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Green route for efficient synthesis of metal complexes of 4-bromo-2-((*E*)-((2-hydroxyphenyl)imino)methyl)-6-((*E*)-(3--nitrophenyl)diazenyl)phenol and its anti-hyperglycemia, anticancer and antimicrobial assessment

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Abstract The world is battling cancer and diabetes, prompting global research into effective drugs. Studies show coordination compounds, especially substituted salicylaldehydes, exhibit strong biological activity, which increases when treated with amines. In the presented article, the preparation of metal complexes involving Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and VO(II) was carried out using a Schiff base ligand that had been previously synthesized by grinding method of (*E*)-5-bromo-2-hydroxy-3-((3-nitrophenyl)diazenyl)benzaldehyde and 2-aminophenol. The synthesized Schiff base ligand was confirmed by mass, 1H-NMR and FT-IR spectra. The confirmation of the Schiff base ligand was followed by synthesis of metal complexes using metal salts of Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and VO(II). The synthesized metal complexes were analyzed by elemental analysis, FT-IR and electronic spectra, thermal analysis, X-ray powder diffraction, molar conductivity, *etc*. In the course of the biological studies, anti-hyperglycaemia and anticancer assessments of Schiff base ligand and metal complexes were carried out by alpha amylase inhibition assay and MTT assay against standard reference drug acarbose and 5-flourouracil (5-FU), respectively. The findings of the anti-hyperglycaemia suggest that Co(II) shows higher activity than other metals, wheras all metal complexes show more significant activity than free ligand. In the anticancer activity it is clear that Co(II) shows higher activity than other meal complexes; also, all metal complexes show higher activity than that of free ligand. In addition to this, the antimicrobial properties were examined against two Gram-positive bacterial strains (*Staphylococcus aureus* and *Bacillus subtilis*), two Gram-negative bacterial strains (*Klebsiella pneumoniae* and *Pseudo-*

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monas aeruginosa) and three fungal strains (*Penicillium chrysogenum*, *Trichoderma viride* and *Aspergillus niger*). From all the results and observations, it is clear that metal complexes exhibit better biological activity than Schiff base ligand.

Keywords: acarbose; 5-flourouracil; tetracycline; Schiff-base; anti-diabetic.

INTRODUCTION

The diseases, cancer and diabetes, have emerged as significant global health challenges, affecting population worldwide over the past three decades. Developing effective pharmaceutical interventions to combat these diseases presents a complex and critical task for researchers. Over the last two decades, coordination chemistry has gathered substantial scientific interest due to its extensive applications in the fields of biology and medicine. Schiff base ligands, when coordinated with transition metal ions, exhibit remarkable bioactive properties that amplify various pharmacological activities including anticancer,[1] antidiabetic,[2] antifungal,[3] antibacterial,[4–6] antioxidant,[2,7] antiviral, antimalarial, antitumor, antituberculosis,[8] anthelmintic, anti-HIV, antidiuretic, anti-inflammatory, antiprotozoal, anticonvulsant, analgesic, anti-Alzheimer's, anti-hypertensive, anti-ulcerative and other therapeutic functions. The versatility and efficacy of Schiff base metal complexes highlight their potential as promising candidates in drug discovery and development.[9–21] The azomethine linkage, in the presence of oxygen, nitrogen and sulfur donor atoms, plays a critical role in enhancing biological properties and facilitating the coordination of metal complexes. The interaction of metal ions with such biologically active compounds can significantly augment their pharmacological efficacy.[22] Green chemistry provides a sustainable alternative to traditional methods of drug molecule synthesis, emphasizing eco-friendly and non-toxic approaches. This methodology not only minimizes environmental hazards but also enhances reaction efficiency by reducing time consumption and achieving a product yield of 70–90 %. Furthermore, green chemistry promotes environmental sustainability by eliminating the use of harmful solvents and excessive energy consumption, aligning with the principles of resource conservation and ecological balance.

