

RESEARCH ARTICLE

Anticancer, Antidibetic and Antimicrobial Activity Study of Biologically Active Vanadium(IV) Mixed Ligand Complexes

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Abstract: Introduction: Cancer and diabetes are proving to be lethal to human society and have attracted attention of researchers around the world. Synthesis of mixed ligand complexes is a challenging area owing to their potential applications as drugs against various diseases.

Methods: Synthesis and biological evaluation of mixed ligand complexes of Vanadium(IV) with heterocyclic bidentate molecule 8-hydroxyquinoline as primary ligand and L-Amino acids such as L-cysteine, L-alanine, L-phenylalanine, L-threonine and L-serine as secondary ligands is reported here. All the complexes were characterized using IR, electronic, Mass, TGA/DTA method, powder XRD analysis, molar conductance and magnetic susceptibility measurements and were screened for their biological activities.

Results: The synthesized mixed ligand complexes were screened for their antibacterial activity against *E. coli* and antifungal activity against *C. albicans*. They were also evaluated for *in vitro* antidibetic activity, anticancer activity against HepG2 (human liver cancer cell line) by MTT assay.

Conclusion: The synthesized mixed ligand complexes were thermally stable, paramagnetic, non-electrolytic in nature and proposed to have square pyramidal geometry. They also exhibited potential as antibacterial, anticancer and antidibetic agents.

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1. INTRODUCTION

Cancer and diabetes are two major health issues in human society and hence are the primary concerns of medicinal chemistry research. Cancer is a group of diseases leading to abnormal cell growth, which is one of the serious issues as it spreads to other body parts. The platinum-based complex 'Cisplatin' has attracted researchers owing to its anticancer properties and since then, it has been a primary focus of research in chemotherapy agents. Synthesis of metal complexes with less side effects and better cytotoxicity is a need of the day [1].

Diabetes Mellitus (DM), mainly identified as resulting from insulin deficiency or insulin resistance, is a serious chronic disorder around the world [2-4]. The increasing population failing to this disease around the world has become a serious issue today. Two types of diabetic situations are identified viz. insulin dependent or type 1 and non-insulin dependent or type 2 diabetes. The complications such as kidney failure, micro- and macrovascular disease, retinopathy, neuropathy and atherosclerosis involved during the treatment

using available drugs have created an urgent need to search for new orally active drugs [2-4].

Vanadium is an important trace element and essential for human body [2, 5]. Literature survey indicated towards the potential of Vanadium compounds to possess insulin mimetic activity, to inhibit lipolysis, to cause decreased blood glucose levels (BGL) in animals and in clinical trials, and to stimulate insulin secretion in experimental models [6-11].

8-hydroxyquinoline is a monoprotic bidentate ligand and is widely used in complex formation [12]. 8-hydroxyquinoline and its metal complexes exhibit antiseptic, disinfectant and pesticide properties [13]. Amino acids mixed ligand complexes are significant owing to their potential as models for enzyme metal ion substrate complexes [14].

We report room temperature synthesis of five new biologically active Vanadium(IV) mixed ligand complexes using primary ligand 8-hydroxyquinoline and secondary ligands amino acids such as L-cystein, L-alanine, L-phenylalanine, L-threonine and L-serine in 1:1:1 molar ratio, their characterization using various characterization methods and their screening for antimicrobial, antidibetic, and anticancer activities using MTT assay.

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2. EXPERIMENTAL SECTION

2.1. Materials and Methods

All the chemicals were purchased from S. D. Fine Chemicals, Spectrochem Private Limited, Qualigens Fine Chemicals and Merck Chemicals. All the chemicals used were of AR grade. All the solvents used were double distilled and dried using molecular sieves before use [15].

The melting point or decomposition temperatures of all the synthesized complexes were determined using a simple capillary tube method. Thermo Finnigan (Model: Flash EA 1112 series) analyzer was used to perform elemental analyses of all the synthesized mixed ligand complexes. Room temperature molar conductance values of all the synthesized complexes were measured by preparing 10^{-3} M solutions in DMSO solvent using Equiptronics conductivity meter with an inbuilt magnetic stirrer (Model:Eq-664). Room temperature magnetic susceptibilities were determined using copper(II) sulphate as an internal standard using the SES Instrument's magnetic susceptibility Gouy's balance (Model:EMU-50).

A Shimadzu spectrophotometer was used to record IR spectra of all the synthesized complexes in the region of $4000-400\text{ cm}^{-1}$ using KBr pellets. The electronic spectra of all the complexes were recorded using Shimadzu UV-1800 UV/Visible Scanning spectrophotometer (double beam) by preparing 10^{-3} M solutions in DMSO. Mass spectra were recorded using Alliance 2795 Q-TOF Micromass mass spectrometer. The TGA/DTA curves were recorded using DTG 60H module with a heating rate of 10.00 k/min . Nitrogen atmosphere was maintained while conducting experiments with a heating rate of 10.00 K/Min and a temperature range of $30\text{ to }1000^\circ\text{C}$ using alumina crucible. The sample amount selected for the experiment was 9 mg . The powder XRD spectra of all the complexes were recorded using an Ultima IV instrument with X-Ray $40\text{ kV}/20\text{ mA}$.

2.2. General Procedure

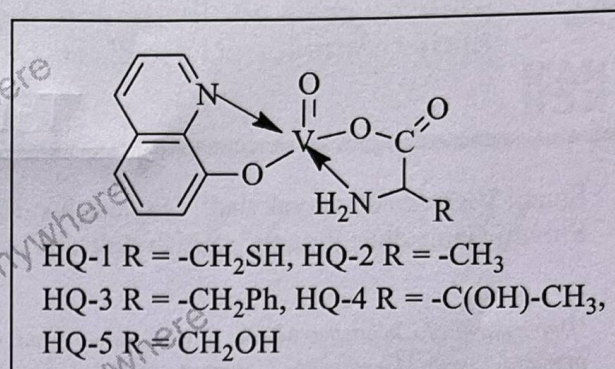
In a round bottom flask, an aqueous solution (20 mL) of Vanadyl sulphate (1.63 g , 0.01 mol) was taken. To it was added an ethanolic solution (20 mL) of 8-hydroxyquinoline (1.45 g , 0.01 mole). The resultant mixture was allowed to stir for 30 min at room temperature and an aqueous solution (20 mL) of respective amino acid (0.01 mol) was added in a dropwise manner with constant stirring. The resulting mixture was then stirred at room temperature for 5 h . The black coloured complexes were precipitated. They were filtered, first washed with cold distilled water and then followed by ethanol, dried at room temperature and then were used for further study.

Scheme 1 represents the generalized proposed structure for all the synthesized Vanadium(IV) mixed ligand complexes.

2.3. Antimicrobial Activity

All the synthesized mixed ligand complexes were screened for their *in vitro* antibacterial activity against *E. coli*

using well plate method [16] and for antifungal activity against *C. albicans* using well diffusion method [16].



Scheme 1. Proposed generalized structure of complexes.

2.4. Antidiabetic Activity by α -Amylase Inhibition

All the synthesized mixed ligand complexes were tested for their antidiabetic activity using Bernfeld method [17] to study α -amylase inhibition. Spectrophotometric determination of the absorbance at 540 nm was carried out and the percentage inhibition of α -amylase enzyme was calculated using equation (1) given below:

$$\text{Percent Inhibition (\%)} = \frac{[\text{Abs } 540 (\text{control}) - \text{Abs } 540 (\text{extract})]}{\text{Abs } 540 (\text{control})} \times 100 \quad (1)$$

Simultaneous determination of suitable reagent blank and inhibitor controls were also carried out.

2.5. Anticancer Study using MTT Assay

Two complexes HQ-4 and HQ-5 were screened for their anticancer activity and cytotoxicity study using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay. The human liver cell line HepG2 was used to assess the cytotoxicity [18-19]. The cancer cell line used in this work was selected based on easy availability and wide use found in the literature survey with cisplatin. Analysis was done by measuring the absorbance of each sample using microplate reader at a wavelength of 550 nm in triplicate. Measurements were performed and IC_{50} i.e. the concentration required for a 50% inhibition of viability, was determined graphically.

3. RESULTS AND DISCUSSION

3.1. Physicochemical Data

All the synthesized complexes were obtained in 70-78% yield, black coloured and non-hygroscopic. The thermal stability of all the synthesized complexes indicated the presence of strong metal-ligand bonding in all these complexes. All the complexes were soluble in DMSO and DMF.

3.2. Molar Conductance

The recorded values of molar conductance for all the synthesized complexes (0.12–0.29 (Cm²/Ohm.Mol) are very low indicating their non-electrolytic nature [20].

3.3. Magnetic Measurements

The observed values of magnetic moments (1.72 to 1.87 B.M.) indicated presence of one unpaired electron in these complexes [20]. Table 1 represents results obtained from molar conductance and magnetic susceptibility measurements, along with elemental analysis data recorded for all the synthesized mixed ligand complexes.

3.4. IR Spectra

The broad peak observed in the range of 3410 to 3442 cm⁻¹ can be assigned due to the symmetric stretching of O-H bond in free 8-hydroxyquinoline molecule. This peak was absent in case of complexes which indicated complex formation between vanadium and 8-hydroxyquinoline through oxygen atom of –OH group.

The broad peak at 2920–2972 cm⁻¹ due to –NH vibrations in free amino acids are shifted to higher wave number in the range 2981–3057 cm⁻¹ in IR spectra of metal complexes. This indicated that amino group is bonded to the metal through nitrogen atom [14]. The C=N stretching vibration peak observed at 1580 cm⁻¹ in the free 8-hydroxyquinoline ligand is shifted to lower wave number up to 1460–1465 cm⁻¹ in IR spectra of complexes indicating coordination of 8-hydroxyquinoline molecule with vanadium metal through ternary nitrogen.

