

Synthesis, Spectroscopic Characterization, Thermogravimetric and Biological Activity Evaluation of Te(IV), Se(IV), V(III), Nb(V), Ta(V) Complexes With Indole-3-Acetic Acid Plant Hormone Ligand

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Abstract Te(IV), Se(IV), V(III), Nb(V) and Ta(V) complexes of indole-3-acetic acid (IAAH) ligand were synthesized, characterized by elemental analysis and various spectroscopic techniques like, IR, ¹H-NMR, X-ray powder diffraction, UV-Visible, thermogravimetry analysis, magnetic measurements, molar conductance and surface morphology using SEM. All the synthesized complexes of IAAH ligand have 1 : 2 stoichiometry of the types [Te(IAA)₂(NH₃)₂] · 2Cl (I), [Se(IAA)₂(NH₃)₂] · 2Cl (II), [V(IAA)₂(NH₃)(Cl)] (III), [Nb(IAA)₂(Cl)₃] (IV), and [Ta(IAA)₂(Cl)₃] (V). Spectral analysis indicates octahedral geometry for the Te(IV), Se(IV) and V(III) complexes, whereas both Nb(V) and Ta(V) have a seven-coordination. The bonding sites are the oxygen atoms of carboxylate group for the deprotonated indole-3-acetic acid (IAA) ligand. The thermogravimetry analysis studies gave evidence for the presence of other coordinated molecules (Cl or NH₃) in the composition of IAA complexes, which were further supported by IR and micro analytical measurements. The higher molar conductance data of tellurium and selenium (IV) complexes reveal that these chelates are electrolytes, while low conductivity values for the vanadium(III), niobium and tantalum(V) chelates indicated a non-electrolytes. To test the antibacterial property of the five complexes in this study, four bacterial strains *Klebsiella* (G⁻), *Escherichia coli* (G⁻), *Staphylococcus aureus* (G⁺) and *Staphylococcus epidermidis* (G⁺) were used in the investigation. The effects of the five complexes in the cytotoxicity of Caco-2 and MCF-7 human cancer cell lines were studied Neutral red uptake assay for the estimation of cell viability/cytotoxicity protocol.

Keywords Indole-3-acetic acid; chelation; IR; Metal ions; TEM; Antimicrobial test

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Introduction

The indole-3-acetic acid (IAAH; Fig. 1) is a dominant type of auxin found in plants and is involved in the growth responses of plants for the regulation of cell elongation, cell

division, cell differentiation, root initiation and synthetic auxins are an important class of selective herbicides^[1-2]. IAAH has been produced not only in plants, but also by plant-associated microorganisms including ectomycorrhizal, endophytic, pathogenic, phyllosphere and rhizospheric microbes^[3-6].

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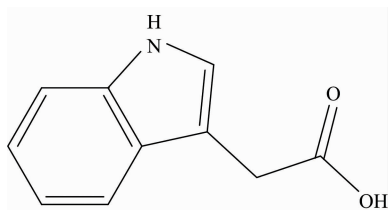


Fig. 1 Structure of indole-3-acetic acid (IAAH)

Indole-3-acetic acid is a monocarboxylic acid that is acetic acid in which one of the methyl hydrogens has been replaced by a ^1H -indol-3-yl group. It has a role as a plant hormone, a human metabolite, a plant metabolite, a mouse metabolite and an auxin. It is a monocarboxylic acid and a member of indole-3-acetic acids. Metal complexes have important applications in many aspects of life. In recent years, the successful development of metal-based pharmaceuticals has attracted more attention on metal complexes in microbial treatment^[7-9]. Carboxylate ligands can bind to metal ions in several ways, such as monodentate, bidentate, bridging etc. These binding modes complicate selective synthesis of metal carboxylate complexes^[10-12]. A literature survey reveals that few research papers has been reported on the metal chelation of indole-3-acetic acid^[10-12], so it seems important to conduct investigations of IAAH metal complexes. In continuation of our published work^[7-9] on the coordination chemistry of pharmaceutical and bioactive ligands, we report in the present article a synthesis, spectroscopic characterization, and thermogravimetric measurements of Te(IV), Se(IV), V(III), Nb(V), Ta(V) complexes with indole-3-acetic acid plant hormone ligand. The study also includes an antimicrobial and anticancer investigations.