The Azo-Schiff base ligand has garnered significant scientific attention for its role in the formation of coordination compounds, as well as its broad spectrum of biological activities when complexed with metal ions. These activities include antibacterial, antifungal, anticonvulsant, antimalarial and anticancer properties.[23–26] Previously, various types of Azo-Schiff base ligands, along with their metal complexes, have been effectively employed as catalysts in numerous organic reactions, such as the oxidation and reduction of both saturated and unsaturated compounds.[27–29] Building on this foundation and after an extensive literature review, we synthesized the ligand 4-bromo-2-((*E*)-((2-hydroxyphenyl)imino)methyl)-6-

-((*E*)-(3-nitrophenyl)diazenyl)phenol using the azo aldehyde (*E*)-5-bromo-2-hydroxy-3-((3-nitrophenyl)diazenyl)benzaldehyde. The synthesis was accomplished *via* a green chemistry approach using a simple grinding method and was characterized through various spectroscopic techniques to confirm the structure of the products. Furthermore, we coordinated this ligand with transition metal salts to generate corresponding metal complexes.

These metal complexes, along with the ligand, were subjected to an array of biological assays, including antimicrobial, anticancer and anti-hyperglycemic evaluations, against standard drugs references. The results revealed that the metal complexes exhibit superior pharmacological potential compared to the Schiff base ligand alone when benchmarked against standard drugs.

EXPERIMENTAL

Material and methods

All the chemicals such as aldehyde (5-bromosalicylaldehyde), amines (2-aminophenol) were used as received from the Sigma Aldrich Private Limited. The various metal salts such as manganese (II), cobalt (II), nickel (II), copper (II) and zinc (II) acetate and vanadium (II) oxysulphate were procured from Sigma Aldrich and utilized without any further modifications. The solvents like ethyl alcohol, *n*-hexane, ethyl acetate, and petroleum ether were demanded from the local vendor and used after purification by distillation method. The reaction progress was periodically monitored using thin layer chromatography (TLC) with silica gel coated on aluminum foil. A mixture of *n*-hexane and ethyl acetate served as the mobile phase. The physical constant of the synthesized Schiff base ligand as well as metal complexes were taken on digital melting point instrument named as Optic Technology. The elemental analysis was carried out on Vario EL Cube. ^{1}H-NMR spectra were recorded on the instrument Bruker 400 MHz ^{1}H-NMR by using $CDCl_3$ solvent. The MALDI TOF-mass spectrum instrument was utilized for the observation of EI-MS spectrum of the Schiff base ligand. The Bruker Alpha T. FTIR spectrophotometer was used to obtain FTIR spectra of Schiff base ligand as well as metal complexes by utilizing potassium bromide disk. The electronic spectrum has been recorded on the instrument Perkin Elmer UV light level meter. To check the stability of synthesized metal complexes stability test was done by using TGA instrument in the nitrogen atmosphere. The instrument utilized powder X-ray diffraction analysis using the Rigaku-Japan Miniflex 600.

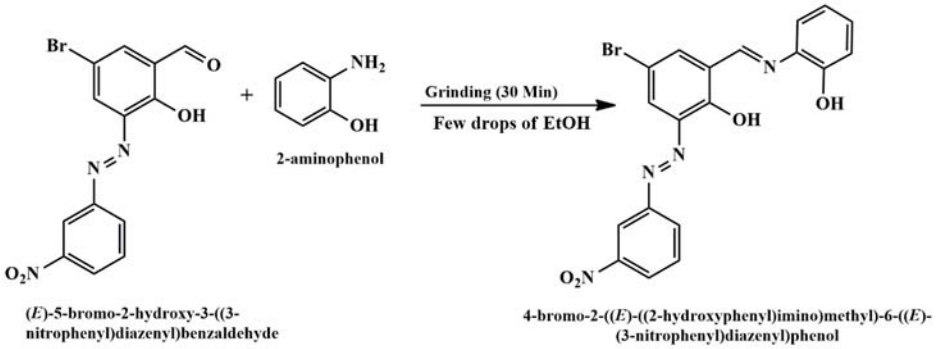
Synthesis of Schiff base ligand (L)

