and $[\text{Co}(\text{Isttscab})_2] \cdot 2\text{H}_2\text{O}$ showed strong absorption below 390-400 nm. A weak broad shoulder near 420-440 nm and weak absorption band near 520-530 nm were assigned to ${}^4\text{T}_{1g} \rightarrow {}^4\text{T}_{2g}$ and ${}^4\text{T}_{1g} \rightarrow {}^4\text{A}_{2g}$ transitions, respectively confirming octahedral environment around Co(II) . In inclusion complexes, these transitions were not affected. The observation confirmed that octahedral structure of Ni(II) and

TABLE-2
ANALYTICAL RESULTS, ELECTRICAL CONDUCTANCE VALUES, MAGNETIC MOMENT AND MOLECULAR WEIGHT OF SYNTHESIZED β -CYCLODEXTRIN INCLUSION COMPLEX PRODUCTS

Compound & Formula	Element analysis (%): Found (calcd.)					m.w. (g): Found (calcd.)	Electrical conductance ($\text{ohm}^{-1} \text{ mol}^{-1} \text{ cm}^2$)	μ_{eff} (BM) at 301 K
	C	H	N	S	M			
$[\text{Co}(\text{Istscab})_2(\beta\text{-CD})_2] \cdot 2\text{H}_2\text{O}$ [$\text{Co}(\text{C}_{60}\text{H}_{88}\text{N}_8\text{O}_{41})$]	44.35 (44.04)	5.63 (5.42)	6.92 (6.85)	—	3.85 (3.66)	1610.1 (1636.35)	85	5.08
$[\text{Ni}(\text{Istscab})_2(\beta\text{-CD})] \cdot 2\text{H}_2\text{O}$ [$\text{Ni}(\text{C}_{60}\text{H}_{88}\text{N}_8\text{O}_{41})$]	44.31 (44.07)	5.60 (5.42)	6.92 (6.85)	—	3.73 (3.59)	1607.2 (1635.11)	85	3.28
$[\text{Co}(\text{Isttscab})_2(\beta\text{-CD})] \cdot 2\text{H}_2\text{O}$ [$\text{Co}(\text{C}_{60}\text{H}_{88}\text{N}_8\text{O}_{39}\text{S}_2)$]	43.40 (43.19)	5.35 (5.31)	6.92 (6.72)	3.95 (3.84)	3.63 (3.59)	1645.1 (1668.47)	73	5.12
$[\text{Ni}(\text{Isttscab})_2(\beta\text{-CD})] \cdot 2\text{H}_2\text{O}$ [$\text{Ni}(\text{C}_{60}\text{H}_{88}\text{N}_8\text{O}_{39}\text{S}_2)$]	43.40 (43.22)	5.40 (5.36)	6.91 (6.72)	3.98 (3.84)	3.80 (3.52)	1638.1 (1667.23)	76	3.18
$[\text{Zn}(\text{Istscab})_2(\beta\text{-CD})]$ [$\text{Zn}(\text{C}_{60}\text{H}_{84}\text{N}_8\text{O}_{39})$]	44.95 (44.85)	5.43 (5.27)	7.20 (6.98)	—	4.23 (4.07)	1591.1 (1606.77)	78	Dia
$[\text{Zn}(\text{Isttscab})_2(\beta\text{-CD})]$ [$\text{Zn}(\text{C}_{60}\text{H}_{84}\text{N}_8\text{O}_{37}\text{S}_2)$]	44.10 (43.97)	5.24 (5.16)	6.92 (6.84)	4.01 (3.91)	4.10 (3.99)	1607.2 (1638.87)	74	Dia
$[\text{Cd}(\text{Istscab})_2(\beta\text{-CD})]$ [$\text{Cd}(\text{C}_{60}\text{H}_{84}\text{N}_8\text{O}_{39})$]	43.65 (43.57)	5.16 (5.12)	6.85 (6.78)	—	6.95 (6.80)	1671.1 (1653.79)	74	Dia
$[\text{Cd}(\text{Isttscab})_2(\beta\text{-CD})]$ [$\text{Cd}(\text{C}_{60}\text{H}_{84}\text{N}_8\text{O}_{37}\text{S}_2)$]	42.93 (42.74)	5.13 (5.02)	6.93 (6.65)	3.97 (3.80)	6.92 (6.66)	1641.3 (1685.89)	77	Dia

