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Efficient synthesis and characterization of new ligand and their transition metal complexes derived from 4-methyl-1,2,3-thiadiazoles-5-carboxylic acid hydrazide

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ABSTRACT

Synthesis of the new metal complexes, by allowing the condensation of Ligand, HL, (E)-N'-(2-hydroxy-5-methoxybenzylidene)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide (**3**) with some transition metals. Here an attempt is also made to compare reported conventional methods with microwave irradiation for synthesized compounds. Spectroscopic technique, IR, ¹H-NMR, C¹³NMR, elemental analysis and TGA-DTA were used to characterize synthesized ligands and their complexes. The metal complexes were also evaluated for in vitro antimicrobial screening.

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1. Introduction

The development of coordination chemistry has been significantly influenced by metal complexes of schiff bases. Schiff bases are becoming more significant due to their wide range of biological activity, which includes antibacterial, antitumor, antifungal, anticancer,¹⁻³ antitubercular⁴ etc. Schiff base having spectacle ability to form stable complexes with transition metals⁵⁻⁹ and behave chelating characteristics property with metal have more biological importance.¹⁰ In addition, transition metal complexes of Schiff bases are used to control the extension of bacteria and fungus¹¹⁻¹⁵ and have exhibit potential therapeutics properties.¹⁶ Now a day metal complexes of schiff bases bearing heterocycles have occupied an important place in drug industry due to its application in biological and chemical sciences. Literature revealed that there is little information about 1,2,3-thiadiazole molecule and have displayed antitumor, antiviral, systematic acquired resistance, insecticidal, fungicidal, herbicidal¹⁷⁻²⁸ activities and its derivatives is a good necroptosis inhibitor.²⁹ With this we have planned to syntheses 1,2,3-thiadiazole based ligand and their metal complexes.

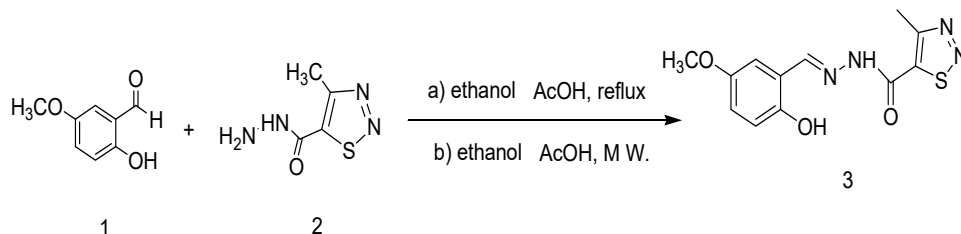
Several methods have been reported in the literature for the synthesis of Schiff bases and their metal complexes. The Schiff bases and their metal complexes were synthesized conventionally in ethanol or methanol as a reaction medium. However, these methods often require long reaction times and increase environmental impact. Literature survey revealed that microwave technique is considered as an important approach toward green chemistry. Under microwave irradiation conditions, synthesis of schiff bases and metal complexes can be accelerated, and selectivity of the ensuing products can be obtained by choosing appropriate microwave parameters, thus offering several advantages over conventional heating, such

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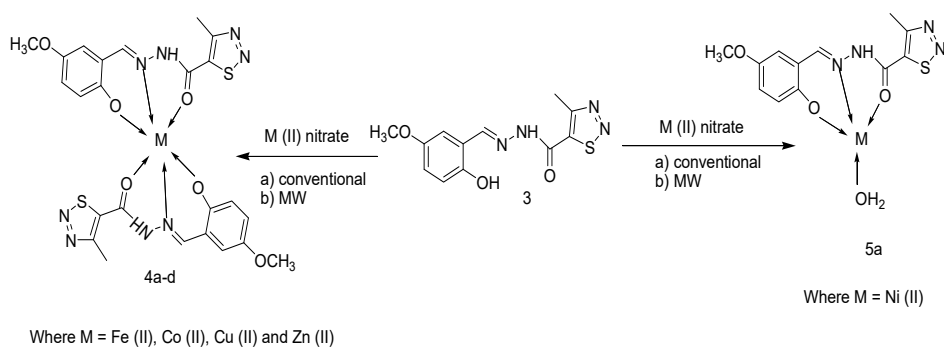
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as instantaneous and rapid heating (deep inside heating), homogeneity, selective heating, shorter reaction time and better yields.³⁰⁻³³

Taking into account the biological significance of these heteryl nuclei, Schiff bases, metal complexes and ongoing our work.³⁴ We report the synthesis and characterization of Fe(II), Zn(II), Cu(II), Co(II), and Ni(II) complexes (**4a-d** and **5a**) and thiadiazoles based ligand (HL) (**3**). Herein new ligand (**3**) derived from carrying condensation of 4-methyl-1,2,3-thiadiazoles-5-carboxylic acid hydrazide with 5-Methoxy-2-Hydroxy benzaldehyde. The desired compounds were synthesized by conventional as well as microwave irradiation. The reaction sequence is outlined in scheme 1 & 2.