The asymmetric and symmetric (COO⁻) bands observed in the region 1580–1597 and 1402–1408 cm⁻¹ in spectra of free amino acids were shifted to lower wave numbers region of 1571–1575 and 1373–1377 cm⁻¹ respectively in complexes. This indicated the bonding of COO⁻ group with vanadium

metal with oxygen atom of the carboxylic group of amino acids. The peak due to $\nu(V=O)$ stretching vibrations was observed between 945–950 cm⁻¹ in the spectra of complexes. Finally the bands observed in the range of 445–447 cm⁻¹ and 621–632 cm⁻¹ indicated $\nu(M-N)$ and $\nu(M-O)$ bonding in complexes, respectively Figs. (1A-E).

3.5. Electronic Spectra

Room temperature electronic absorption spectra of all the synthesized mixed ligand complexes were recorded using a freshly prepared solution in DMSO. Three absorption bands were observed in case of all the five complexes.

The first band at 203–264 nm indicated $\pi \rightarrow \pi^*$ transition due to aromatic rings of ligand. The second peak observed in the range 364–501 nm in electronic spectra of complexes indicated charge transfer transition from ligand to metal atom (LMCT) [20].

Third absorption band observed in the region 479–791 nm in electronic spectra of complexes can be caused due to $d \rightarrow d^*$ transition of the central metal vanadium [21]. The results obtained from electronic spectra of all the complexes indicated the presence of square pyramidal geometry in all these complexes [22] Figs. (2A-E).

3.6. Mass Spectra

The ESI-MS spectra of complexes HQ-4 and HQ-5 were recorded as a representative case. The peaks of appreciable intensity were observed in both these complexes viz. peaks at m/z 146, 252, 301, 338, 355, 437, 453, 582, 727 and 749 for HQ-4 complex and 146, 252, 355, 301, 413, 582, 727 and 749 for HQ-5 complex. The peak at m/z 338 in mass spectrum of HQ-4 and at m/z 301 in mass spectrum of HQ-5 complexes is nearest to the compositions of complexes HQ-4 [C₁₃H₁₄N₂O₅V] and HQ-5 [C₁₂H₁₂N₂O₅V], respectively [23] Figs. (3A-B).

Table 1. Physicochemical data of the synthesized complexes.

Proposed Molecular Formula	Elemental Analysis Percentage of Elements Obtained						Percentage Yield (%)	Molar Conductance (Mhos mol ⁻¹ cm ²)	M _{eff} (B.M.)
	C	H	N	O	S	M(V)			
HQ-1 C ₁₂ H ₁₂ N ₂ O ₄ SV	43.51 (43.47)	3.65 (3.62)	8.46 (8.45)	19.32 (19.34)	9.68 (9.66)	15.38 (15.39)	78%	0.12	1.75
HQ-2 C ₁₂ H ₁₂ N ₂ O ₄ V	48.18 (48.13)	4.04 (4.01)	9.36 (9.35)	21.39 (21.39)	---	17.03 (17.04)	72%	0.21	1.84
HQ-3 C ₁₈ H ₁₆ N ₂ O ₄ V	57.61 (57.56)	4.30 (4.26)	7.46 (7.45)	17.05 (17.05)	---	13.57 (13.59)	70%	0.18	1.87
HQ-4 C ₁₃ H ₁₄ N ₂ O ₅ V	47.43 (47.38)	4.29 (4.25)	8.51 (8.50)	24.30 (24.30)	---	15.47 (15.49)	75%	0.26	1.72
HQ-5 C ₁₂ H ₁₂ N ₂ O ₅ V	45.73 (45.68)	3.84 (3.80)	8.89 (8.88)	25.38 (25.38)	---	16.16 (16.18)	78%	0.29	1.73

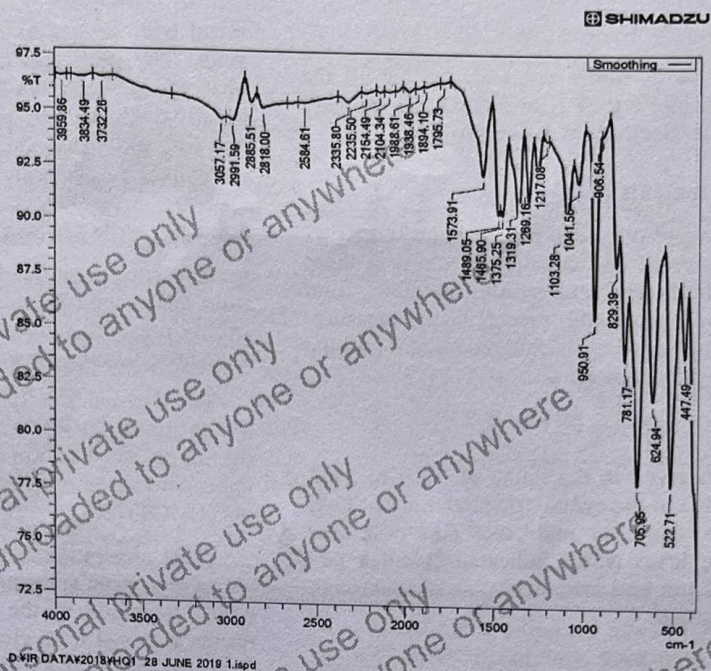


Fig. (1A). IR Spectra of HQ-1.

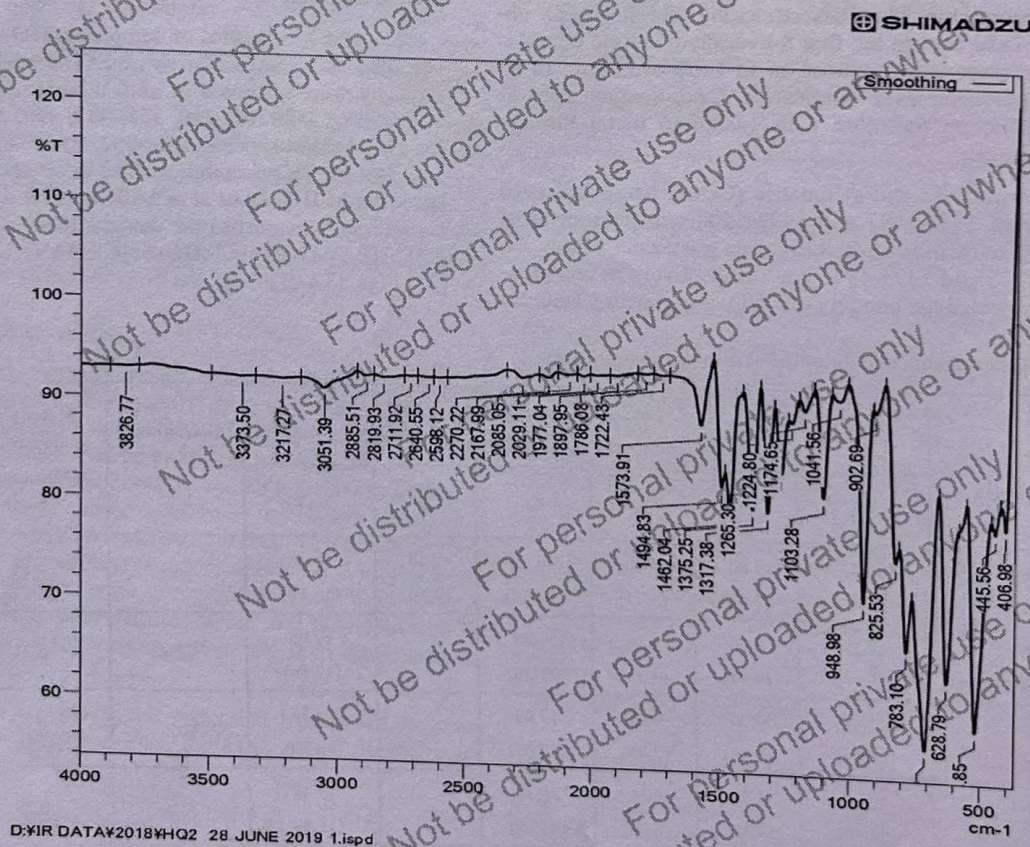


Fig. (1B). IR Spectra of HQ-2.

(Fig. 1) contd....

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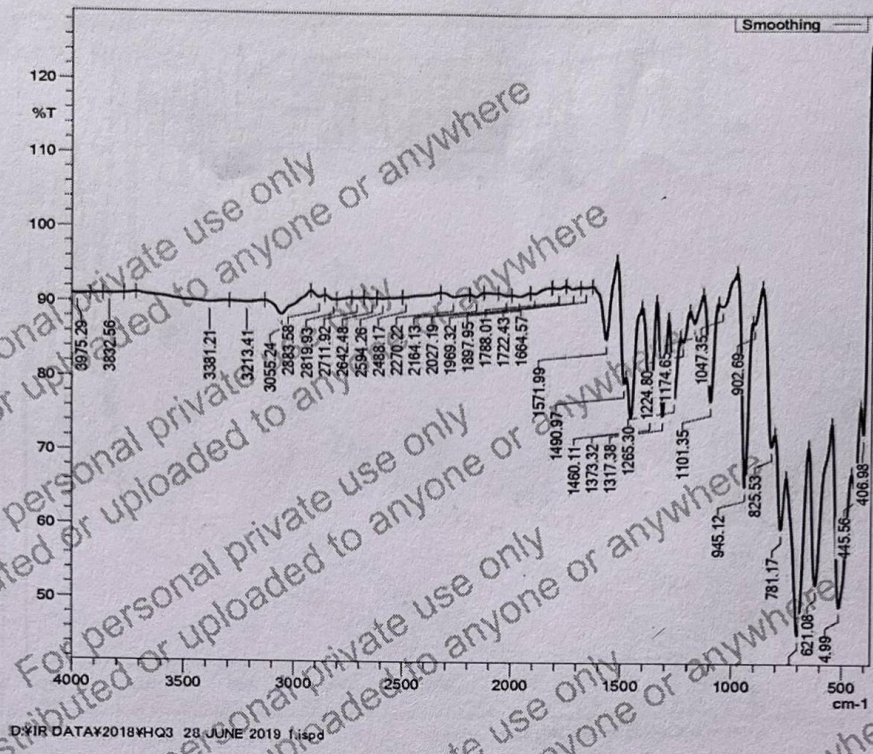


Fig. (1C). IR Spectra of HQ-3.