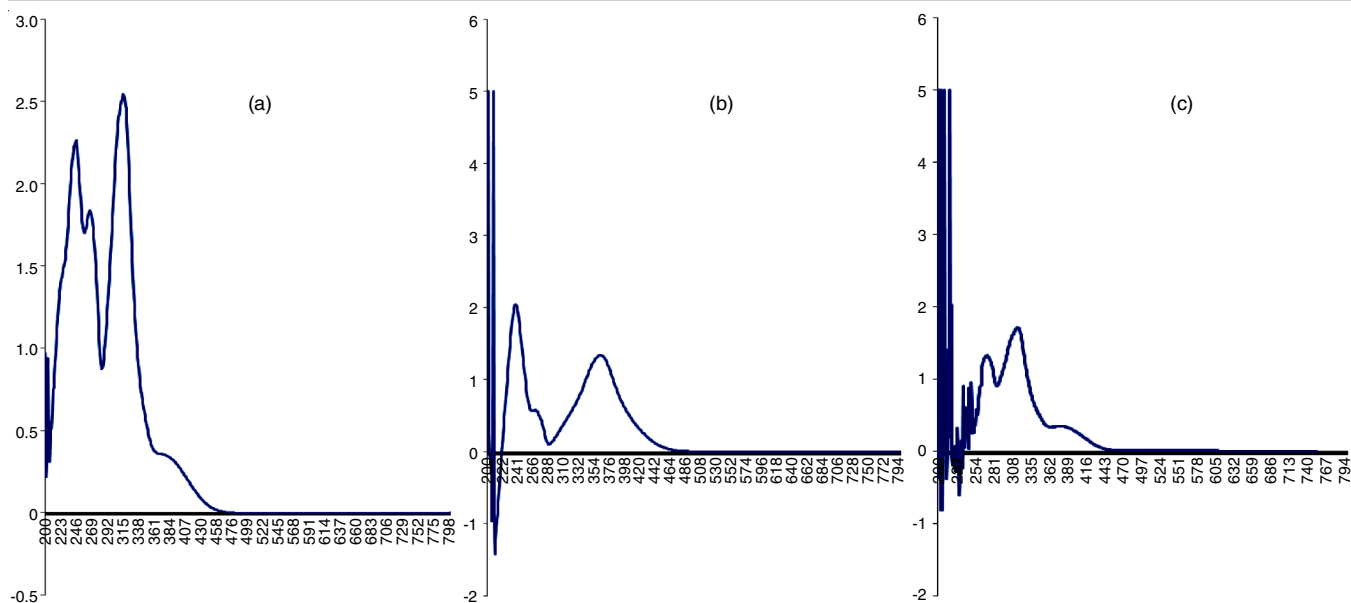


Fig. 1. Electronic spectrum of the ligand (a) isatinylsemicarbazone (IstscabH), ($C_9H_8N_4O_2$) (b) isatinylthiosemicarbazone (IsttscabH), ($C_9H_8N_4OS$) and (c) cadmium isatinylthiosemicarbazone [$Cd(C_9H_7N_4OS)_2$] complex

TABLE-3
ELECTRONIC TRANSITIONS ASSIGNMENT (nm) OF THE LIGANDS (IstscabH AND IsttscabH)
AND ITS METAL COMPLEXES AND INCLUSION COMPOUND

Compounds	$\sigma-\sigma^*$	$\pi-\pi^*$	$n-\pi^*$	Charge transfer	$d-d$ Transition
IstscabH	204, 206, 209	239, 246, 315	330	–	–
IsttscabH	202, 204, 210	240, 268	–	364	–
[(IstscabH)(β -CD)]	205, 207, 210	238, 245	–	399	–
[Cd(isttscab) $_2$]	–	254, 312	335	400	–
[Ni(Istscab) $_2$] $\cdot 2H_2O$	–	266	–	375	$395^3A_{2g} \rightarrow ^3T_{1g}$ (P); $570^3A_{2g} \rightarrow ^3T_{1g}$ (F)
[Ni(Isttscab) $_2$] $\cdot 2H_2O$	–	–	–	420	$420^3A_{2g} \rightarrow ^3T_{1g}$ (O); $580^3A_{2g} \rightarrow ^3T_{1g}$ (F)
[Ni(Istscab) $_2$](β -CD) $\cdot 2H_2O$	–	260	–	410	$410^3A_{2g} \rightarrow ^3T_{1g}$ (P); $590^3A_{2g} \rightarrow ^3T_{1g}$ (F)
[Co(Isttscab) $_2$] $\cdot 2H_2O$	–	275	–	390	$420^4T_{1g} \rightarrow ^4T_{2g}$; $475^4T_{1g} \rightarrow ^4A_{2g}$
[Co(Istscab) $_2$](β -CD) $\cdot 2H_2O$	–	265	–	380	$430^4T_{1g} \rightarrow ^4T_{2g}$; $480^4T_{1g} \rightarrow ^4A_{2g}$

Co(II) complexes were very much retained in the inclusion complexes.