The Schiff base ligand B106 was synthesized by utilizing 3.501 g (0.01 mol) of (*E*)-5--bromo-2-hydroxy-3-((3-nitrophenyl)diazenyl)benzaldehyde and 1.090 g (0.01 mol) of 2-aminophenol ground with pestle in mortar at a ambient temperature for 30 min by adding few drops of ethyl alcohol (Scheme 1). The reaction progress was periodically tracked using thin layer chromatography (TLC). After the 30 min brown colored paste was obtained and poured in to crushed ice, the solid product observed. Filtration was used to separate this solid product. To obtain an analytically pure product with high yields, the material was vacuum-dried overnight using anhydrous $CaCl_2$.[30]

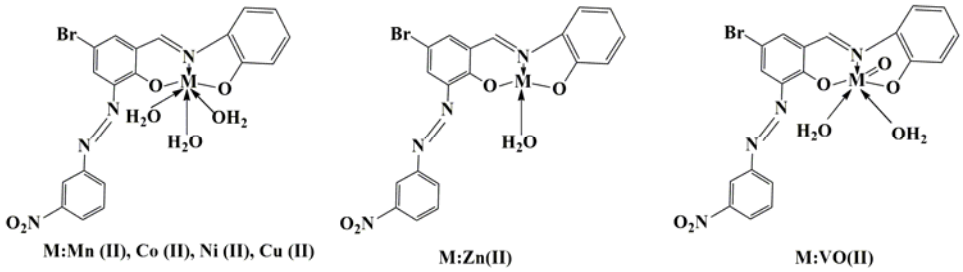
Synthesis of metal complex (M)

A mixture of 0.440 g (0.001 mol) of the Schiff base ligand B106 and 0.001 mol of metal acetate salts, including Mn (II), Co (II), Ni (II), Cu (II), Zn (II) and VO (II) sulfate, was ground together in a mortar with a pestle at ambient temperature for 40–45 min, few drops of ethanol

were added during the process of grinding for mixing the reactant (Scheme 2). Various coloured metal complexes formed.[30]



Scheme 1. Synthesis of Schiff base ligand (L).



Scheme 2. Synthesis of metal complexes.

Anti-hyperglycemia assessment

The anti-hyperglycemia assessment of Schiff base ligand B106 and Mn (II), Co (II), Ni (II), Cu (II), Zn (II) and VO(II) complexes was done by utilizing amylase inhibition assay. For this study, 500 µL of 0.1 M phosphate buffer solution having pH of 6.9 containing 0.5 % *α*-amylase enzyme was made first.. The test sample of 500 µL was taken and added in the above solution allowed to react and incubated for 10 min at 25 ℃. After this 500 µL of 1 % starch solution, extra pure 0.1 M phosphate buffer was mixed and placed in incubator for 10 min at 25 ℃. The comparable procedure was conducted for the controls where 500 µL of the enzyme were substituted with buffer. After incubation, 1000 µL of DNS was transferred to both test and control samples. The drug acarbose was used as standard drug. The absorbance at 540 nm was recorded using a spectrophotometer, and the percentage inhibition of the α-amylase enzyme was determined using the specified formula:

$$\text{Inhibition (\%)} = Abs540\ (\text{control}) - Abs540\ (\text{extract}) \times 100 Abs540\ (\text{control}) \quad (1)$$

Anticancer activity

The MTT assay has been used to test of the anticancer assessment of the synthesized Schiff base ligand B106 along with the Mn (II), Co (II), Ni (II), Cu (II), Zn (II) and VO(II) complexes on the MCF-7 human breast cancer cell line. The growing cell line was incubated for 24 h in a