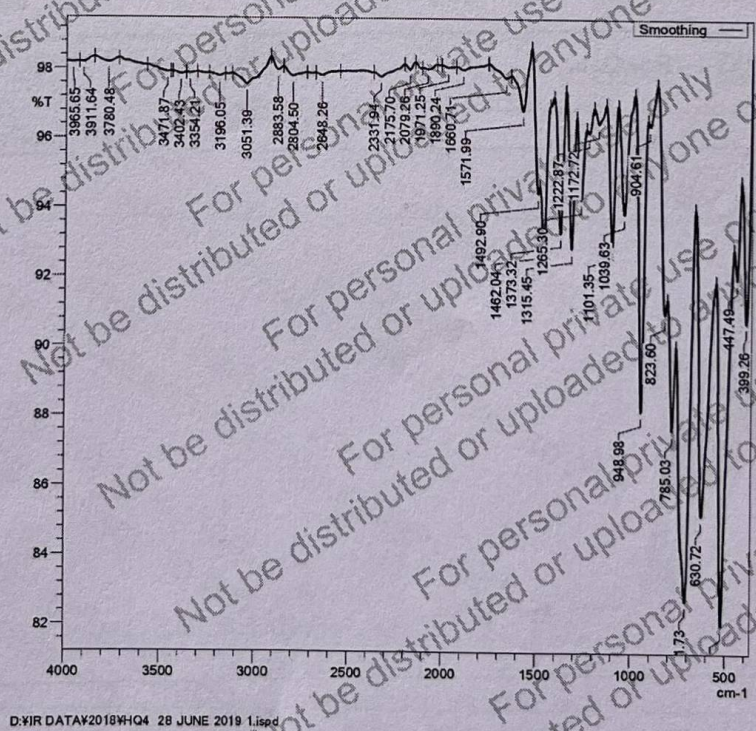
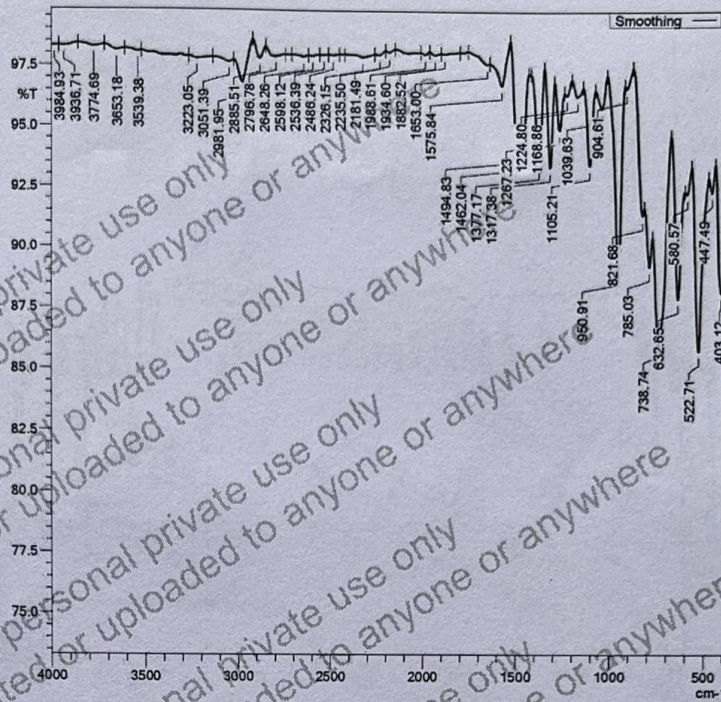


Fig. (1D). IR Spectra of HQ-4.

(Fig. 1) contd....

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Fig. (1E). IR Spectra of HQ-5.

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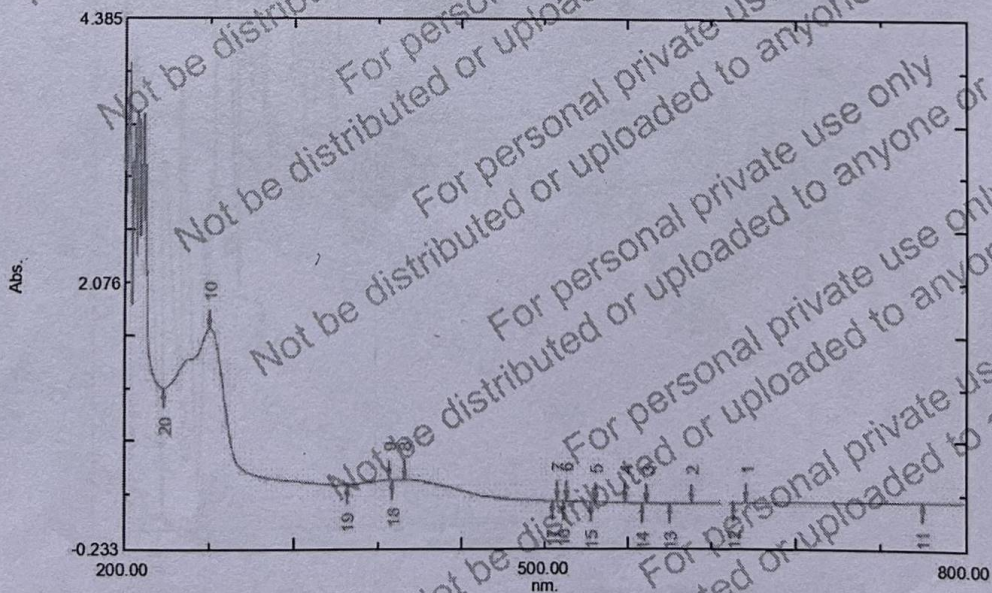


Fig. (2A). UV Visible Spectra of HQ-1. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

(Fig. 2) contd....

Spectrum Peak Pick Report

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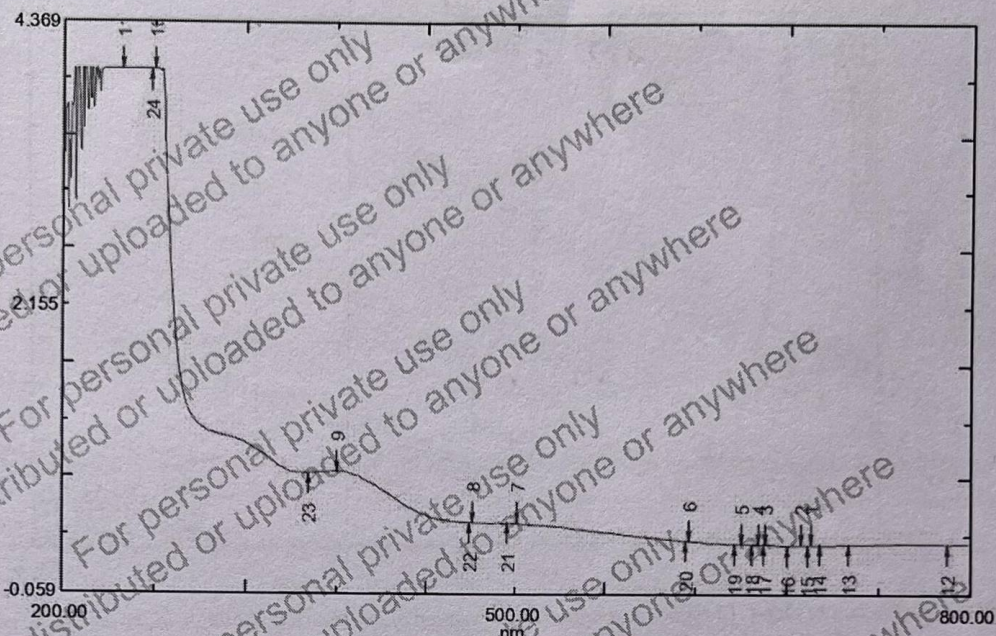


Fig. (2B). UV Visible Spectra of HQ-2. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

Spectrum Peak Pick Report

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Data Set: HQ-3 - RawData

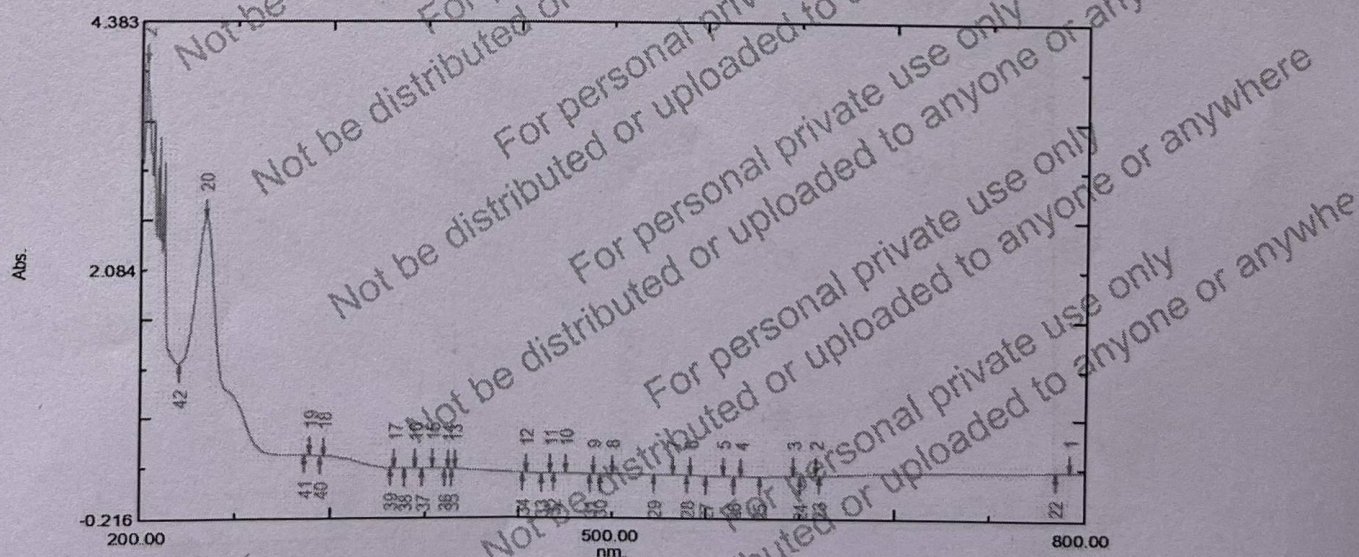


Fig. (2C). UV Visible Spectra of HQ-3. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

(Fig. 2) contd....