Scheme 1 Synthesis of ligand HL, (**3**)



Scheme 2 Synthesis of metal complexes (**4a-d** and **5a**) metal-ligand ratio 1:2 and 1:1

2. Results and Discussion

In the present work, firstly we optimized the reaction condition of the formation, Ligands, HL, (**3**) and their metal complexes (**4a-d** and **5a**). The Ligand (HL) (**3**), synthesized by carrying condensation of 5-Methoxy-2-Hydroxy Benzaldehyde (**1**) with 4-methyl-1,2,3-thiadiazoles-5-carboxylic acid hydrazide (**2**) in presence of glacial acetic acid in ethanol under reflux condition, it observed the desired compound (**3**) obtained after 4h. Herein the complexes (**4a-d** and **5a**) were produced by heating metal nitrate with thiadiazoles-5-carboxylic acid hydrazide based ligand (HL) (**3**) in a 1:1 and 1:2 molar ratio under reflux condition, by this method its required 5 h. for generate metal complexes (**4a-d** and **5a**). When we carried the same reaction under microwave irradiation at 160 W. It observed that ethanol and methanol attribute more polar reaction mixture, have greater ability to couple with the microwave energy and accelerate the rate of reaction compared with conventional heating. The formation of ligand was completed within 3.5 min. and complexes were obtained within 4-5 min. with better yields. The clean reaction conditions, shorter reaction time, high yields and consumes less solvent, making it more suitable for principles of green chemistry are unique features of this method. Optimization reaction conditions are given in **Table 1**.

Table 1. Optimization condition of ligand HL (**3**) and their metal complexes. (**4a-d** and **5a**)

Entry	Compound	Conventional			Microwave		
		Solvent	Time (h) ^a	Yield (%)	Solvent	Time (min) ^b	Yield (%)
3	C ₁₂ H ₁₂ N ₄ O ₃ S (HL)	Ethanol	4	78	Ethanol	3.5	83
4a	[Fe (C ₁₂ H ₁₁ N ₄ O ₃ S) ₂]	Methanol	6	70	Methanol	5	79
4b	[Zn (C ₁₂ H ₁₀ N ₄ O ₃ S) ₂]	Methanol	6	73	Methanol	5	82
4c	[Cu (C ₁₂ H ₁₁ N ₄ O ₃ S) ₂]	Methanol	6	69	Methanol	5	81
4d	[Co (C ₁₂ H ₁₁ N ₄ O ₃ S) ₂]	Methanol	6	71	Methanol	5	80
5a	[Ni (C ₁₂ H ₁₂ N ₄ O ₄ S)]	Methanol	5	75	Methanol	4	82

^aReaction carried under conventional heating. ^bReaction carried under microwave irradiation.

All synthesized compounds were characterized by using spectroscopic techniques such as IR, $^1\text{H-NMR}$, $^{13}\text{C NMR}$, UV-visible and elemental analyses, they have good agreement with the structure of the synthesized compounds, ligand (**3**) and complexes (**4a-d** and **5a**). Melting point and elemental analysis of synthesized compounds are given in **Table 2**.

Table 2. Physical and Analytical data of Ligand HL (**3**) and Complexes (**4a-d** and **5a**)

Compound	M.W.	Colour	M.P. (°C)	Elemental analysis (%) Calcd. (Found)					
				C	H	N	S	M	O
$\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_3\text{S}$ (HL)	292	Yellow	272	49.31 (50.31)	4.14 (4.70)	19.17 (18.17)	10.97 (11.28)	---	16.42 (15.78)
$[\text{Fe}(\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S})_2]$	638	Black	>300	45.15 (44.52)	4.14 (3.98)	17.55 (18.25)	10.04 (11.05)	8.73 (7.83)	16.42 (15.78)
$[\text{Zn}(\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}_3\text{S})_2]$	648	Yellow	>300	44.48 (45.25)	3.42 (4.45)	17.29 (18.10)	9.90 (10.75)	10.09 (11.05)	14.81 (13.25)
$[\text{Cu}(\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S})_2]$	646	Green	>300	44.61 (43.61)	3.43 (3.05)	17.34 (17.25)	9.92 (9.01)	9.83 (10.02)	14.86 (14.02)
$[\text{Co}(\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S})_2]$	641	Dark brown	>300	44.93 (43.94)	3.46 (3.30)	17.47 (17.10)	10.00 (9.89)	9.19 (9.90)	14.96 (15.08)
$[\text{Ni}(\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_3\text{S})]$	368	Orange	>300	39.16 (40.78)	3.56 (2.98)	15.22 (14.52)	8.71 (9.25)	15.95 (16.23)	17.93 (18.25)