1 Experimental

1.1 Chemicals and instruments

The chemicals presented in this article are of analytical grade and were used without further purification. These chemicals (Indole-3-acetic acid, TeCl_4 , SeCl_4 , VCl_3 , NbCl_5 and TaCl_5) were received from Sigma-Aldrich Chemical Company, USA. The analyses and the corresponding models are summarized as follows:

Type of analysis	Models
Elemental analyses	Perkin Elmer CHN 2400
Conductance	Jenway 4010 conductivity meter
FTIR spectra	Bruker FTIR Spectrophotometer
^1H NMR spectra	Varian Mercury VX-300 NMR spectrometer, 300 MHz
Electronic spectra	UV2 Unicam UV/Vis Spectrophotometer

Magnetic moment	Magnetic Susceptibility Balance
Thermo gravimetric	TG/DTG-50H, Shimadzu thermo-gravimetric analyzer
SEM	Quanta FEG 250 equipment
XRD	X'Pert PRO PAN analytical, with copper target
TEM	JEOL 100 s microscopy

1.2 Synthesis

The five IAA solid complexes were prepared by mixing 1.0 mmol of TeCl_4 , SeCl_4 , VCl_3 , NbCl_5 or TaCl_5 in 25 mL of methanol solvent with 2.0 mmol IAAH (0.350 g) in 25 mL of methanol. The reaction mixtures were neutralized between $\text{pH}=7\sim 8$ by 5% ammonia solution, then refluxed in a water bath for about 2 h to give the precipitate. After cooling to room temperature, the solid complexes were filtered as fine precipitates. The precipitates were washed with hot methanol. Then they were dried and stored in a desiccators containing dry calcium chloride. The yield of the products was about 80%~87%. The solid products have a higher melting point $>250\text{ }^\circ\text{C}$. The micro analytical (calculated/Calc. and experimental/Found) and physical data of the five synthesized complexes are summarized in Table 1.

1.3 Biological tests

Based on disc diffusion method^[13], an antibacterial screening for the five IAA complexes was performed against four bacterial strains *Klebsiella*, *Escherichia coli*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*. Inhibition zones diameters around the disc were determined. In vitro the cytotoxic activity of the tested IAA complexes against two human cancer cell lines (colorectal adenocarcinoma (Caco-2) and breast cancer (MCF-7)) was evaluated using the standard neutral red uptake assay^[14].

2 Results and discussions

2.1 Elemental analysis and conductance measurements

Elemental analysis was applied to further confirm the composition of these IAA complexes. The contents of carbon, hydrogen, nitrogen and chloride in each complex were consistent with the calculated values (Table 1), which supported the proposed structure of these complexes (Fig. 2). The IAAH ligand and its complexes were stable in air. Furthermore, Te(IV), Se(IV), V(III), Nb(V) and Ta(V) complexes were soluble in DMSO with gently heating and their molar conductivities (Δ_m) were 96, 105, 14, 10, and 12 $\text{ohm}^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$, respectively. Consequently, the V(III), Nb(V) and Ta(V) IAA complexes were considered as non-electrolytes while the Te(IV) and Se(IV) complexes have an electrolyte feature^[15]. The obtained complexes were characterized

by IR, $^1\text{H-NMR}$, TG analysis and elemental analysis. structure was not performed. Because these compounds were not crystallized, X-ray crystal