Spectrum Peak Pick Report

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Data Set: HQ-4 - RawData

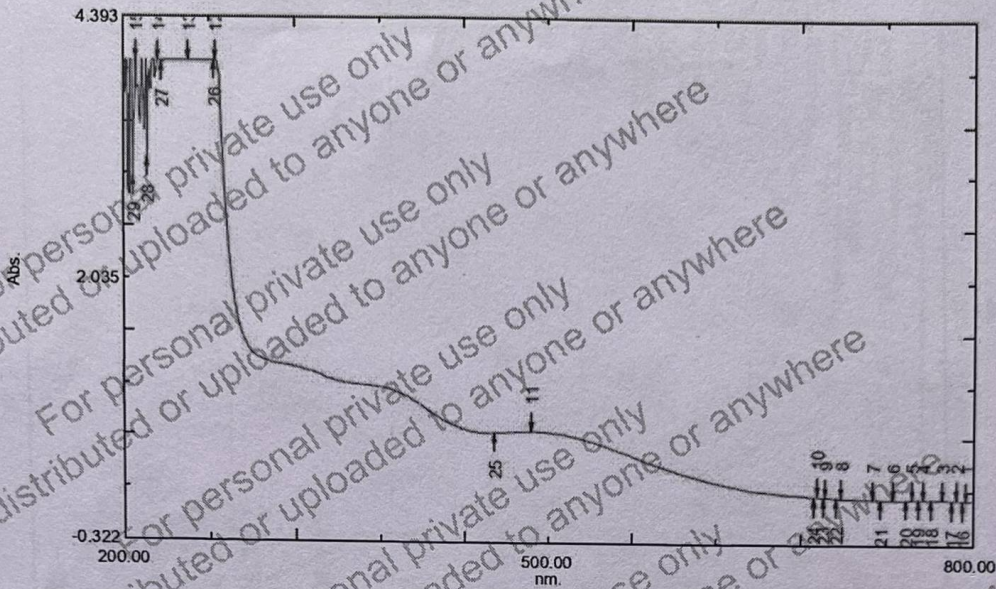


Fig. (2D). UV Visible Spectra of HQ-4. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

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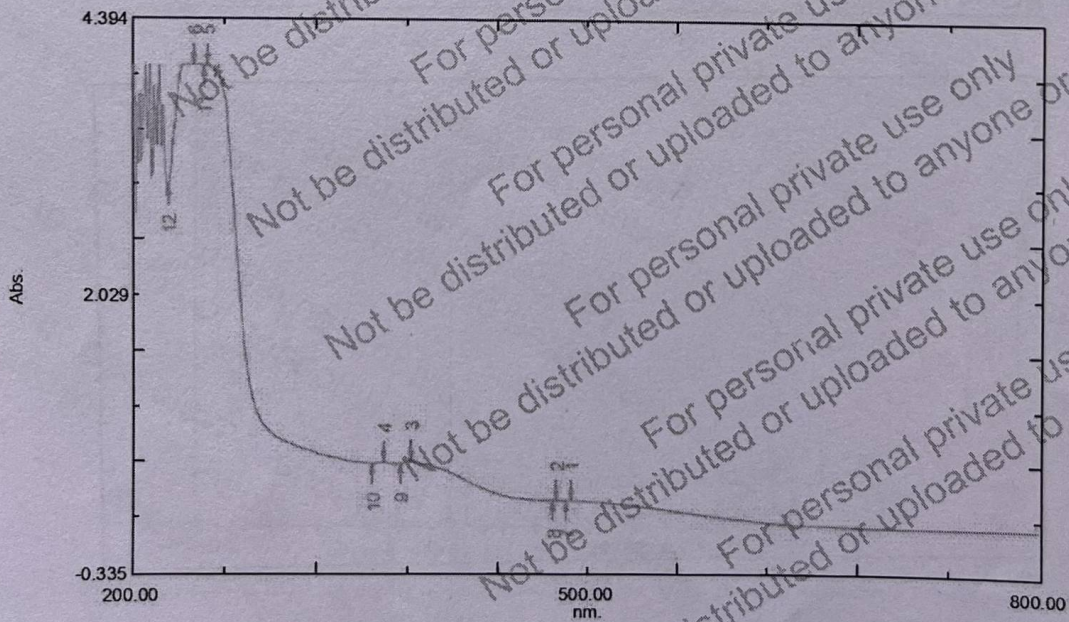


Fig. (2E). UV Visible Spectra of HQ-5. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

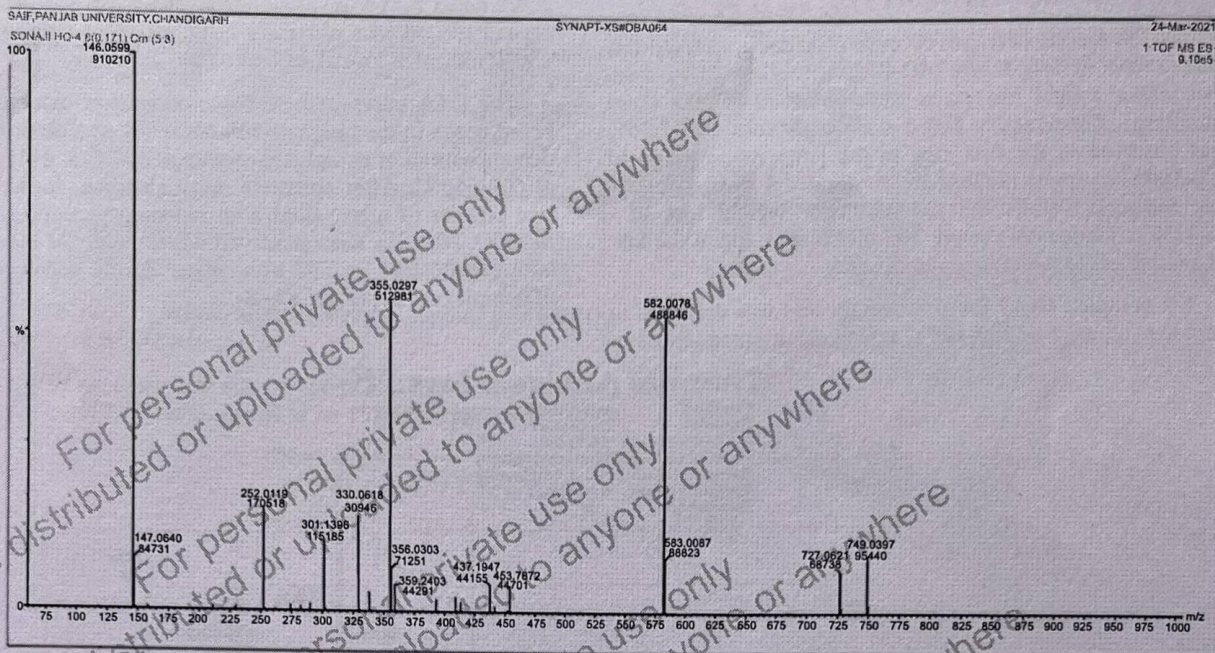


Fig. (3A). Mass Spectra of HQ-4. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