medium with 10 % FBS and L-glutamine at 37 °C, 5 % CO_2, 5 % air and 100 % relative humidity. The Mn (II), Co (II), Ni (II), Cu (II), Zn (II) and VO(II) complexes and ligand B106 were diluted in water to a maximum of 100 μg/mL and dissolved in to 1mg/mL of DMSO before being applied to the microtiter wells and placed in incubator for 48 h. After adding trichloroacetic acid (TCA) to finish the procedure, the cell line was fixed and incubated for an hour at 4 ℃. 1 % acetic acid was used to create the MTT solution and after 20 min of incubation at room temperature, the unbound dye was removed. MCF-7 cells were seeded at a density of 5×10^3 cells per well in a 96-well plate. 10 mM trizma base was used to elute the bound dye stain. The analysis was done on the different concentration such as 10, 40 and 100 μg/mL. A reference wavelength of 690 and 540 nm were used to measure absorbance and calculated by using following formula:

$$\text{Inhibition (\%)} = 100(\text{Control } OD - \text{Sample } OD)/\text{Control } OD \quad (2)$$

Antimicrobial activity

The National Committee for Clinical Laboratory Standards (NCCLS) 2002 standards were followed for conducting the antimicrobial assessment using the agar disc diffusion method. In order to prepare McFarland turbidity standards, first sterilize the PDA+MHA mediums and autoclave them for the time of 15 min. Then added 0.5 mL of 1.175 % $BaCl_2{\cdot}2H_2O$ solutions to 99.5 mL of 0.18 mol/L sulfuric acid and stirring continuously. Standardized bacterial and fungal inoculums were swabbed onto Petri dishes containing MHA + PDA to initiate the inoculation process. After applying the sample to the inoculated agar plate, the plates have been then kept in an incubator that had been preheated to 30 °C. Each plate was carefully inspected after 24 h and we discovered that the inhibition zone was uniformly round with a lawn of growth. We were able to measure the inhibition zone diameter with our unaided eyes. Sliding callipers are used to measure the zones in mm on the reverse side of a petri dish.

RESULTS AND DISCUSSION

Sophisticated techniques such as mass spectrometry, ^{1}H-NMR and FTIR were employed to analyze the synthesized Schiff base ligand and its associated complexes labeled A1 through A6 (A1 = Mn (II), A2 = Co (II), A3 = Ni (II), A4 = Cu (II), A5 = Zn (II), A6 = VO(II)). For biological assessments, including anti-hyperglycemia, anticancer and antimicrobial assessment, various instruments were utilized. The Schiff base ligand B106 along with its complexes A1 to A6 exhibits a range of distinct colors. The A1–A6 complexes are not soluble in water, ethyl alcohol and methyl alcohol but are soluble in various organic solvents including chloroform, dimethylsulfoxide and dimethylformamide.

Physical and spectral data

Physical and spectral data are given in Supplementary material to this paper.

Spectroscopic analysis

Mass spectra of Schiff base ligand B106. The mass spectrometry analysis reveals molecular ion peaks at *m*/*z* 440.34, 441.15 (M+1) and 443.15 (M+3). These peaks are attributed to the successful formation of Schiff base ligand B106 as shown in Fig. S-1 of the Supplementary material.

^{1}H-NMR of Schiff base ligand B106. The ^{1}H-NMR of Schiff base ligand B106 was recorded in $CDCl_3$ solvent. The spectrum revealed the important signal, the signal at 8.65 ppm attributed to imine proton (HC=N–). Peaks found at 12.37 and 5.72 ppm, which correspond to the phenolic-OH groups are observed within the salicylaldehyde and amine moiety. Peaks observed at 6.94–7.58 ppm attributed to presence of proton of aromatic ring[31] as shown in Fig. S-2 of the Supplementary material.

IR spectra of Schiff base ligand B106 and A1–A6 complexes. The imine group (>C=N–) in the Schiff base ligand B106 exhibited a band at 1619 cm^{-1} which shifted to lower frequencies ranging between 1580–1615 cm^{-1} in the A1–A6 complexes. This change is attributed to the metal ion and nitrogen of the Schiff base ligand B106 in the coordination and resulting in the formation of complexes.[32] The band of phenolic-OH group was found at 3432 and 3502 cm^{-1}, this band disappeared in all A1–A6 complex indicating that the phenolic oxygen atom coordinated by deprotonation and this was further corroborated by the IR spectra of the Schiff base ligand B106, where the >C–O band observed at 1271 cm^{-1} shifted to higher frequencies ranging from 1275 to 1292 cm^{-1} in all A1–A6 complexes.[33,34] The >C–Br band was found at 742–747 cm^{-1}. The band of azo group (–N=N–) was found at 1368–1381 cm^{-1}. The –OH rocking band found at 821–828 cm^{-1} suggests that all A1–A6 complexes contain coordinated water molecule.[35] According to overall data, Schiff base ligand chelated to the central metal ion by tridentate manner as shown in Figs. S-3–S-9 of the Supplementary material.