Table 1 Micro analytical and physical data of IAA complexes

Complex	Color	Magnetic moment (BM)	Conductance/ ($\text{ohm}^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$)	Element	Calc.	Found
I	Orange red	—	96	%C	41.35	41.12
				%H	3.82	3.77
				%N	9.64	9.65
				%Cl	12.21	12.09
II	Orange	—	105	%C	45.13	45.03
				%H	4.17	4.03
				%N	10.53	10.45
				%Cl	13.32	13.21
III	Olive green	1.11	14	%C	53.17	53.06
				%H	4.24	4.11
				%N	9.30	9.23
				%Cl	7.85	7.70
IV	Yellow	—	10	%C	43.87	43.65
				%H	2.94	2.88
				%N	5.12	5.06
				%Cl	19.42	19.35
V	Yellow	—	12	%C	37.79	37.81
				%H	2.54	2.43
				%N	4.41	4.38
				%Cl	16.73	16.60

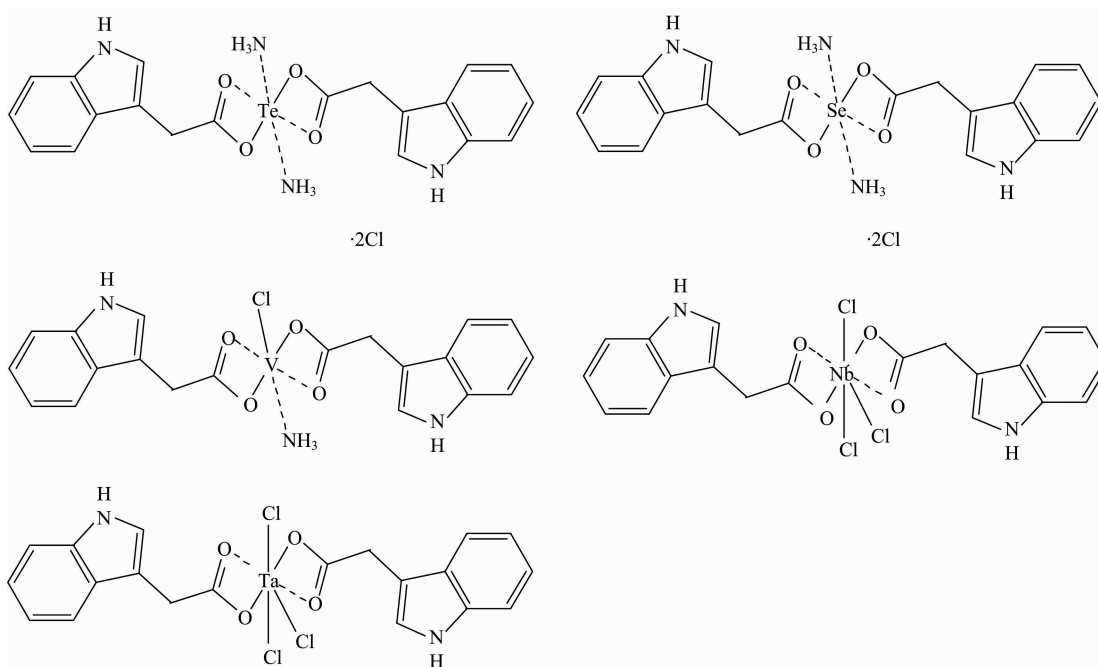


Fig. 2 Suggested structures of IAA complexes

2.2 FTIR spectra

The IR spectra of IAA complexes are shown in Fig. 3. The important IR spectral bands of IAA complexes are pres-

ented in Table 2. According to the IR spectra data of IAAH ligand and complexes (IAA-Te, IAA-Se, IAA-V, IAA-Nb and IAA-Ta), the strong absorption peaks at $\sim 3\ 400\ \text{cm}^{-1}$

belong to the —NH group. No significant shifts were observed on the peaks among this ligand, suggesting that nitrogen atom in the indole ring didn't coordinate with metal ions. Compared with the IR spectra of the IAA ligand, two new peaks at 1 549 and 1 403 cm^{-1} were assigned to ν_{as} (COO^-) and ν_{s} (COO^-), respectively^[16]. According to Deacon and Phillips^[17], a difference larger than $>200 \text{ cm}^{-1}$ indicates monodentate coordination, whereas one smaller than $<200 \text{ cm}^{-1}$ indicates a bidentate coordination mode. Regarding IAA complexes (I—V), $\Delta\nu = \nu_{\text{asym}} - \nu_{\text{sym}} < 200 \text{ cm}^{-1}$, which confirms that the coordination is bidentate. The absorption vibration frequencies appeared within the 630~500 cm^{-1} range in these complexes were attributed to the formation of M—O bond. A new peak located in the range of 500~