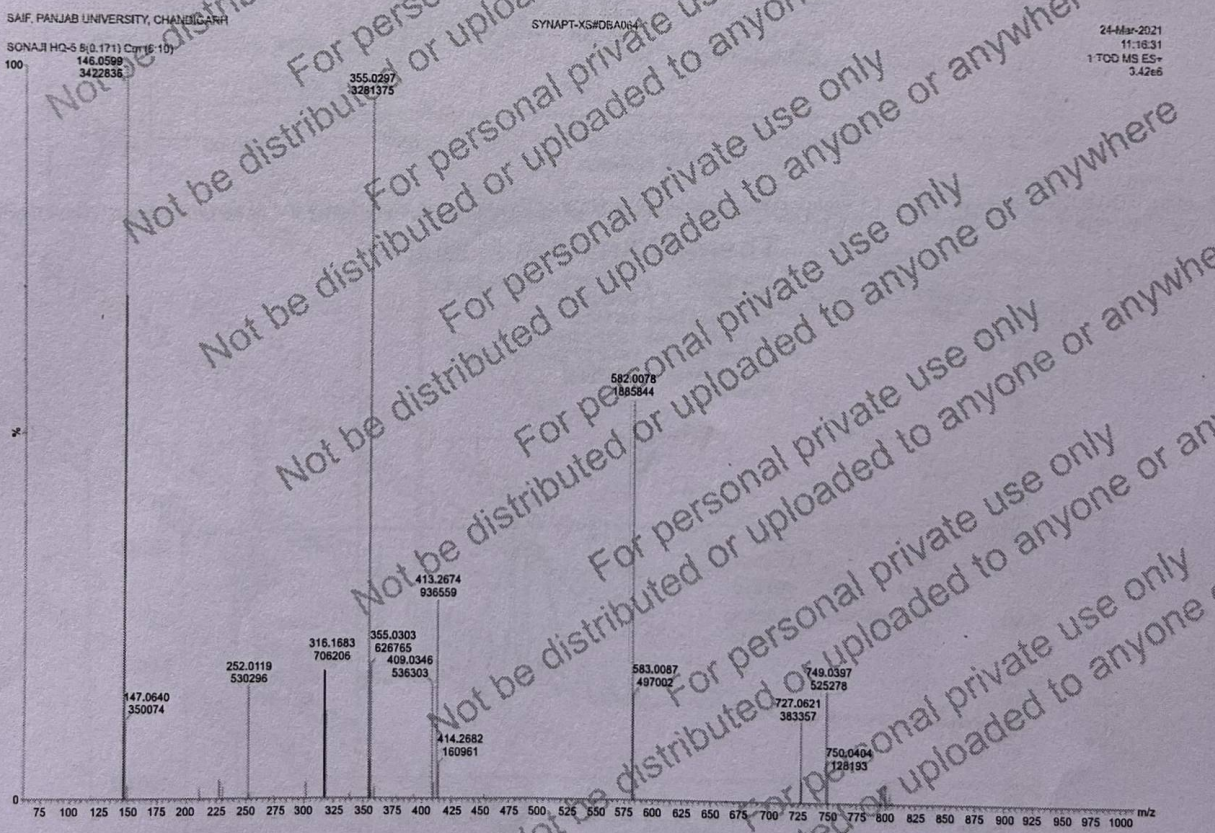


Fig. (3B). Mass Spectra of HQ-5. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

3.7. Thermal Analysis (TGA/DTA)

The TGA and DTA curves were recorded for mixed ligand complexes **HQ-1** and **HQ-2** as a representative case. Two major weight loss steps were observed in both these complexes. For complex **HQ-1** the weight loss of -37.36% was observed in the first step in the temperature range of 220-300°C owing to the loss of coordinated 8-hydroxyquinoline molecule. While the second major weight loss of -47.13% in temperature range 300-600°C was due to the loss of another coordinated ligand molecule.

For complex **HQ-2** the first weight loss was observed in temperature range of 250-400°C which is attributed to loss of

coordinated 8-hydroxyquinoline ligand molecule. While the second weight loss observed in temperature range of 400-650°C indicated loss of second ligand molecule.

The DTA curve of both these complexes exhibited two broad peaks in the range of 300-650°C. It was observed that decomposition of complex is started at 300°C and completed at 600-650°C. After complete decomposition, formation of fine powder of metal atom with reducing gaseous products like CO, NH₃ etc. were observed which confirms the loss of both coordinated ligands from metal during decomposition of complexes [24] (Figs. 4A-B).

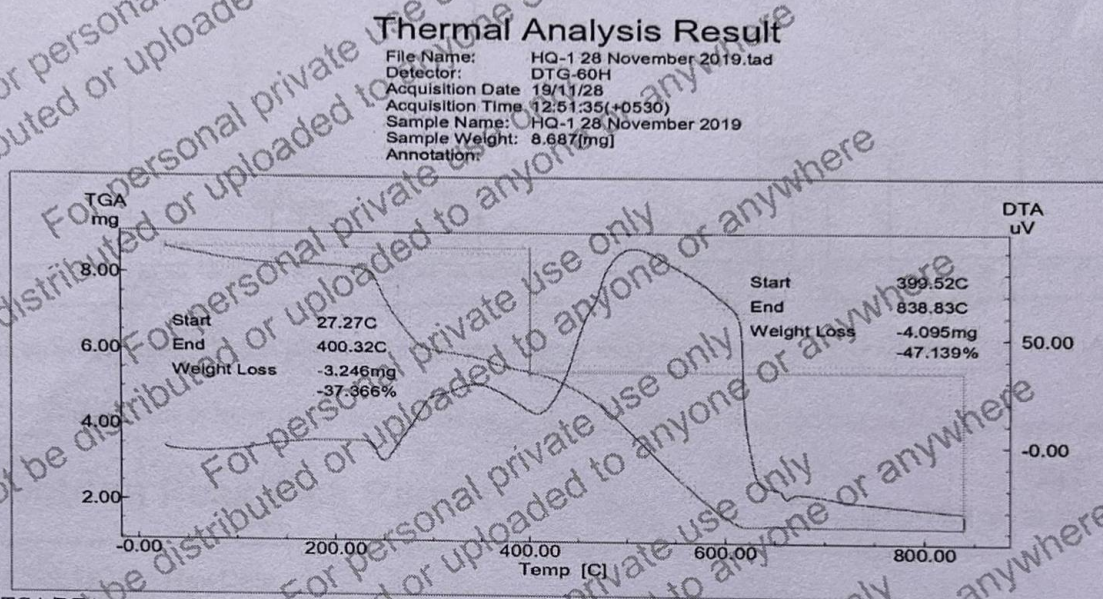


Fig. (4A). TGA/DTA curves of HQ-1. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

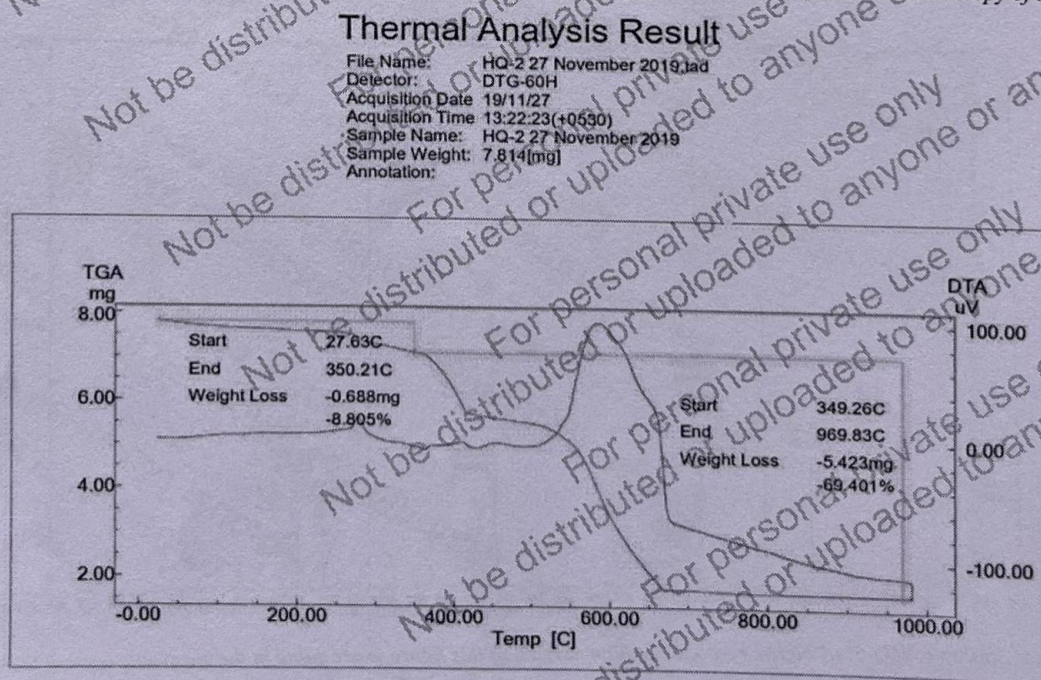


Fig. (4B). TGA/DTA curves of HQ-2. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

3.8. Powder XRD Analysis

Powder XRD analysis was performed to study the nature of synthesized mixed ligand complexes. The XRD pattern indicated microcrystalline nature of complexes. The particle sizes of complexes were calculated using Scherer's formula [25] given as in equation (2)

$$\text{Particle size (D)} = \frac{0.9 \lambda}{\beta \cos \theta} \quad (2)$$

Where, λ = wavelength of x-ray radiation, β = FWHM and θ = diffraction angle.

The mean particle size of complexes HQ-1, HQ-2, HQ-3, HQ-4 and HQ-5 was found to be 15.75, 24.98, 10.60, 37.26

and 25.86 nm respectively. The inter planner spacing (d) of complexes were calculated by using equation proposed by Bragg (3). All the synthesized complexes show microcrystalline nature Figs. (5A-E)

$$n\lambda = 2d\sin\theta \quad (3)$$

Where, λ = Wavelength of x-ray, and θ = angle of diffraction.

Table 2 represents the results obtained from powder XRD analysis for all the synthesized mixed ligand complexes.