2.1 Infrared and $^1\text{H NMR}$ Spectra of ligand and their metal complexes

The IR spectral data of the ligand and their metal complexes are given in **Table 3**. In free Schiff bases (Ligand) characteristic bands of IR were found 3303, 1602, 3160, 1656 corresponding to $\nu(\text{Ph-OH})$, $\nu(\text{C=N})$, $\nu(\text{N-H})$, and $\nu(\text{C=O})$. In all metal complexes IR band of $\nu(\text{C=N})$ shifted to lower frequency in the regions 1527-1596 cm^{-1} . These can be attributed to delocalization of metal electron density (t_{2g}) to the π system of ligand.³⁵⁻³⁶ Indicating coordination nitrogen of the C=N moieties to the metal atom.³⁷ The characteristic and $\nu(\text{N-H})$ and $\nu(\text{C=O})$ stretches in complexes Fe(II), Cu(II) and Co(II) are observed at 3153, 3064, 3153 and 1616, 1614, 1604 respectively. whereas disappearance of $\nu(\text{N-H})$ and $\nu(\text{C=O})$ bands observed in Ni(II) and Zn(II) complexes, it is due to enolisation and followed by deprotonation.³⁸ Moreover, the phenolic $\nu(\text{C-O})$ vibration appear at 1262 in ligand and these phenolic $\nu(\text{C-O})$ band seemed at higher frequency by (15-20 cm^{-1}) 1282, 1276, 1284, 1281 and 1277 corresponding to Fe(II), Zn(II), Cu(II), Co(II) and Ni(II) complexes respectively. This shift confirmed phenolic oxygen are directly linked to metal.^{32,39} In ligand HL, IR band appear at 3303 cm^{-1} attributed by OH group, this band disappeared in all synthesized metal complexes which is confirmed -O- linked to central metal atom.⁴⁰ In Ni(II) IR broad bands was found at 3409 cm^{-1} these can be attributed due to the $\nu(\text{OH})$ of water molecule, which indicate the presence of coordinated water molecule.⁴¹ The complexes exhibit lower frequency IR bands at 527, 520, 547, 518, 536 cm^{-1} and 462, 474, 416, 474, 484 cm^{-1} this is due to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ respectively. This shift confirms the formation of metal-nitrogen and metal-oxygen bond.⁴²⁻⁴³

Table 3. FT-IR data of Ligand HL (**3**) and complexes (**4a-d** and **5a**).

Entry	Molecular formula [Empirical formula]	$\nu(\text{PhOH})$	$\nu(\text{C=N})$	$\nu(\text{N-H})$	$\nu(\text{C=O})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$	$\nu(\text{H}_2\text{O})$
3	$\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_3\text{S}$	3303 cm^{-1}	1602 cm^{-1}	3160 cm^{-1}	1656 cm^{-1}	----	-----	
4a	$\text{C}_{24}\text{H}_{22}\text{N}_8\text{O}_6\text{S}_2\text{Fe}$ [$\text{Fe}(\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S})_2]$	-----	1527 cm^{-1}	3151 cm^{-1}	1616 cm^{-1}	527 cm^{-1}	462 cm^{-1}	
4b	$\text{C}_{24}\text{H}_{20}\text{N}_8\text{O}_6\text{S}_2\text{Zn}$ [$\text{Zn}(\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}_3\text{S})_2]$	-----	1562 cm^{-1}	-----	-----	520 cm^{-1}	474 cm^{-1}	
4c	$\text{C}_{24}\text{H}_{22}\text{N}_8\text{O}_6\text{S}_2\text{Cu}$ [$\text{Cu}(\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S})_2]$	-----	1596 cm^{-1}	3064 cm^{-1}	1660 cm^{-1}	547 cm^{-1}	416 cm^{-1}	
4d	$\text{C}_{24}\text{H}_{22}\text{N}_8\text{O}_6\text{S}_2\text{Co}$ [$\text{Co}(\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S})_2]$	-----	1536 cm^{-1}	3153 cm^{-1}	1604 cm^{-1}	518 cm^{-1}	474 cm^{-1}	
5a	$\text{C}_{12}\text{H}_{12}\text{O}_4\text{N}_4\text{SNi}$ [$\text{Ni}(\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_4\text{S})]$	-----	1536 cm^{-1}	-----	-----	536 cm^{-1}	484 cm^{-1}	3409 cm^{-1}