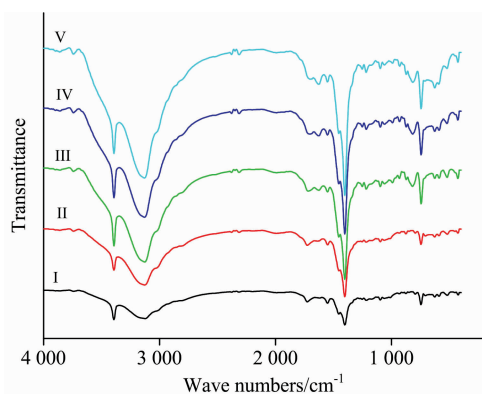


Fig. 3 FTIR spectra of IAA complexes I—V

Table 2 Infrared spectral data (cm^{-1}) of IAA complexes I—V

Compounds	Frequencies/ cm^{-1}				
	$\nu(\text{N—H})$	$\nu_{\text{as}}(\text{COO})$	$\nu_{\text{s}}(\text{COO})$	$\nu(\text{M—O})$	$\nu(\text{M—N})$
I	3 400	1 549	1 403	585, 517	429
II	3 400	1 550	1 403	517	429
III	3 400	1 549	1 403	595, 517	419
IV	3 390	1 549	1 403	634	—
V	3 400	1 549	1 403	624	—

Table 3 ^1H NMR spectral data (cm^{-1}) of IAA and its complexes (I, II, IV, and V)

Assignments	Compounds				
	IAAH	I	II	IV	V
1H, COOH	12.16	—	—	—	—
1H, NH	10.91	10.909	11.100	10.909	10.948
5H, C ₆ H ₄ , C=CH	7.51~6.97	6.914~7.485	7.473	7.292	6.945~7.481
2H, CH ₂	3.64	3.721	3.434	3.353	3.728

2.5 Thermo gravimetric analysis

The TG analyses of IAA complexes I—V were performed in the temperature range of 30~700 $^{\circ}\text{C}$. The TG curves of the five IAA complexes are difference, further indicating that the five complexes possess a difference metal

400 cm^{-1} in case of tellurium(IV), selenium(IV) and vanadium (III) complexes, suggesting the formation of M—N bond because of presence NH_3 group inside the coordination sphere.

2.3 Electronic spectra and magnetic susceptibility

The UV-Vis spectrum of indol-3-acetic acid dissolved in DMSO solvent has displayed a two distinguish peaks at 219 and 280 nm that assigned to $\pi-\pi^*$ electronic transitions^[10]. For the Te(IV)-IAA, Se(IV)-IAA, Nb(V)-IAA, and Ta(V)-IAA complexes, both the $\pi-\pi^*$ electronic transition peaks showed a hyperchromic effect with red shifted to 227 and 280~293 nm. This data revealed the involvement of indol-3-acetic acid in the chelation with metal ions. In addition, the IAA complexes show two electronic transition peaks at 330 and 380 nm related to charge transfer MLCT. The effective magnetic moments (μ_{eff}) data regarding to Te(IV), Se(IV), Nb(V), and Ta(V) IAA complexes were less than 1.00 B. M. These results deduced that all of these complexes are a diamagnetic properties with a six-coordination for Te(IV) and Se(IV) complexes, whereas Nb(V) and Ta(V) have a seven-coordination mode^[18]. Concerning the vanadium (III) IAA complex, the μ_{eff} data is 1.11 B. M. due to a six-coordination structure for the speculated chelation^[19-20].