Infrared spectra: The infrared spectra of the free ligands IstscabH and IsttscabH and metal complexes of Co(II), Ni(II), Zn(II) and Cd(II) were recorded as KBr optics. The prominent IR data of both ligands and all the metal complexes and their inclusion complexes are given in Table-4. Isatinylsemicarbazone (IstscabH) shows NH_2 and NH stretching bands at 3286, 3162 and 3678 cm^{-1} . The $\nu(CO)$ of isatin ring and semicarbazone $\nu(CO)$ of ($CONH_2$) group were observed at 1715 and 1693 cm^{-1} , respectively [31]. The ($-NH-CO$) group, $\nu(CO)$ band of semicarbazone at 1715 cm^{-1} disappears in almost all complexes indicating coordination of semicarbazone ($-NH-CO$) oxygen on deprotonation of semicarbazone ($-NH-CO$) proton after enolization [32,33]. The isatin ring $\nu(CO)$ band at 1693 cm^{-1} in Ni(II) and Co(II) complexes is shifted to lower frequency by 10-30 cm^{-1} indicating coordination of isatin ring (CO) oxygen in Ni(II) and Co(II) complexes leading to formation of $[M(Istscab)_2] \cdot 2H_2O$ type of complexes. In Zn(II) and Cd(II) complexes, the isatin ring $\nu(CO)$ vibration is raised to higher wavenumber by 10-15 cm^{-1} indicating that isatin ring CO oxygen is free and not coordinated to Zn(II) and Cd(II). The $\nu(CO)$ of

semicarbazone ($-NH-CO-$) disappears in Zn(II) and Cd(II) complexes due to deprotonation. The shift of isatin ring $\nu(CO)$ vibration at higher wave number indicated that ligand coordinated as bidentate donor molecule and isatin ring (CO) oxygen is not bonded in Zn(II) and Cd(II) unlike Ni(II) and Co(II) complexes. The $\nu(C=N)$ of ligand istscabH is located at 1603 cm^{-1} and it is shifted to lower wave number in all the metal complexes (Table-4) supporting coordination of azine ($C=N$) nitrogen. The $\delta(NH_2)$ located at 1471 cm^{-1} in IstscabH is not affected appreciably in metal complexes. This indicated that the azine nitrogen is not involved in bonding. The $\delta(C-H)$, $\nu(C-N)$, $\nu(C-C)$ and $\nu(N-N)$ vibrations of the ligand IstscabH were observed at 1396, 1350, 1197, 1163, 1109, 1052 and 951 cm^{-1} , respectively and are retained in the metal complexes. The phenyl and isatin ring ($C-H$) out of plane bending and deformation vibrations of ligand are assigned to IR bands at 787, 749, 664 and 620 cm^{-1} . In metal complexes, the sharp bands at 1096 and 1010 cm^{-1} are attributed to $\nu(C-O)$ band of coordinated and deprotonated enolic $\nu(N=C-OH)$ group. The inclusion complexes showed similar pattern of IR spectra (Table-4). The IR spectra of isatinylthiosemicarbazone displayed NH_2 and NH stretching bands at 3268, 3182 and 3112 cm^{-1} . The