$^1\text{H-NMR}$ of Schiff base HL, (**3**) reveals the presence of a phenolic proton at δ 12.33 (1H, s). While the signal due to the NH group appeared at δ 9.83 (1H, s), azomethine proton (HC=N) at δ 8.51 (1H, s), aromatic protons at δ 6.86-6.94 (2H, dd) and δ 7.37 (1H, s), methoxy protons at δ 3.80 (3H, s) and methyl protons of CH_3 appeared at δ 2.97. In $^{13}\text{C NMR}$ spectrum, the signal of 163.0 ppm is due to the phenolic carbon, amide carbon at δ 160.0 ppm, δ 152.0 ppm (C=N) is due to carbon atom in the azomethine groups, aromatic carbons at δ 151.0, 142.0, 135.0, 120.0, 119.0, 117.0, 109.0, methoxy carbon at δ 55.0 ppm and methyl carbon at δ 15.0 ppm. The $^1\text{H-NMR}$ spectrum of the complexes differs from that of the free ligands. The disappearance of the phenolic OH signal due to its involvement in the coordination sphere with the corresponding metal ions.⁴⁴⁻⁴⁵ The N-H proton (CONH) appears at a higher region in Fe(II), Cu(II) and Co(II) complexes. Whereas the disappearance of N-H proton of hydrazide observed in complexes (**4b**), Zn(II) and (**5a**), Ni(II) confirms the deprotonation of amide proton via enolate.⁴⁶ All this spectral data, FT-IR, $^1\text{H-NMR}$ and Elemental analysis supported the following structures of the synthesized ligand and their complexes. Details of the spectral interpretation of ligand and metal complexes are given in the experimental section.

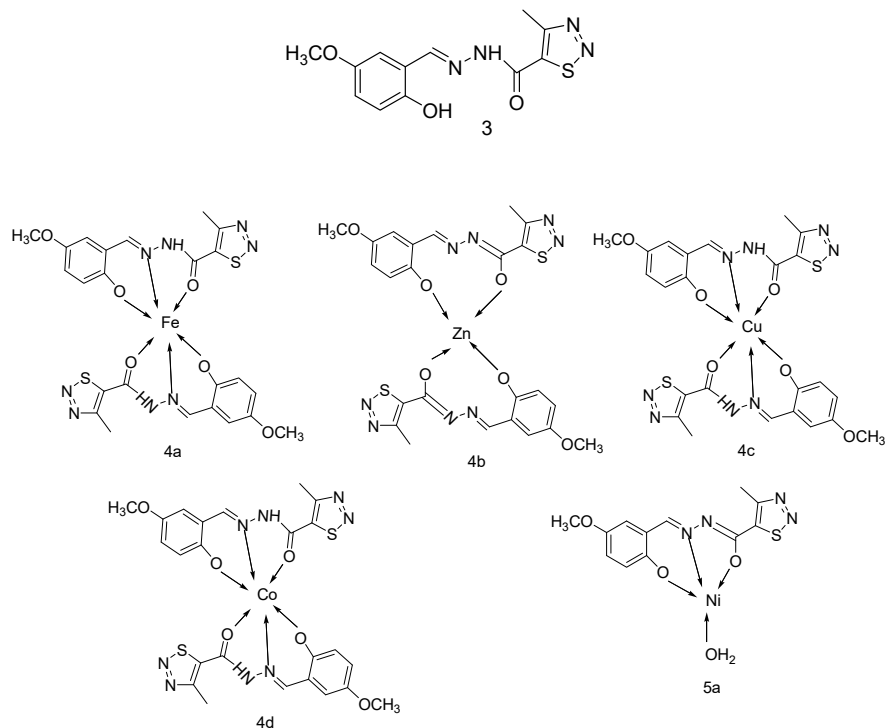


Fig.1. Structure of ligand (3) and their metal complexes (4a-d) and (5a)