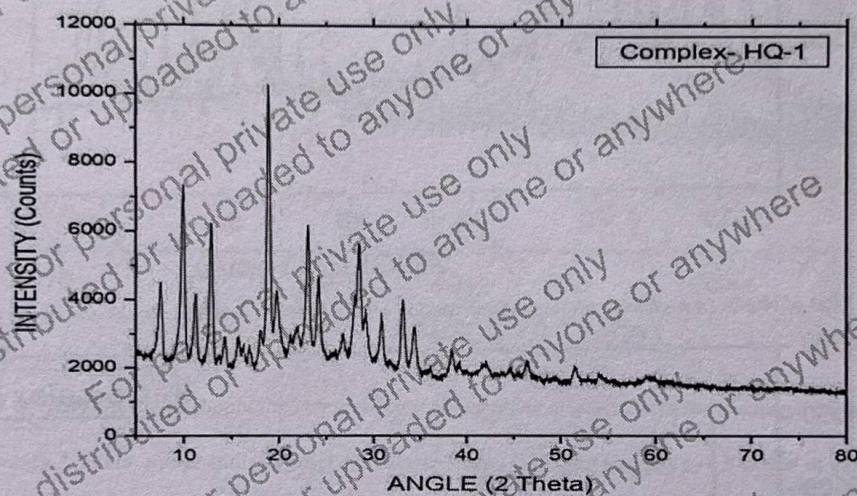


Fig. (5A). Powder XRD of HQ-1. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

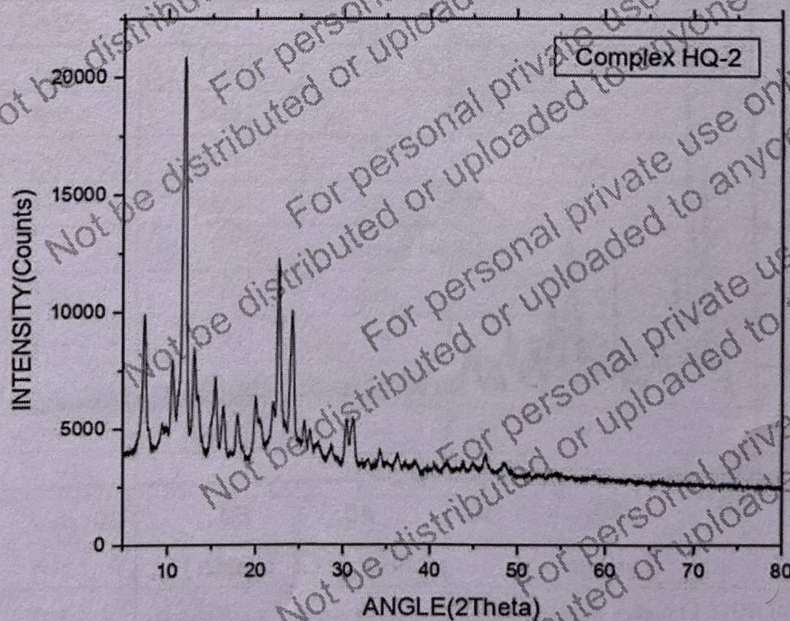


Fig. (5B). Powder XRD of HQ-2. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

(Fig. 5) Contd....

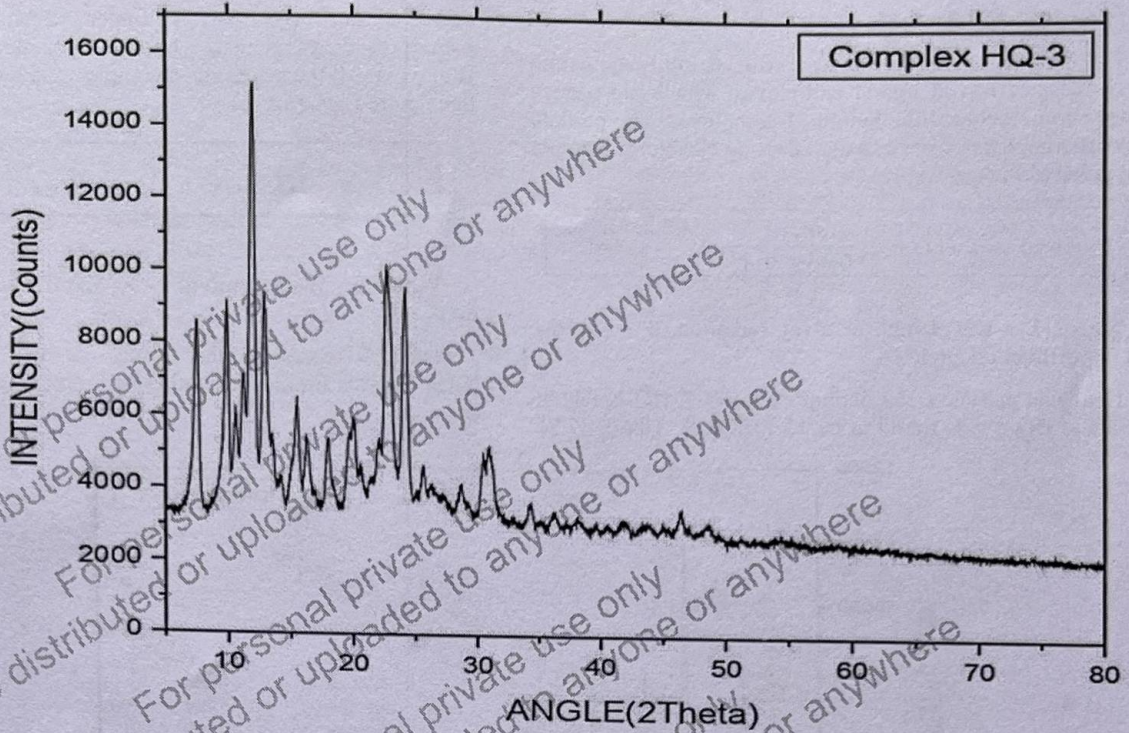


Fig. (5C). Powder XRD of HQ-3. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

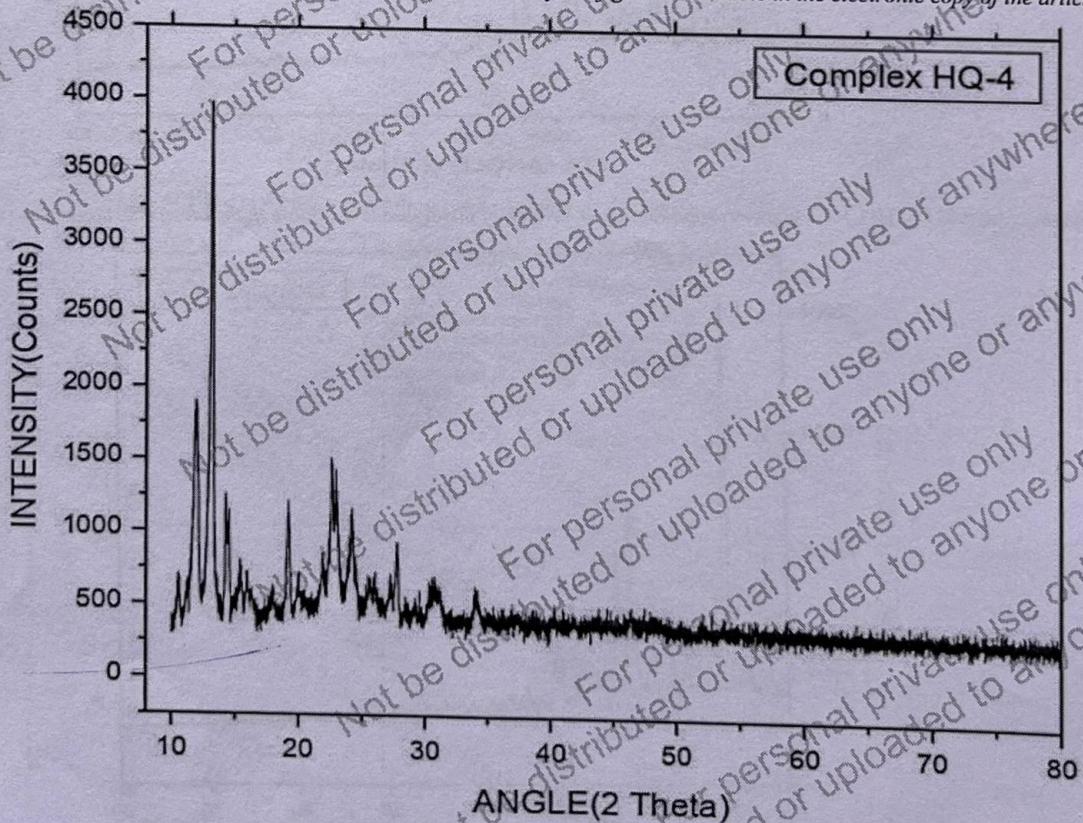


Fig. (5D). Powder XRD of HQ-4. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

(Fig. 5) Contd....

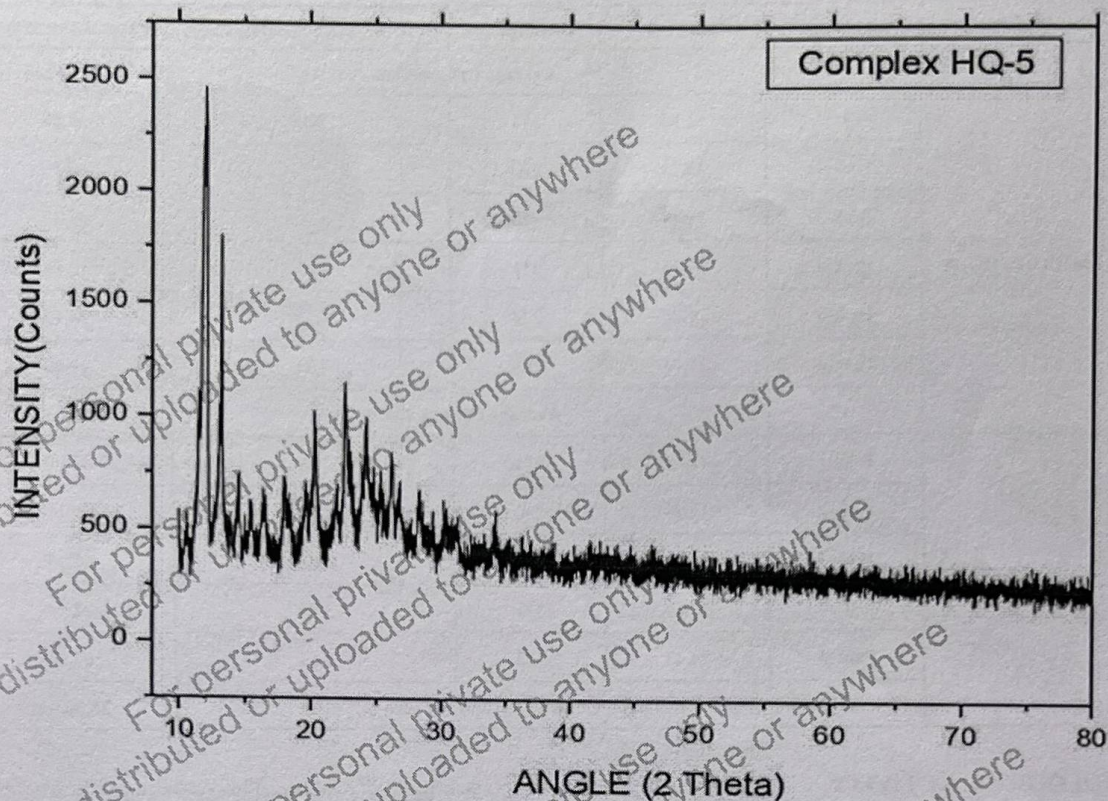


Fig. (5E). Powder XRD of HQ-5. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

Table 2. Powder XRD data 2 Theta, miller indices, Inter planner spacing (d) crystal size (D) and FWHM of complexes.