UV–Vis spectra, magnetic susceptibility of A1–A6 complexes

The UV–Vis spectra of A1–A6 complexes are presented in the Figs. S-10–S--14 of the Supplementary material. The A1 complex shows band at 335 nm and indicates an octahedral geometry around the central metal atom suggesting metal to ligand charge transfer transition (MLCT). The UV spectra of the A2 complexes display broad absorption bands at 383, 350 and 267 nm, corresponding to the transitions $^{4}T_1g \rightarrow {}^{4}T_2g$, $^{4}T_1g \rightarrow {}^{4}T_1g(P)$ and $^{4}T_1g \rightarrow {}^{4}A_2g$, respectively. The magnetic moment ($\boldsymbol{\mu}$) value of 3.90 μ_B indicates a paramagnetic nature and suggests an octahedral geometry. The UV spectra of A3 complexes exhibit bands at 398, 366 and 335 nm which attributed to $^{3}A_{2g} \rightarrow {}^{3}T_{2g}$, $^{3}A_{2g} \rightarrow {}^{3}T_{1g(f)}$ and $^{3}A_{2g} \rightarrow {}^{3}T_{1g(P)}$. The value of magnetic moment ($\boldsymbol{\mu}$) at 3.05 μ_B indicates paramagnetic nature and suggests an octahedral geometry. The A4 complexes exhibit bands at 435 and 363 nm which attributed to $^{2}E_g \rightarrow {}^{2}T_{2g}$ and ligand to metal charge transitions (LMCT). The magnetic moment value of 1.70 μ_B indicates a paramagnetic nature and points to a distorted octahedral geometry likely influenced by Jahn–Teller distortion. The absorption band of the A5 complexes observed at 396 nm is attributed to the metal to ligand charge transfer (MLCT). The diamagnetic property indicates the presence of a tetrahedral geometry. The A6 complex exhibits absorption bands at 435 and

325 nm potentially corresponding to the $^2B_2 \rightarrow {}^2E$ and $^2B_2 \rightarrow {}^2B_1$ transitions. The magnetic moment value of 1.72 μ_B indicates a square pyramidal geometry.[31]

Molar conductivity of A1–A6 complexes

The molar conductance of A1–A6 complexes were measured at ambient temperature in a 10^{-3} M dimethylsulfoxide (DMSO) solution. The findings were obtained by utilizing the relation $\Lambda_M = K/C$. The molar conductance values ranged between 7.2 to 19.5 $S \cdot mol^{-1} \cdot cm^2$ clearly indicate that A1–A6 complex are non-electrolytic in nature. This is consistent with non-electrolyte molar conductivity values in DMSO solution being less than 50 $S \cdot mol^{-1} \cdot cm^2$. The structure of stable metal complexes does not dissociate into ions in DMSO, leading to non-electrolytic properties of the metal complexes[36] shown in Table I.

TABLE I. Magnetic moment and molar conductance of A1–A6 complexes

Sr. No.	Complex	Conductance S mol^{-1} cm^2	Magnetic moment μ_B	Assigned geometry
1.	A1	15.20	5.00	Octahedral
2.	A2	14.35	3.90	Octahedral
3.	A3	17.25	3.05	Octahedral
4.	A4	19.5	1.70	Octahedral
5.	A5	7.2	Diamagnetic	Tetrahedral
6.	A6	13.20	1.72	Square pyramidal