2.2 UV-visible spectra of ligand and their metal complexes

The electronic spectral data of the metal complexes were recorded in DMSO solution using JASCO UV wavelength from 200 nm to 900 nm at room temperature are given in **Table 4**. The nature of the ligand field about the metal ion has been derived from the electronic spectra. The electronic spectra of free ligand bands observed at 262, 276 nm attribute to $\pi-\pi^*$ transition and 351 nm due to $n-\pi^*$ transition. Here all metal complexes exhibit bands at 268-301, 368-372 and 408-460 nm. The first two bands are assigned to $\pi-\pi^*$ and $n-\pi^*$ electronic transition, but the last third band is due to LMCT transition.⁴⁷ In metal complexes $\pi-\pi^*$ and $n-\pi^*$ transition were shifted to longer wavelength as a consequence of coordination to metal center.⁴⁸ The electronic spectrum of Ni(II) complex exhibits three bands at 271, 368, and 408 nm recognized to ${}^3T_1(F) \rightarrow {}^3T_1(P)$, ${}^3T_1(F) \rightarrow {}^3A_2(F)$, and ${}^3T_1(F) \rightarrow {}^3T_2(F)$ transitions, respectively. The Ni(II) complex was reliable with two unpaired electrons confirming the tetrahedral geometry around Ni(II) ion.^{49,50}

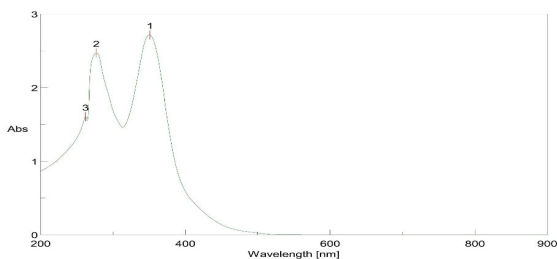


Fig. 2. Electronic spectra of Ligand, HL(3)

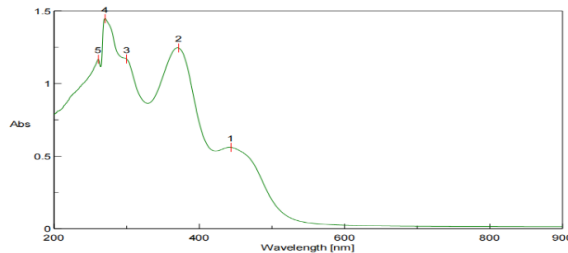


Fig. 3. Electronic spectra of Ni (II) complex (5a)

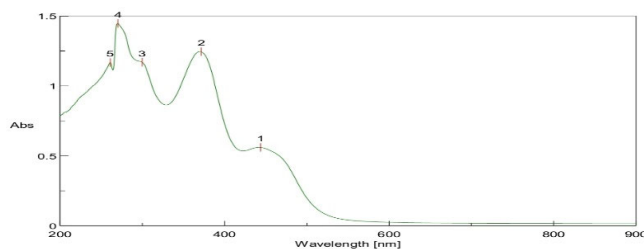


Fig. 4. Electronic spectra of Zn (II) complex (4b)

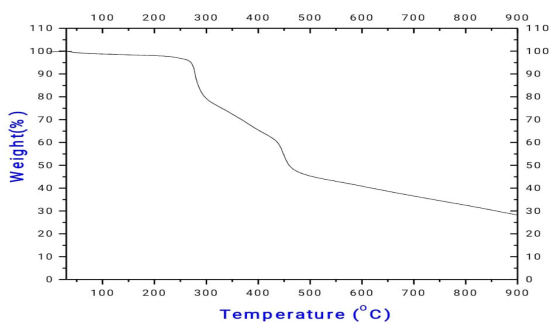
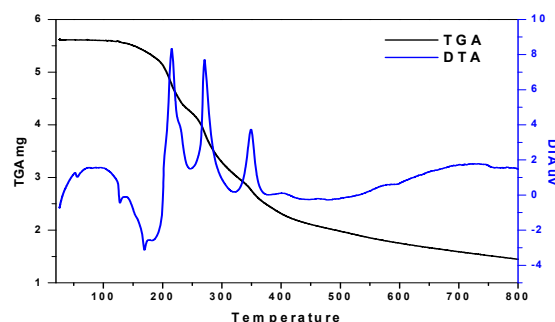
Table 4. Electronic absorption spectral bands of the ligands (**3**) and their complexes (**4a–b** and **5b**)