Complex	Reflexes	2-Theta	Miller Indices	Inter Planner Spacing d (Å)	Crystal Size D (nm)	FWHM
C ₁₂ H ₁₂ N ₂ O ₄ SV (HQ-1)	Peak-1	9.94	111	8.89	08.92	1.5587
	Peak-2	12.81	210	6.90	31.18	0.4474
	Peak-3	18.85	311	4.70	26.62	0.5278
	Peak-4	22.79	400	3.95	03.18	4.9398
	Peak-5	28.50	422	3.12	08.85	1.6146
	Average Crystal Size					15.75 nm
C ₁₂ H ₁₂ N ₂ O ₄ V (HQ-2)	Peak-1	7.41	111	11.9	24.50	0.5669
	Peak-2	11.90	220	7.42	28.51	0.4888
	Peak-3	22.65	511	3.92	22.52	0.6275
	Peak-4	24.15	521	3.68	24.38	0.5813
	Average Crystal Size					24.98 nm
C ₁₈ H ₁₆ N ₂ O ₄ V (HQ-3)	Peak-1	11.96	111	7.39	07.60	1.8320
	Peak-2	19.90	220	4.45	12.97	1.0847
	Peak-3	22.97	311	3.86	07.42	1.9058
	Peak-4	30.80	420	2.89	14.68	0.9789

(Table 2) contd....

Complex	Reflexes	2-Theta	Miller Indices	Inter Planner Spacing d (Å)	Crystal Size D (nm)	FWHM
		Average Crystal Size			10.60 nm	
C ₁₃ H ₁₄ N ₂ O ₅ V (HQ-4)	Peak-1	11.89	111	7.44	32.68	0.4265
	Peak-2	13.13	200	6.74	47.59	0.2932
	Peak-3	19.18	220	4.62	55.17	0.2548
	Peak-4	22.73	311	3.90	15.84	0.8920
	Peak-5	24.20	222	3.67	24.19	0.5859
	Peak-6	27.75	400	3.21	48.09	0.2969
		Average Crystal Size			37.26 nm	-
C ₁₂ H ₁₂ N ₂ O ₅ V (HQ-5)	Peak-1	11.96	111	7.39	33.08	0.4213
	Peak-2	13.21	200	6.70	49.11	0.2842
	Peak-3	20.24	221	4.38	17.44	0.873
	Peak-4	22.64	311	3.92	22.14	0.6385
	Peak-5	24.43	222	3.63	07.54	1.8807
			Average Crystal Size			25.86 nm

4. BIOLOGICAL ACTIVITY

4.1. Antimicrobial Activity

All the synthesized mixed ligand complexes were screened for their antibacterial activity against *E. coli* using well plate method [16] and for antifungal activity against *C. albicans* using well diffusion method [16]. Graph-1 represents graphical representation of antibacterial activity.

The complexes HQ-3 and HQ-4 exhibited zones of inhibition 21 and 20 mm respectively which is almost equal to that of standard drug streptomycin (21 mm). Hence, these two complexes exhibit excellent antibacterial activity against *E. Coli*.

Out of the remaining complexes, HQ-1 and HQ-5 complexes exhibited moderate to good activity with a zone of inhibition values of 17 and 12 mm respectively, whereas HQ-2 complex exhibited moderate activity with zone of inhibition 9 mm. All the synthesized mixed ligand complexes were found to be poor in terms of antifungal activity with zone of inhibition values ranging from 0 to 7 mm as compared to standard drug with zone of Inhibition value of 16 mm [14, 26-27].

4.2. Antidiabetic Activity by α -Amylase Inhibition

Graph 2 represents graphical presentation of the results obtained from antidiabetic activity i.e. percent inhibition of α -amylase inhibitory assay for all the synthesized mixed ligand complexes.

The complexes HQ-4 and HQ-5 have recorded percent inhibition values of 46.80 and 57.44%, indicating good activity exhibited by these complexes as compared to standard

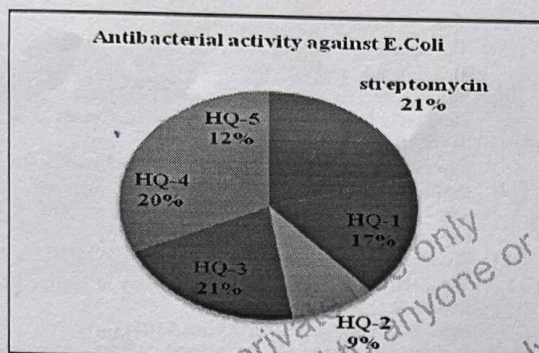
acarbose (72.34%). The remaining three complexes HQ-1, HQ-2 and HQ-3 exhibited poor activities (i.e. 19.14, 21.27 and 02.21% inhibition), respectively.

Two complexes HQ-4 and HQ-5 were screened for their anticancer activity and cytotoxicity study using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay. The human liver cell line HepG2 was used to assess the cytotoxicity [18-19]. The cancer cell line used in this work was selected based on easy availability and wide use found in literature survey with cisplatin. Analysis was done by measuring the absorbance of each sample using microplate reader at a wavelength of 550 nm in triplicate. Measurements were performed and IC₅₀ i.e. the concentration required for a 50% inhibition of viability, was determined graphically.

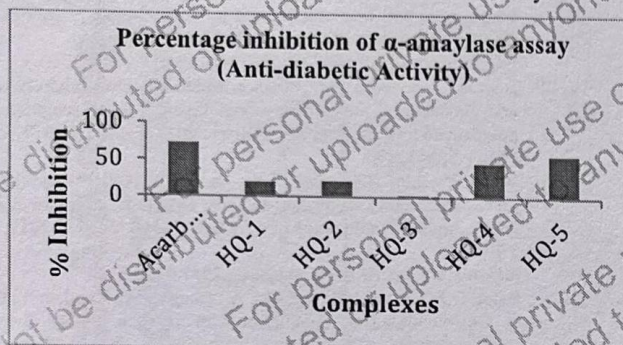
4.3. Anticancer Study using MTT Assay

To evaluate cytotoxicity against human hepatocarcinoma (HepG2) cells, the complexes HQ-4 and HQ-5, were incubated with different doses (10, 30 and 100 μ g/mL) for 24h and MTT assay was used to determine the cell viability. Graph-3 represents graphical presentation of the results obtained from anticancer activity.

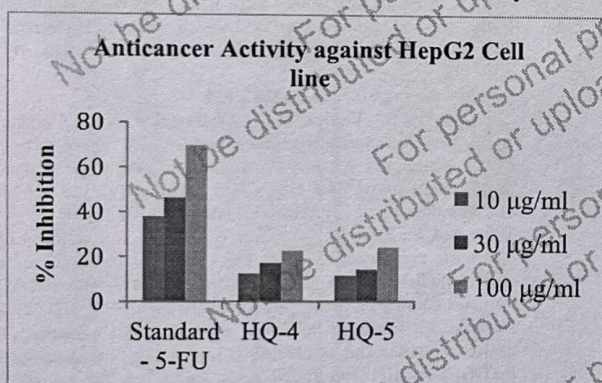
The IC₅₀ values above 100 μ M are noted for both these complexes, which indicates both these complexes were able to inhibit proliferation of the HepG2 cancer cells [18]. The cell viability values were within the expected range i.e. 75-90%, indicating these complexes were more toxic i.e. 75-90% than normal cells. The observed results indicated that both these complexes can be considered potential anticancer agents.



Graph 1. Graphical representation of antibacterial activity.



Graph 2. Graphical representation of Antidiabetic activity.



Graph 3. Graphical representation of anticancer activity.

CONCLUSION

The obtained results indicated square pyramidal geometry for all the synthesized mixed ligand complexes (HQ-1 to HQ-5). The complexes HQ-3 and HQ-4 exhibited excellent antibacterial activities against *E. coli* i.e. close to that of standard streptomycin which seems to be inspiring and indicates towards antibacterial potential of these complexes. The complexes HQ-4 and HQ-5 exhibited good percent inhibition of α -amylase activities as compared to standard acarbose and have good antidiabetic activities. The IC_{50} values recorded for complexes HQ-4 and HQ-5 indicated the potential of these complexes as anticancer agents.