Thermal analysis of A1–A6 complexes

For the stability of synthesized A1–A6 complexes; the complexes were tested by thermogravimetric analysis in presence of nitrogen atmosphere. For this test the temperature was changed from ambient to 800 °C. As a result of decomposition, it was observed that the A1–A6 complexes decompose at two distinct steps, Table

TABLE II. Thermogravimetric data

Sr. No.	Complex	TG range, °C	Mass loss in % (Calc. %)	Decomposition of molecule	Metallic residue
1.	A1	27–190	9.13(9.85)	H_2O	MnO
		240–580	77.78(77.19)	$C_{19}H_{11}BrN_4O_4$	
2.	A2	27–200	9.14(9.78)	H_2O	CoO
		250–580	77.06(76.63)	$C_{19}H_{11}BrN_4O_4$	
3.	A3	27–190	9.65(9.80)	H_2O	NiO
		240–540	76.18(76.58)	$C_{19}H_{11}BrN_4O_4$	
4.	A4	27–190	10.76 (9.71)	H_2O	CuO
		200–550	75.25(76.08)	$C_{19}H_{11}BrN_4O_4$	
5.	A5	27–195	3.10(3.44)	H_2O	ZnO
		200–570	81.65(81.04)	$C_{19}H_{11}BrN_4O_4$	
6.	A6	27–150	5.67(6.64)	H_2O	VO
		180–520	81.98(80.99)	$C_{19}H_{11}BrN_4O_4$	

II. In the initial stage, the loss of the coordinated water molecule occurs between ambient temperature and 200 °C influenced by the nature of the metal to water bonds. In the second step consecutive loss of Schiff base ligand takes place from the temperature range of 200 to 600 °C and at temperatures exceeding 600 °C the formation of metal oxides takes place.[37] The graphs derived from the data are presented in Figs. S-15–S-17 of the Supplementary material.

Powder X-ray diffraction

The powder X-ray diffraction study was carried out by sophisticated instrument in the 2θ range of 20–80° at wavelength of 1.540 Å. This is given in Table III and Figs. S-18–S-20 of the Supplementary material. The A1 and A2 complex shows monoclinic crystal system. The metal complexes A3 and A6 complex show orthorhombic crystal system; A4 and A5 complexes show the triclinic crystal system.[35]

TABLE III. XRD spectral data of metal complexes; M – monoclinic; O – orthorhombic; T – triclinic

Complex	No. of reflections	Maxima (2θ / °)	*d*-Value nm	Lattice constant, Å	Unit cell volume, Å^3	Axis and axis angle	*Z*-Value	Crystal system
A1	14	5.53	15.962	a = 15.9729 b =17.5388 c =11.5710	3229.366	$a \neq b \neq c$ and $\alpha = \gamma = 90°$ $\neq \beta$	4	M
A2	17	10.50	8.415	a = 8.4087 b = 13.6230 c = 17.1860	1631.359	$a \neq b \neq c$ and $\alpha = \gamma = 90°$ $\neq \beta$	2	M
A3	9	22.10	4.018	a = 6.9600 b = 7.8514 c = 9.5124	337.154	$a \neq b \neq c$ and $\alpha = \beta = \gamma$ = 90°	4	O
A4	13	6.82	12.956	a = 26.3197 b = 9.4184 c = 13.3606	3260.708	$a \neq b \neq c$ and $\alpha \neq \beta \neq \gamma$ $\neq$ 90°	8	T
A5	14	7.31	17.627	a = 14.3633 b = 12.2982 c = 11.7339	3521.568	$a \neq b \neq c$ and $\alpha \neq \beta \neq \gamma$ $\neq$ 90°	2	T
A6	17	6.97	12.672	a = 15.3440 b = 8.4152 c = 11.2140	3021.568	$a \neq b \neq c$ and $\alpha = \beta = \gamma$ = 90°	4	O

Biological studies of Schiff base ligand(L) and its metal complexes(M)

Anti-hyperglycemia assessments. The anti-hyperglycemia assessments of synthesized Schiff base ligand and A2, A4 and A5 complexes was done by α-amylase inhibition assay and demonstrated in Table IV. The A2 complex shows higher inhibition than Schiff base ligand. Cobalt is commonly known to show the good antidiabetic activity. Other metal complexes such as A4 and A5 also exhibit better inhibition than Schiff base ligand compared with standard drug acarbose.[38]