Compound	Ligand and its complexes	Electronic absorption bands		Electronic transition
		λ_{max} (nm)	λ_{max} (cm^{-1})	
3	$\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_3\text{S}$ (HL)	262	38167	$\pi \rightarrow \pi^*$
		276	36232	$\pi \rightarrow \pi^*$
		351	28490	$n \rightarrow \pi^*$
4a	[Fe ($\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S}$) ₂]	268	37313	$\pi \rightarrow \pi^*$
		301	33223	$\pi \rightarrow \pi^*$
		370	27027	$n \rightarrow \pi^*$
		417	23981	CT
4b	[Zn ($\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}_3\text{S}$) ₂]	270	37037	$\pi \rightarrow \pi^*$
		371	26954	$n \rightarrow \pi^*$
		443	22573	CT
4c	[Cu ($\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S}$) ₂]	268	37313	$\pi \rightarrow \pi^*$
		368	27174	$n \rightarrow \pi^*$
		440	22727	CT
4d	[Co ($\text{C}_{12}\text{H}_{11}\text{N}_4\text{O}_3\text{S}$) ₂]	271	36900	$\pi \rightarrow \pi^*$
		372	26882	$n \rightarrow \pi^*$
		460	21739	CT
5a	[Ni ($\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_4\text{S}$)]	271	36900	$\pi \rightarrow \pi^*$
		368	27173	$n \rightarrow \pi^*$
		408	24509	CT

2.3 Thermal analysis

Thermogravimetric examination of respective metal complexes has been deliberate as a purpose of temperature from room temperature to 800°C beneath a nitrogen atmosphere at a heating tempo of 10°C/min. This aspect is employed to put forward a general mechanism for the thermal breakdown of these complexes. TG-DTA of the Fe (II), Ni (II), Zn (II), Co (II) and Cu (II) complexes were carried out to study thermal strength and decomposition manners. The complexes of Fe (II), Zn (II), Co (II) and Cu (II) displayed comparable patterns of thermal decomposition. In Zn (II) a complex, thermal curves display mass losses in three steps and the thermal events corresponding to these losses are due to chemical phenomena. The first step of degradation was observed in a temperature range of 240–300°C, which indicates a corresponding to the loss of organic moiety in the complexes. In second step of decomposition, occurred in a temperature 440–470 °C pointing to the loss of ligand part of the complexes. In third step, above 470 °C weight loss occurred upto temperature 540 °C, this informs the removal of the remaining thermally degradable part of the complex. After 540 °C, a plateau has been observed which corresponds to metal oxide as an ultimate pyrolysis product.^{51–52}

In Ni (II) a complex, in the first step of decomposition up to in the 187°C was almost certainly indicates the loss of coordinated water. The complex does not illustrate any loss in weight between 187 and 268 °C. In the second step after 268 °C, a loss in weight has been in general up to 300°C corresponding to the loss of moderately decomposed ligand part from the complex. In third step decomposition steps starts at 300°C and terminates at on 410°C indicates thermal decomposition of ligand leaving behind metal oxide as the product.⁵³

**Fig. 5.** TGA of Zn (II) complex (**4b**)**Fig. 6.** TG-DTA of Ni(II) complex (**5a**)

2.4 Antimicrobial screening of metal complexes

All synthesized compounds screened in vitro for their antibacterial and antifungal activities against three strains of bacteria and two strains of fungus. The petri plate (stains) containing 30 mL nutrient agar and potato dextrose agar (PDA) medium for bacteria and fungi were incubated for 20–24 h and 24–48 h respectively at 37 °C and the zones of inhibition were measured in terms of mm. The results were compared with the standard antibiotics and antifungal. The complexes of Co(II), Fe (II) Cu (II) and Zn (II) exhibited moderate activity against *S. aureus* bacteria but less than the standard against. The complexes Fe (II) and Cu (II) also displayed moderate activities against *S. pyogenes* and *E. coli* respectively. Similarly,

only two complexes of Co (II) and Cu (II) exhibited moderate activity against fungus *T. rubrum*. Zones of inhibition in mm are given in **Table 4**.

Table 4. Antimicrobial screening of the synthesized compounds.

Compound	Antibacterial Activity (Zone of inhibition in mm)			Antifungal Activity (Zone of inhibition in mm)	
	<i>S. aureus</i>	<i>S. pyogenes</i>	<i>E. coli</i>	<i>Candida</i>	<i>Trychophtyon rubrum</i>
[Fe(C ₁₂ H ₁₁ N ₄ O ₃ S) ₂]	10	12	-	-	-
[Ni(C ₁₂ H ₁₂ N ₄ O ₄ S)]	-	-	-	-	-
[Zn(C ₁₂ H ₁₀ N ₄ O ₃ S) ₂]	12	-	-	-	-
[Cu(C ₁₂ H ₁₁ N ₄ O ₃ S) ₂]	10	-	10	-	12
[Co(C ₁₂ H ₁₁ N ₄ O ₃ S) ₂]	11	-	-	-	10
Reference Antibiotic	20 Ampicillin-sulbactam	23 Ampicillin-sulbactam	22 Aztreonam		
Antifungal				22 Fluconazole	22 Fluconazole