2.4 ^1H NMR spectra

The ^1H NMR spectrum of free IAAH ligand (400 MHz, DMSO-d₆): δ 12.16 [1H, COOH], 10.91 [1H, NH], 7.51~6.97 [5H, —C₆H₄, —C=CH], 3.64 [2H, CH₂]. The ^1H NMR spectra of IAA-Te, IAA-Se, IAA-Nb, and IAA-Ta complexes (Table 3) showed that there were upfield or downfield shifts in the signals among IAA ligand, suggesting the interaction between IAA ligand and metal ion. In addition, the signal for NH proton in the spectra of complexes I, II, IV, and V are 10.909, 11.100, 10.909, and 10.948 ppm, respectively were still present, while the signal for the COOH proton of the IAA ligand was absent in these complexes, indicating the hydrogen atom of carboxyl group were displaced by metal ion.

ions and structures. For clarity's sake, only the TG curve of complex III has been shown in Fig. 4. From 30 to 700 $^{\circ}\text{C}$, the weight loss of complex III is 71%, corresponding to the decomposition of IAA, and release of NH_3 and HCl molecules, in a good accordance with the calculated value

(71.02%). It was found that the five complexes (I–V) are thermally decomposed with DrTGA at 260, 307, 257, 450, and 254 °C, respectively. Thermal analysis (TG) of IAA complexes IAA-Te, IAA-Se, IAA-V, IAA-Nb, and IAA-Ta were recorded in the range from 30-to-700 °C. These complexes were all decomposed actually in one or two steps and the residue rates of them were 21.97%, 0.0%, 28.98%, 16.97%, and 28.47%, respectively, which were assigned to tellurium metal, sublimated selenium, VO₂ polluted with few carbon atoms, niobium metal, and tantalum metal.

2.6 Morphological analysis

The X-ray powder diffraction patterns of IAA complexes (I–V) at the range of $2\theta = 5^\circ \sim 90^\circ$ are shown in Fig. 5, these patterns have three types of structures as semi-crystalline for tellurium(IV) complex (I), crystalline nature for selenium(IV) and vanadium(III) complexes while both niobium

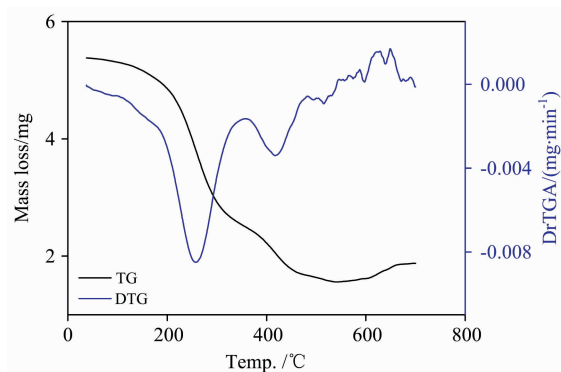


Fig. 4 TG-DrTGA curve of $[V(IAA)_2(NH_3)(Cl)]$ complex

(V) and tantalum(V) complexes have an amorphous structure (Fig. 5). The particle size was calculated dependent on Scherrer relationship^[21] using full-width at half-maximum (FWHM).