TABLE-4
KEY IR BANDS (cm^{-1}) OF LIGANDS AND SOME OF THEIR COMPLEXES AND INCLUSION PRODUCTS

Compounds	$\nu(\text{NH}_2) +$	$\nu(\text{CO})$	$\nu(\text{C}=\text{N})$	$\delta(\text{NH}_2)$	$\nu(\text{N}-\text{H}) +$	$\nu(\text{N}-\text{N}) +$	$\nu(\text{C}-\text{O})$	$\nu(\text{C}=\text{S})$	$\delta(\text{C}-\text{H}) +$
	$\nu(\text{NH}) +$				$\nu(\text{C}-\text{H})$	$\nu(\text{C}-\text{N}) +$		or	$\delta(\text{C}-\text{N}) +$
	$\nu(\text{OH})$					$\nu(\text{C}-\text{C})$	$\nu(\text{C}-\text{S})$	$\nu(\text{N}-\text{N})$	
IstscabH	3286, 3162, 3078	1715, 1693	1603	1471, 1451	1396, 1350	1197, 1163, 1109, 1052	–	–	787, 749, 664
IsttscabH	3268, 3182, 3112	1727	1615	1460	1331, 1332	1201, 1153, 1079, 999	–	1026	768, 734, 659
[Cd(Istscab) ₂]	3266, 3189	1726	1601	1461	1331	1201, 1193	1096	–	758, 741, 652
[Zn(Isttscab) ₂]	3262, 3180	1735	1598	1462	1332	1215, 1161	–	742	768, 731, 656
[Ni(Istscab) ₂].2H ₂ O	3354, 3216	1682	1608	1464	1354, 1316	1198, 1152	1077	–	777, 750, 685
[Co(Istscab) ₂].2H ₂ O	3347, 3207	1686	1594	1463	1349, 1310	1180, 1150	1073	–	777, 747, 680
[Cd(Isttscab) ₂](β -CD)]	3418, 3331, 3261, 3160	1698, 1670	1621, 1593	1471, 1463	1347, 1302	1252, 1214	1101, 1062	–	797, 855, 757, 741, 685, 650
[Zn(Istscab) ₂](β -CD)]	3410, 3350, 3152, 3206	1726, 1684	1586	1547, 1454	1350, 1301	1246, 1190, 1152	1077, 1022	–	744, 673, 631
[Zn(Isttscab) ₂](β -CD)]	3345, 3209, 3076	1735, 1682	1606	1550, 1464	1352, 1350	1201, 1154	1078, 1023	–	751, 650, 623
[Ni(Isttscab) ₂].2H ₂ O	3440, 3286, 3186	1685	1590	1454	1353, 1308	1221, 1154	–	741	768, 652
[Ni(Istscab) ₂](β -CD)].2H ₂ O	3420, 3282, 1380, 3120	1691	1601, 1585	1540, 1451	1361, 1340, 1306	1254, 1205, 1150	1070, 1021	–	798, 748, 653, 701

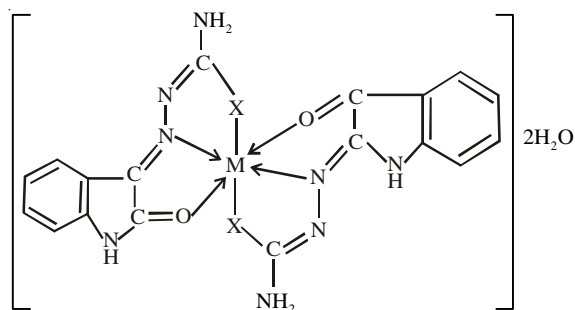
$\nu(\text{CO})$ of isatin ring is located as strong band 1727 cm^{-1} which is shifted to lower wave number in case of Ni(II) and Co(II) complexes as well as in their inclusion complexes while it is raised slightly to higher wave number in Zn(II) and Cd(II) complexes and their inclusion complexes with β -cyclodextrin (Table-4). This observation suggested that isatin ring CO is coordinated to Ni(II) and Co(II) in their complexes while it is free in Zn(II) and Cd(II) complexes and their inclusion complexes. The $\nu(\text{C}=\text{N})$ of the ligand (IsttscabH) observed at 1615 cm^{-1} shifted to lower wave number in almost all the metal complexes supporting the bonding of IsttscabH through azine (C=N) nitrogen. The $\delta(\text{NH}_2)$ of IsttscabH ligand located at 1460 cm^{-1} and in its metal complexes as well as its inclusion products is not involved in bonding. The $\nu(\text{C}=\text{S})$ of thiosemicarbazone thione group is observed as a very strong band at 1026 cm^{-1} , but disappears in all complexes of IsttscabH and appeared at $745 \pm 5 \text{ cm}^{-1}$ suggesting the deprotonation of thiol tautomer of thione group and bonding of ligand through deprotonated thiol sulphur [32]. In β -cyclodextrin inclusion complex, the hydrogen bonded (OH) stretches is observed between $2850\text{--}2250 \text{ cm}^{-1}$. A number of prominent IR bands of IsttscabH have been observed in finger print region at $1331, 1322, 1201, 1153, 1079, 999, 946, 768, 734$ and 659 cm^{-1} due to various mode of vibrations in ligand and are retained with slight change in the complexes and inclusion complexes. The hydrated complexes display broad band due to $\nu(\text{OH})$ at $3450\text{--}3500 \text{ cm}^{-1}$ supporting the presence of H₂O in complexes [31]. Thus IR spectral studies supported tridentate nature of the ligands IsttscabH and IstscabH in Ni(II) and Co(II) complexes while as bidentate bonding in Zn(II) and Cd(II) complexes and their inclusion complexes.