3. Conclusion

We have synthesized a series of complexes, using transition metal ion Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) with ligand, (E)-N'-(2-hydroxy-5-methoxybenzylidene)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. In the present study the proposed method has an advantage over existing conventional methods with high yield and shorter reaction time with good to excellent yields. The synthesized compounds characterized by various spectral techniques and TG analysis. The spectral data of ligands and their metal complexes shows Octahedral geometry of Fe(II), Co(II), Cu(II), and Zn(II) complexes and Ni(II) complexes exhibit tetrahedral geometry. Complexes tested by in vitro antimicrobial activity, except Ni(II) complexes all metal complexes shows moderate activity against *Streptococcus aureus* GM +ve bacteria and two complexes Co(II) and Cu(II) shows reasonable antifungal activity against *Trychophtyon rubrum*.

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4. Experimental

4.1 Materials and Method

All chemicals were obtained from commercial sources and used without any further purification. The melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on a FT-IR (JASCO FT-IR 4100) Japan. The ¹H and ¹³C NMR was measured on Bruker Avance II 400 MHz FT NMR with low and high temperature in DMSO using TMS as internal reference. Mass spectra were recorded on GC-MS spectrometers. Elemental analyses were performed on a Perkin-Elmer 2400 CHN analyser.

4.2 General procedures

4.2.1 Synthesis of Schiff base, (E)-N'-(2-hydroxy-5-methoxybenzylidene)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide, HL (3)

4.2.2 Conventional synthetic route

A mixture of 5-Methoxy-2-Hydroxy Benzaldehyde (1) (0.01 mol, 1.52 g) and 4-methyl-1,2,3-thiadiazoles-5-carboxylic acid hydrazide (2) (0.01 mol, 1.58 g) was dissolved in ethanol (25 mL). To this solution a few drops of glacial acetic acid were added and it was then refluxed for 4 h. The progress of the reaction was monitored by TLC. After completion of reaction mixture was poured into the crushed ice. The obtained solid was filtered, dried and crystallized from methanol.

4.2.3 Microwave Irradiation synthetic route

In a conical flask, 5-Methoxy-2-Hydroxy Benzaldehyde (**1**) (0.002 mol), 4-methyl-1,2,3-thiadiazoles-5-carboxylic acid hydrazide (**2**) (0.002 mol) and catalytic amount of glacial acetic acid was dissolved in ethanol. The reaction mixture was irradiated using a microwave at 160 Watt. The progress of the reaction was monitored on a TLC plate. After completion, the reaction mixture was poured in ice cold water and was extracted with EtOAc. The solvent was removed and the crude product was crystallized using methanol.

Analysis for HL, Ligand (**3**)

M.F. $C_{12}H_{12}N_4O_3S$ Yield 83 %; M. P. 270 °C; yellow powder; FT-IR (KBr, cm^{-1}): 3303 ν (Ph-OH), 3160 ν (N-H), 1656 ν (C=O), 1602 ν (C=N) 1285 ν (C-O); 1H NMR (400 MHz, DMSO-*d*6) = δ 2.97 (3H, CH₃), δ 3.80 (3H, s, -OCH₃), δ 6.86-6.94 (2H, dd, Ar-H), δ 7.37 (1H, s, Ar-H), δ 8.51 (1H, s, -CH=N), δ 9.83 (1H, s, -CONH), δ 12.33 (1H, s, Phenolic -OH). ^{13}C -NMR (400 MHz, DMSO, ppm) 163.52 (Phenolic carbon), 160.28 (amide carbon), 152.69 (azomethine carbon), 151.60, 142.69, 135.76, 120.39, 119.05, 117.69, 109.55, (aromatic carbon), 55.64 (methoxy carbon) 15.41(methyl carbon); Elemental analysis found (%) C, 50.31; H, 4.70; N, 18.17; O, 15.78 calculated for. $C_{12}H_{12}N_4O_3S$: C, 49.31; H, 4.14; N, 19.17; O, 16.42; MS (*m/z*): 292 (M^+).