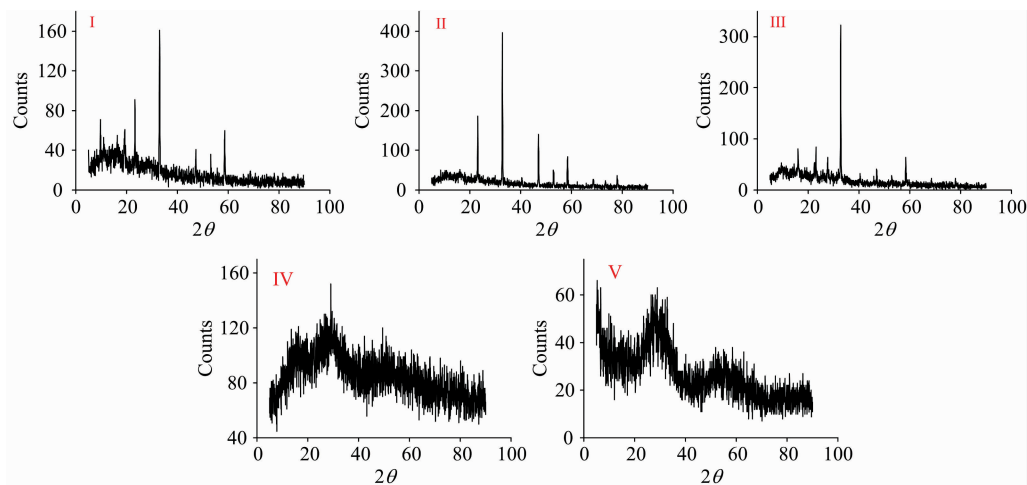


Fig. 5 XRD pattern of IAA complexes I–V

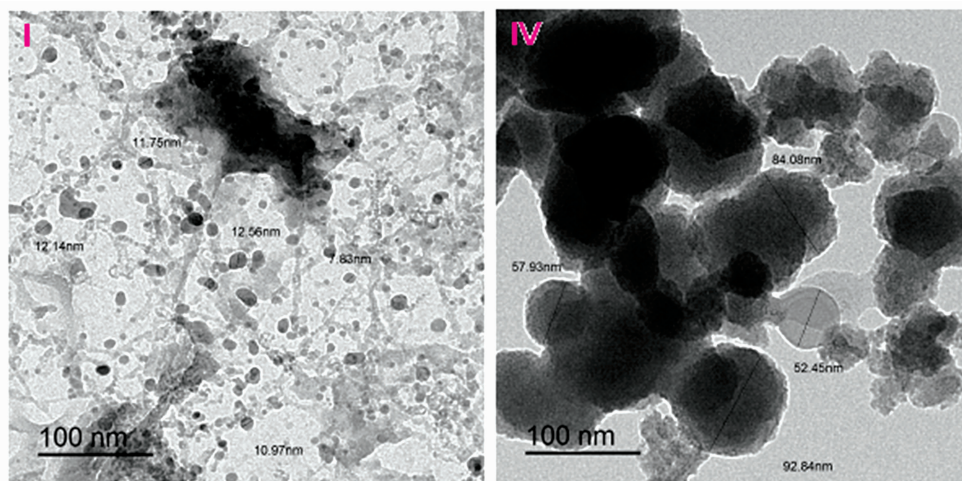


Fig. 6 TEM images of (I): tellurium and (IV): niobium complexes

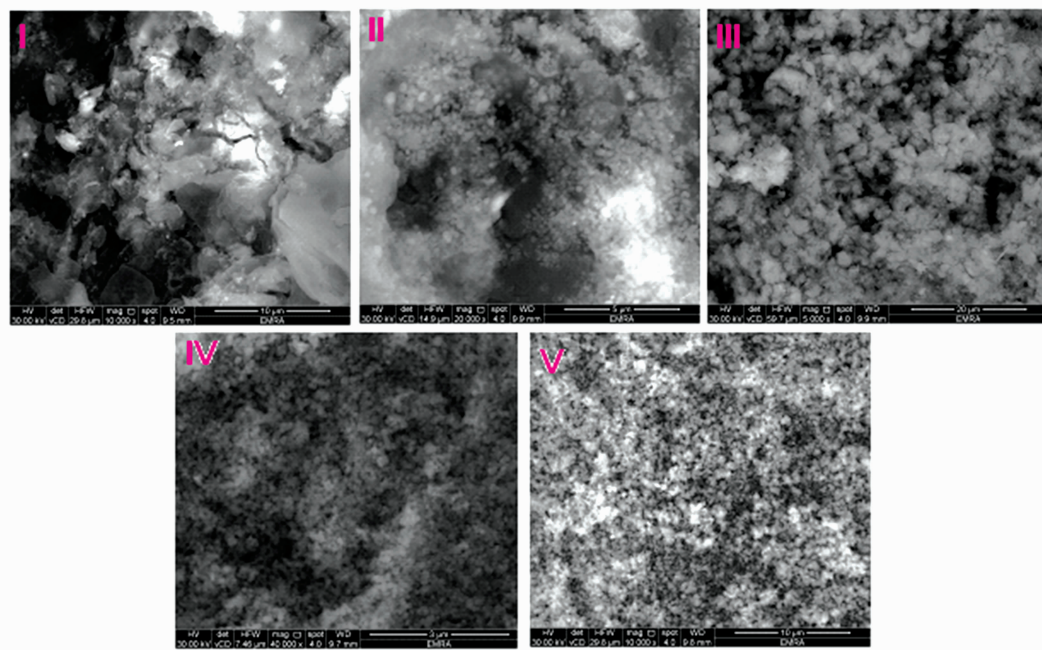


Fig. 7 SEM images of IAA complexes I — V

TEM photos of the $[\text{Te}(\text{IAA})_2(\text{NH}_3)_2] \cdot 2\text{Cl}$ (I) and $[\text{Se}(\text{IAA})_2(\text{NH}_3)_2] \cdot 2\text{Cl}$ (IV) complexes are displayed in Fig. 6, the complexes refer to a black spots with spherical shape nanoparticles within 7~12 and 50~90 nm, respectively. SEM images of all IAA complexes (Fig. 7) were scanned at energy 30 kV with magnification $\times 5\,000 \sim 40\,000$. Figure 7 show the aggregation of tremendous micro-size fine powders and homogeneous uniform.

2.7 Biological results

To test the antibacterial property of the five IAA complexes in this study, four bacterial strains *Klebsiella* (g^-),

Escherichia coli (g^-), *Staphylococcus aureus* (g^+) and *Staphylococcus epidermidis* (g^+) were used in the investigation. Disc diffusion method was used to evaluate the antibacterial activity for the selected strains. Gentamicin and Ceftriaxone were used as positive controls and DMSO, the solvent, was used as negative control in this test. As shown in Table 4 marginal antibacterial activity was observed in all complexes against *Klebsiella* strain only, whereas no antibacterial effect was seen in all complexes against the rest of the tested bacterial strains.