LIST OF ABBREVIATION

BGL	=	Blood Glucose Levels
DM	=	Diabetes Mellitus
DMF	=	Dimethyl Formamide
DMSO	=	Dimethyl Sulfoxide
DTA	=	Differential Thermal Analysis
FWHM	=	Full Width Half Maximum
TGA	=	Thermogravimetric Analysis
XRD	=	X-ray Diffraction

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that were the basis of this research.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

REFERENCES

- [1] Jevtović, V.; Ivković, S.; Kaisarević, S.; Kovačević, R. Anticancer activity of new copper(II) complexes incorporating a pyridoxal-semicarbazone ligand. *Contemp. Mater.* **2010**, *1*(2), 133-137. <http://dx.doi.org/10.5767/anurs.cmat.100102.en.1331>
- [2] Zhang, H.; Yuefao, Y.; Dawei, F.; Yipeng, W.; Song, Q. Hypoglycemic properties of Oxovanadium (IV) coordination compounds with carboxymethyl-carrageenan and carboxymethyl-chitosan in alloxan-induced diabetic mice. *Evid Based Complement Alternat Med*, **2011**, *2011*, 691067. <http://dx.doi.org/10.1155/2011/691067>
- [3] Mariappan, G.; Saha, B.P.; Datta, S.; Kumar, D.; Haldar, P.K. Design, synthesis and antidiabetic evaluation of oxazolone derivatives. *J. Chem. Sci.* **2011**, *123*(3), 335-341. <http://dx.doi.org/10.1007/s12039-011-0079-2>
- [4] Shukla, S.N.; Gaur, P.; Jhariya, S.; Chaurasia, B.; Vaidya, P.; Debariya, D.; Azam, M. Synthesis, characterization, *in vitro* anti-diabetic, antibacterial and anticorrosive activity of some Cr(III) complexes of

- schiff bases derived from isoniazid. *Chem. Sci. Trans.*, **2018**, *7*(3), 424-444.
<http://dx.doi.org/10.7598/cst2018.1509>
- [5] Mukherjee, B.; Patra, B.; Mahapatra, S.; Banerjee, P.; Tiwari, A.; Chatterjee, M. Vanadium—an element of atypical biological significance. *Toxicol. Lett.*, **2004**, *150*(2), 135-143.
<http://dx.doi.org/10.1016/j.toxlet.2004.01.009>
 PMID: 15093669
- [6] Korbecki, J.; Baranowska-Bosiacka, I.; Gutowska, I.; Chlubek, D. Biochemical and medical importance of vanadium compounds. *Acta Biochim. Pol.*, **2012**, *59*(2), 195-200.
http://dx.doi.org/10.18388/abp.2012_2138 PMID: 22693688
- [7] Crans, D.C. Chemistry and insulin-like properties of vanadium(IV) and vanadium(V) compounds. This manuscript summarizes the presentation given at the symposium 'Biological Aspects of Vanadium Chemistry — Chemistry, Biochemistry and Therapeutic Applications of Vanadium Compounds' and recently communicated in original research articles. The original research articles describing the experimental details of this work are given in Refs: [1-5]. *J. Inorg. Biochem.*, **2000**, *80*(1-2), 123-131.
[http://dx.doi.org/10.1016/S0162-0134\(00\)00048-9](http://dx.doi.org/10.1016/S0162-0134(00)00048-9) PMID: 10885472
- [8] Willsky, G.R.; Chi, L.H.; Gódzala, M., III; Kostyniak, P.J.; Smec, J.J.; Trujillo, A.M.; Alfano, J.A.; Ding, W.; Hu, Z.; Crans, D.C. Anti-diabetic effects of a series of vanadium dipicolinate complexes in rats with streptozotocin-induced diabetes. *Coord. Chem. Rev.*, **2011**, *255*(19-20), 2258-2269.
<http://dx.doi.org/10.1016/j.ccr.2011.06.015> PMID: 23049138
- [9] Yuan, C.; Lu, L.; Gao, X.; Wu, Y.; Guo, M.; Li, Y.; Fu, X.; Zhu, M. Ternary oxovanadium(IV) complexes of ONO-donor Schiff base and polypyridyl derivatives as protein tyrosine phosphatase inhibitors: Synthesis, characterization, and biological activities. *J. Biol. Inorg. Chem.*, **2009**, *14*(6), 841-851.
<http://dx.doi.org/10.1007/s00775-009-0496-6> PMID: 19290551
- [10] Li, M.; Ding, W.; Smec, J.J.; Baruah, B.; Willsky, G.R.; Crans, D.C. Anti-diabetic effects of vanadium(III, IV, V)-chlorodipicolinate complexes in streptozotocin-induced diabetic rats. *Biomaterials*, **2009**, *22*(6), 895-905.
<http://dx.doi.org/10.1007/s10534-009-9241-4> PMID: 19404749
- [11] Fedorova, E.V.; Buryakina, A.V.; Zakharov, A.V.; Filimonov, D.A.; Lagunin, A.A.; Poroikov, V.V. Design, synthesis and pharmacological evaluation of novel vanadium-containing complexes as antidiabetic agents. *PLoS One*, **2014**, *9*(7), e100386.
<http://dx.doi.org/10.1371/journal.pone.0100386> PMID: 25057899
- [12] Sanoja, W.; Martínez, J.D.; Araujo, M.L.; Brito, F.; Hernández, L.; Del Carpio, E.; Lubes, V. Stability constants of mixed ligand complexes of vanadium(III) with 8-hydroxyquinoline and the amino acids glycine, proline, α -alanine and β -alanine. *J. Mol. Liq.*, **2014**, *197*, 223-225.
<http://dx.doi.org/10.1016/j.molliq.2014.05.012>
- [13] Sarmiento, L.E.; Rodríguez, M.; Echevarría, L.; Lubes, V. Speciation of the Vanadium(III) complexes with 1,10-phenanthroline, 2,2'-bipyridine, and 8-hydroxyquinoline. *J. Solution Chem.*, **2010**, *39*(10), 1484-1491.
<http://dx.doi.org/10.1007/s10953-010-9603-0>
- [14] Patil, S.S.; Thakur, G.A.; Shaikh, M.M. Synthesis, characterization, and antibacterial studies of mixed ligand dioxouranium complexes with 8-hydroxyquinoline and some amino acids. *ISRN Pharm.*, **2011**, *2011*, 168539.
<http://dx.doi.org/10.5402/2011/168539>
- [15] Vogel, A.I. *Textbook of Practical Organic Chemistry*, 5th ed; Longman: London, **1989**.
- [16] Balouiri, M.; Sadiki, M.; Ibsouda, S.K. Methods for *in vitro* evaluating antimicrobial activity: A review. *J. Pharm. Anal.*, **2016**, *6*(2), 71-79.
<http://dx.doi.org/10.1016/j.jpha.2015.11.005> PMID: 29403965
- [17] Bernfeld, P. Amylases, α and β . *Methods Enzymol.*, **1955**, *1*, 149-158.
[http://dx.doi.org/10.1016/0076-6879\(55\)01021-5](http://dx.doi.org/10.1016/0076-6879(55)01021-5)
- [18] Senthilraja, P.; Kathiresan, K. *In vitro* cytotoxicity MTT assay in Yero, HepG2 and MCF -7 cell lines study of Marine Yeast. *J. Appl. Pharm. Sci.*, **2015**, *5*(3), 80-84.
<http://dx.doi.org/10.7324/JAPS.2015.50313>
- [19] Horiuchi, N.; Nakagawa, K.; Sasaki, Y.; Minato, K.; Fujiwara, Y.; Nezu, K.; Ohe, Y.; Saijo, N. *In vitro* antitumor activity of mitomycin C derivative (RM-49) and new anticancer antibiotics (FK973) against lung cancer cell lines determined by tetrazolium dye (MTT) assay. *Cancer Chemother. Pharmacol.*, **1988**, *22*(3), 246-250.
<http://dx.doi.org/10.1007/BF00273419> PMID: 2842080
- [20] Bodkhe, A.S.; Patil, S.S.; Shaikh, M.M. Synthesis, characterization and antibacterial studies on mixed ligand copper complexes with polydentate ligands. *Acta Pol. Pharm.*, **2012**, *69*(5), 871-877.
 PMID: 23061283
- [21] Wang, Y.; Lin, X.M.; Bai, F.Y.; Sun, L.X. Novel vanadium complexes with rigid carboxylate ligands: Synthesis, structure and catalytic bromine dynamics of phenol red. *J. Mol. Struct.*, **2017**, *1149*, 379-386.
<http://dx.doi.org/10.1016/j.molstruc.2017.07.015>
- [22] Bajju, G.D.; Sharma, P.; Kapahi, A.; Bhagat, M.; Kundan, S.; Gupta, D. Oxovanadium(IV) complexes with nitrogen donors: Synthesis, characterization, and biological activities. *J. Inorg. Chem.*, **2013**, *2013*(3).
<http://dx.doi.org/10.1155/2013/982965>
- [23] Mishra, A.P.; Pandey, L.R.; Jain, R.K. Microwave synthesis, reactivity, spectral and thermal analysis of some binary/mixed ligand Oxovanadium(IV) complexes. *Chem. Sci. Trans.*, **2012**, *1*(1), 121-133.
<http://dx.doi.org/10.7598/cst2012.135>
- [24] Shivankar, V.S.; Vaidya, R.B.; Dharwadkar, S.R.; Thakkar, N.V. Synthesis, characterization, and biological activity of mixed ligand Cu(II) complexes of 8-hydroxyquinoline and some amino acids. *Synth. React. Inorg. Met.-Org. Chem.*, **2003**, *33*(9), 1597-1622.
<http://dx.doi.org/10.1081/SIM-120025443>
- [25] Tabassum, S.; Zaki, M.; Arjmand, F.; Ahmad, I. Synthesis of hetero-bimetallic complexes: *In vitro* DNA binding, cleavage and antimicrobial studies. *J. Photochem. Photobiol. B*, **2012**, *114*, 108-118.
<http://dx.doi.org/10.1016/j.jphotobiol.2012.05.017> PMID: 22762922
- [26] Hossain, A.; Islam, M.S.; Alam, A.; Sultan, T. Synthesis, physico-chemical studies and antimicrobial screening of metal complexes of Fe(III) & Au(III) with amino acids. *Int. J. Sci. Techno. Res.*, **2013**, *2*(7), 210-217. [IJSTR]
- [27] Amolegbe, S.A.; Adewuyi, S.; Akinremi, C.A.; Adediji, J.F.; Lawal, A.; Atayese, A.O.; Obaleye, J.A. Iron(III) and copper(II) complexes bearing 8-quinolinol with amino-acids mixed ligands: Synthesis, characterization and antibacterial investigation. *Arab. J. Chem.*, **2015**, *8*(5), 742-747.
<http://dx.doi.org/10.1016/j.arabjc.2014.11.040>



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