Antibacterial activity: It was found that the inclusion complexes showed greater activity than Schiff bases and their metal complexes. The Zn(II) complex and its inclusion products showed higher activity against *Escherichia coli* and *Bacillus subtilis* while Co(II) complex and its inclusion products were active against *Staphylococcus aureus* (Table-5). The better activities of Zn(II) complexes and its inclusion products with β -cyclodextrin compared to Schiff bases of isatin may be due to decrease in polarizability of inclusion product, which enhanced the lipophilicity of product than metal complexes and isatin Schiff bases leading to reduction of permeability of the cells resulting in interference with normal cell process. The result showed that in some cases, the activities are comparable to streptomycin (Table-5).

TABLE-5
ANTIBACTERIAL SCREENING DATA OF ISATIN SCHIFF BASES, THEIR SOME METAL COMPLEXES AND THEIR INCLUSION PRODUCTS

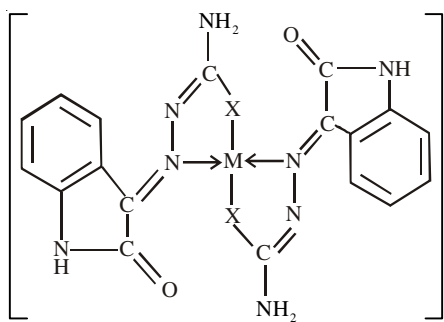
Compounds	Zone of inhibition (mm)		
	<i>E. coli</i>	<i>B. subtilis</i>	<i>S. aureus</i>
IstscabH	6.34	8.12	7.23
IsttscabH	8.14	9.02	8.38
[Zn(Istscab) ₂]	16.21	16.68	14.31
[Zn(Isttscab) ₂]	17.31	15.92	15.23
[Co(Istscab) ₂].2H ₂ O	14.26	12.81	14.82
[Co(Isttscab) ₂].2H ₂ O	15.26	13.81	13.36
[Cd(Istscab) ₂]	12.83	13.12	13.62
[Cd(Isttscab) ₂]	13.63	14.41	13.21
[Zn(Istscab) ₂](β -CD)]	20.28	19.36	15.91
[Zn(Isttscab) ₂](β -CD)]	22.92	19.45	14.61
[Co(Istscab) ₂](β -CD)].2H ₂ O	17.52	16.81	17.21
[Co(Isttscab) ₂](β -CD)].2H ₂ O	17.83	15.81	18.28
Streptomycin	20.84	21.32	18.82

On the basis of analytical results and spectral studies the following possible structures of the metal complexes with IstscabH and IsttscabH are suggested.



where, M = Co(II) and Ni(II), X = S or O

Structure of $[M(\text{istscab}/\text{isttscab})_2] \cdot 2\text{H}_2\text{O}$



where, M = Zn or Cd and X = S or O of IstscabH or Isttscab

Structure of $[M(\text{istscab}/\text{isttscab})_2]$

Conclusion

The synthesized complexes of Co(II), Ni(II), Zn(II) and Cd(II) with isatinysemicarbazone (IstscabH) and isatinythiosemicarbazone (IsttscabH) have been characterized by their elemental analysis, molar mass, molar conductance, magnetic moment, IR and electronic spectral studies. The analytical results and spectral studies suggest that these metal complexes of IstscabH and IsttscabH form 1:1 inclusion complexes with β -cyclodextrin. These ligands were coordinated as tridentate molecules in Ni(II) and Co(II) complexes while as bidentate molecule in Zn(II) and Cd(II) complexes. Overall experimental evidence showed that Co(II) and Ni(II) displayed coordination number six while Zn(II) and Cd(II) complexes are tetra coordinated. The inclusion complexes of Zn(II) showed higher antibacterial activities and are comparable to streptomycin.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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