Anticancer assessments. The anticancer assessments of Schiff base ligand as well as the A2, A4 and A6 complexes have been performed by utilizing the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) test by using MCF-7 human breast cancer cell line. The metal complexes of copper and zinc are commonly known to exhibit good anticancer activities than other metals. The metal complexes involving A1, A4 and A5 demonstrated significantly superior anticancer assessment compared to Schiff base ligand B106 against standard drug 5-FU[39] shown in Table V.

TABLE IV. Anti-hyperglycemia assessment of Schiff base ligand and A2, A4 and A5 complexes

Sr. No.	Compound	Concentration, μg/mL	Cell viability, %
1	Standard acarbose	250	54.54
		500	61.93
		1000	**74.43**
2	B106	250	28.97
		500	35.22
		1000	**44.31**
3	A2 Complex	250	35.79
		500	43.18
		1000	**56.81**
4	A4 Complex	250	35.22
		500	44.88
		1000	**53.97**
5	A5 Complex	250	38.63
		500	44.31
		1000	**47.72**

TABLE V. Anticancer assessment of Schiff base ligand and A2, A4 and A5 complexes

Sr. No.	Compound	Concentration of sample, μg/mL	Cell inhibition, %
1	Standard 5-FU	10	79.14
		40	83.29
		100	**88.79**
2	B106	10	38.06
		40	59.14
		100	**66.52**
3	A2 Complex	10	42.75
		40	57.62
		100	**71.81**
4	A4 Complex	10	38.56
		40	62.81
		100	**70.83**
5	A5 Complex	10	41.34
		40	60.83
		100	**69.84**

Antimicrobial activities. The Schiff base ligand and metal complexes were investigated against antifungal and antibacterial activities.[35] The observation suggest that the metal complexes are more active than the Schiff base ligand (L).

The antimicrobial properties of the synthesized Schiff base ligand B106 and its A1–A6 complexes were evaluated using the disc diffusion method against Gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus*) as well as Gram--negative bacteria (*Klebsiella pneumonia*, *Pseudomonas aeruginosa*) and three fungi (*Penicillium chrysogenum*, *Tricoderma viride* and *Aspergillus niger*). The findings of the antibacterial assessments indicate that all complexes except A5 show better inhibition than Schiff base ligand B106 and standard reference drug tetracycline. In antifungal activity no metal complex shows better or higher inhibition than Schiff base ligand B106 and standard reference drug fluconazole 40, Table VI.

TABLE VI. Antimicrobial assessment of Schiff base ligand and metal complexes; interpretation key: "–" (resistant) = up to 8 mm; intermediate sensitive: 8–12 mm; sensitive: 12–18 mm; highly sensitive: ≥18 mm

Sr. No.	Compound	Antibacterial activity				Antifungal activity		
		S. aureus	*B. subtilis*	*K. pneumoniae*	*P. aeruginosa*	*P. chrysogenum*	*T. viride*	*A. niger*
1	B106	8	8	8	8	8	8	8
2	A1 complex	22	21	19	21	8	8	8
3	A2 complex	13	14	11.5	17	8	8	8
4	A3 complex	17.5	20	20.5	16	8	8	8
5	A4 complex	18	19	15	16.5	8	8	8
6	A5 complex	8	8	8	8	8	8	8
7	A6 complex	21	15	18	15	8	8	8
8	Tetracycline	19	25	20	19	–	–	–
9	Fluconazole	–	–	–	–	25	35	26

CONCLUSION

The current study utilized a green synthetic approach to produce Schiff base ligand and its corresponding transition metal complexes. This environmentally friendly methodology demonstrated notable advantages over conventional techniques, including significantly higher yields ranging from 80 to 90 %. Moreover, the green approach considerably reduced reaction times and eliminates the necessity of hazardous solvents, thereby enhancing safety and sustainability. These factors collectively contribute to a substantial decrease in the overall cost of the reaction process, emphasizing the economic and ecological benefits of the method. The spectroscopic analyses revealed that the Schiff base ligand exhibited tridentate behaviour. Furthermore, powder X-ray diffraction (XRD) studies highlighted the presence of distinct crystal systems such as monoclinic for A1 and A2, triclinic for