4.2.4 Preparation of complexes, (**4a-d** and **5a**)

4.2.5 Conventional synthetic route

Metal nitrate in methanol was added to methanolic solution of (E)-N'-(2-hydroxy-5-methoxybenzylidene)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide (**3**) at hot condition in 1:1 / 1:2 (metal:ligand) molar ratio and reaction mixture slightly adjusted to basic. Then the reaction mass was refluxed for 6 h. The progress of reaction was monitored by TLC and after completion of reaction coloured precipitates were obtained. The obtained solid product was filtered, washed with hot methanol and dried.

4.2.6 Microwave Irradiation synthetic route

In a conical flask, Metal nitrate and (E)-N'-(2-hydroxy-5-methoxybenzylidene)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide dissolved in methanol. The solution of reaction adjusted slightly to basic. Then this reaction mass was irradiated using a microwave at 160 Watt. The progress of the reaction was monitored on a TLC plate. After completion, the reaction mixture was poured in ice cold, coloured precipitates. The obtained solid was filtered, washed with hot methanol and dried.

Analysis for Metal complexes [$Fe(C_{12}H_{11}N_4O_3S)_2$] (**4a**)

M. F. $C_{24}H_{22}N_8O_6S_2Fe$ Yield 79 %; M.P. >300; black powder; FT-IR (KBr, cm^{-1}): 1527 attributed to ν (C=N), 3151 revealed presence of amide ν (N-H), 1616 this due to the carbonyl ν (C=O), 1282 arising new band from phenolic ν (C-O), new lower frequency bands 527 and 464 attributed to ν (M-O) and ν (M-N); 1H NMR (400 MHz, DMSO-*d*6) δ (ppm) = 2.97 this is due to the proton of methyl group, (6H, s, (CH₃)₂), 3.40 attributed to methoxy proton (6H, s, (OCH₃)₂), 6.90-7.92 revealed presence of aromatic proton (6H, m, Ar-H), 8.46 attributed to azomethine proton (CH=N), 10.62 this chemical shift indicate presence of amide proton (CONH) ; Elemental analysis found (%) C, 44.52; H, 3.98; N, 18.25; S, 11.05; Fe, 7.82; O, 15.78 calculated for $C_{24}H_{22}N_8O_6S_2Fe$: C, 45.15; H, 4.14; N, 17.55; S, 10.04; Fe, 8.73; O, 16.42.

Analysis for Metal complexes [$Zn(C_{12}H_{10}N_4O_3S)_2$] (**4b**)

M. F. $C_{24}H_{20}N_8O_6S_2Zn$ Yield 82 %; M.P. >300; yellow powder; FT-IR (KBr, cm^{-1}): 1562 attributed to ν (C=N), 1276 arising new band from phenolic ν (C-O), lower frequency new bands 520 and 474 attributed to ν (M-O) and ν (M-N); 1H NMR (400 MHz, DMSO-*d*6) δ (ppm) = 2.97 this is due to the proton of methyl group, (6H, s, (CH₃)₂), 3.41 attributed to methoxy proton (6H, s, (OCH₃)₂), 6.53-7.90 revealed presence of aromatic proton (6H, m, Ar-H), 8.55 attributed to azomethine proton (CH=N); Elemental analysis found (%) C, 45.25; H, 4.45; N, 18.10; S, 10.75; Zn, 11.05; O, 13.25 calculated for $C_{24}H_{20}N_8O_6S_2Zn$: C, 44.48; H, 3.42; N, 17.29; S, 9.90; Zn, 10.09; O, 14.81.

Analysis for Metal complexes [$Ni(C_{12}H_{12}N_4O_4S)$] (**5a**)

M. F. $C_{12}H_{12}N_4O_4SNi$ Yield 82 %; M.P. >300; orange powder; FT-IR (KBr, cm^{-1}): 3409 vibrational frequency due to the coordinated water, 1536 attributed to ν (C=N), 1277 arising new band from phenolic ν (C-O), lower frequency new bands 536 and 484 attributed to ν (M-O) and ν (M-N); 1H NMR (400 MHz, DMSO-*d*6) δ (ppm) = 2.97 this is due to the proton of methyl group, (3H, s, CH₃), 3.41 attributed to methoxy proton (3H, s, OCH₃), 6.53-7.90 revealed presence of aromatic proton (3H, m, Ar-H), 8.55 attributed to azomethine proton (CH=N); Elemental analysis found (%) C, 40.78; H, 2.98; N, 14.52; S, 9.25; Ni, 16.23; O, 18.25 calculated for $C_{12}H_{12}N_4O_4SNi$: C, 39.16; H, 3.56; N, 15.22; S, 8.71; Ni, 15.22; O, 17.93.

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