Table 4 Inhibition zone diameter of IAA complexes I — V against four bacterial strains

sample	Inhibition zone diameter ($\text{mm} \cdot \text{mg}^{-1}$ sample)			
	<i>Klebsiella</i>	<i>Esherichia Coli</i>	<i>Staphylococcus Epidermidis</i>	<i>Staphylococcus Aureus</i>
Control: DMSO	0.0	0.0	0.0	0.0
Standard	Ceftriaxone	0.0	1.6	1.9
	Gentamycin	0.3	0.0	1.8
I	0.2	0.0	0.0	0.0
II	0.1	0.0	0.0	0.0
III	0.2	0.0	0.0	0.0
IV	0.1	0.0	0.0	0.0
V	0.1	0.0	0.0	0.0

The effects of the five IAA complexes in the cytotoxicity of Caco-2 and Mcf-7 human cancer cell lines were studied by NR assay method. The percentage of cellular viability (IC_{50}) for the five IAA complexes against two tumour cell lines Caco-2 and Mcf-7 deduced that only $[\text{V}(\text{IAA})_2(\text{NH}_3)\text{Cl}]$

complex can be considered as a potential anticancer agent against colorectal adenocarcinoma cell line with IC_{50} value of $21.4 \mu\text{g} \cdot \text{mL}^{-1}$. The IC_{50} values for the rest of IAA complexes against the two tumour cell lines were higher than $>100 \mu\text{g} \cdot \text{mL}^{-1}$.

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