A4 and A5 and orthorhombic for A3 and A6 configurations in the metal complexes, suggesting structural diversity. By the molar conductance measurements, it is confirmed that the metal complexes are non-electrolytic in nature. In the view of biological activity, the synthesized transition metal complexes, labelled A1 to A6, displayed significantly superior biological activities than Schiff base ligand (B106) in comparison with different standard drugs. This enhancement in activity highlights the potential applications of these complexes in various fields, paving the way for advancements in coordination chemistry and material science.

SUPPLEMENTARY MATERIAL

Additional data and information are available electronically at the pages of journal website: https://www.shd-pub.org.rs/index.php/JSCS/article/view/13329, or from the corresponding author on request.

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ИЗВОД

ЗЕЛЕНИ ПРИСТУП У ЕФИКАСНОЈ СИНТЕЗИ КОМПЛЕКСА МЕТАЛА СА 4-БРОМО-2-((*E*)-((2-ХИДРОКСИФЕНИЛ)ИМИНО)МЕТИЛ)-6-((*E*)-(3-НИТРОФЕНИЛ)ДИАЗЕНИЛ)-ФЕНОЛОМ И ИСПИТИВАЊЕ ЊИХОВЕ АНТИХИПЕРГЛИКЕМИЈСКЕ, АНТИТУМОРСКЕ И АНТИМИКРОБНЕ АКТИВНОСТИ

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У данашње време, свет се бори против рака и дијабетеса, што је подстакло глобална истраживања у правцу развоја ефикасних лекова за лечење ових болести. Истраживања показују да координациона једињења, посебно са супституисаним салицилалдехидима, показују значајну биолошку активност, која се додатно повећава након додатка амина. У овом раду приказана је синтеза комплекса метала, Mn(II), Co(II), Ni(II), Cu(II), Zn(II) и VO(II), са Шифовом базом, која је претходно синтетисана методом млевења из (*E*)-5-бромо-2-хидрокси-3-((3-нитрофенил)диазенил)бензалдехида и 2-аминофенола. Синтетисана Шифова база је окарактерисана применом масене спектрометрије, као и ^{1}H-NMR и FT-IR спекртоскопије. Након тога, синтетисани су комплекси метала са овом Шифовом базом у реакцији са одговарајућим Mn(II), Co(II), Ni(II), Cu(II), Zn(II) и VO(II) солима. Добијени комплекси метала су испитивани применом елементалне микроанализе, FT-IR и електронских спектара, термалне анализе, дифракцијом X-зрака са праха, моларне проводљивости и др. У току биолошких испитивања, одређена је антихипергликемијска и антитуморска активности Шифове базе и комплекса метала применом теста инхибиције α-амилазе и MTT теста, користећи стандардне референтне лекове акарбозу и 5-флуороурацил (5-FU). Резултати антихипергликемијског испитивања указују да Co(II) комплекс показује већу активност у поређењу са осталим комплексима, док сви синтетисани комплекси показују већу активност од слободне Шифове базе. Када је реч о антитуморској активности, Co(II) комплекс показује већу активност у односу на остале комплексе, а сви комплекси метала су активнији од некоординоване Шифове базе. Поред тога, испитивана

је и антимикробна активност синтетисаних једињења према две Грам-позитивне бактеријске врсте (*Staphylococcus aureus* и *Bacillus subtilis*), две Грам-негативне врсте (*Klebsiella pneumoniae* и *Pseudomonas aeruginosa*), као и три врсте гљивица (*Penicillium chrysogenum*, *Trichoderma viride* и *Aspergillus niger*). На основу добијених резултата, закључено је да комплекси метала показују бољу биолошку активност у односу на одговарајућу Шифову базу.

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