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Synthesis, Spectral Characterization and Antibacterial Activity of Metal Complexes of 2-Methoxy benzaldehyde isonicotinoylhydrazone

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Abstract: ***2-Methoxy benzaldehyde isonicotinoylhydrazone (MBINH), and its iron(II), cobalt(II) and nickel(II)complexes have been synthesized and characterized based on physico chemical properties, Electronic and IR spectra. The IR observations suggest that the ligands have coordinated through azomethine nitrogen atom, oxygen atom and through methoxy groups. The invitro antibacterial activity of complexes against Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus and Bacillus subtilis bacteria was screened and compared to the activity of the free ligand, the antibacterial activity of iron complex is active than Co & Ni complexes.***

Keywords: 2-Methoxy benzaldehyde isonicotinoylhydrazone, metal complexes, Antibacterial activity

1. Introduction

Hydrazone ligands and their complexes with different transition metal ions have been thoroughly studied due to their biological activity[1–4]. Heteroaroyl hydrazones forms stable metal complexes with transition metal ions and inner transition metal ions due to complexing ability of ligand through keto-enol tautomerism and availability of other donor sites in the ligand. The aroylhydrazones contain in their structure the –CO–NH–N=C< group that imparts on these chelating agents antibacterial[5], antiparasite [6] , antioxidants [7] and anticancerous [8] properties.

Isonicotinoylhydrazone(INH) is the first line medication in the prevention and treatment of tuberculosis. The drug is inexpensive and available worldwide. It is on WHO's list of essential medicine. It shows number of pharmacological properties. In the year 1954 Sah and coworkers[9] synthesized 'isonicotinoylhydrazones' by reacting with various aldehydes and ketones.

In continuation of ongoing studies on complexes with ligands of the isonicotinoylhydrazone class, the synthesis and study of metal complexes of Fe(II), Co(II) and Ni(II) with 2-Methoxy benzaldehyde isonicotinoylhydrazone are presented in this paper.

2. Materials and methods

Isonicotinic acid hydrazide, 2-methoxybenzaldehyde, agarose were purchased from Sigma-Aldrich. All other chemicals were of AR grade and used as provided. The solvents used for the synthesis were distilled before use. Elemental analyses were carried out on a Heraeus Vario EL III Carlo Erba 1108 instrument. Magnetic measurements were taken at 298K using lakeshore VSM 7410 instrument. Molar conductivity measurements at 298 ± 2K in dry and purified DMF were carried out using a ELICO CM model 162 conductivity meter. The electronic spectra were recorded in DMF with a UV lamda50 (Perkin-Elmer) spectrophotometer. IR spectra were recorded in the range 4,000–400 cm^{-1} with a Perkin-Elmer spectrum100 spectrometer on KBr discs.

2.1 Preparation of Ligand

Ligand was prepared by using isoniazid and different 2-Methoxy benzaldehyde. A methanolic solution of isoniazid (5mmol), 2-Methoxybenzaldehyde (5mmol) in methanol was mixed in a round bottom flask. Two drops of glacial acetic acid were added to the reaction mixture. This reaction mixture was refluxed for 3 and the reaction mixture was cooled to room temperature. The Schiff base ligands 2-Methoxy benzaldehyde isonicotinoylhydrazone(MBINH), was obtained as yellow colored crystalline products, which are subsequently used for the synthesis of metal complexes. The scheme of the ligand is shown in **Figure 1**.

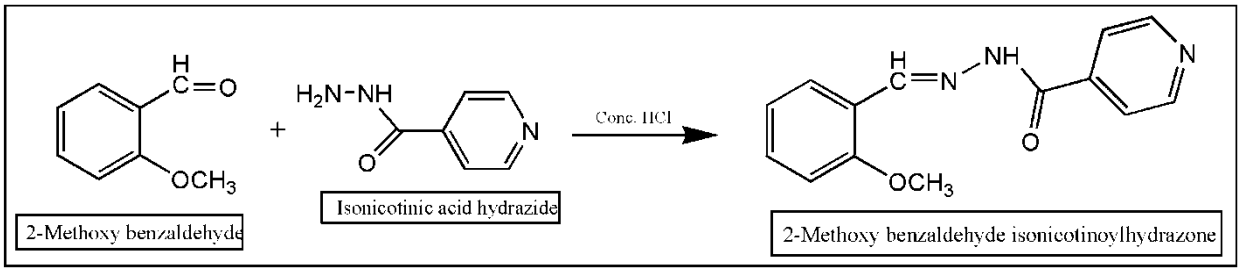

Figure 1: Scheme of 2-Methoxy benzaldehyde isonicotinoylhydrazone

2.2 Charactrization of MBINH

2-Methoxy benzaldehyde isonicotinoyl hydrazone - (MBINH)*)*: *)*: Yield 78%, M.Pt.265-266 °C, Anal (%) Calc.(found): C-65.85(65.88); H-5.06 (5.09); N-16.41(16.64); ^{1}H-NMR spectra: δ(11.51) (singlet 1H), δ(8.2) (multiplet 4H), δ (7.6) (multiplet 4H), δ (3.21)(singlet 3H), δ(2.53) (singlet 1H), assigned to -NH, isonicotine H, benzene H, –OCH_3, azo methine H protons respectively. Mass spectra of MBINH shows molecular ion peak at 255.

2.3 Preparation of complexes

1) **Synthesis of $[Fe(MBINH)_2]Cl_2.H_2O$**
   A methanolic solution of MBINH(1.27g, 5mmol) and metal salt of $FeCl_2.4H_2O$(0.99g, 5mmol) were mixed in a clean 250-ml three necked round bottom flask and the contents were refluxed on water bath under the nitrogen atmosphere for 1hr. On cooling the contents to room temperature, a crystalline black coloured complex was separated out. Then it was collected by filtration, washed with methanol and dried in vaccum. Yield. 71%.
2) **Synthesis of $[Co(MBINH)_2]Cl_2.H_2O$**
   To a methanolic solution of MBINH (1.27g, 5mmol) taken in a 100-ml round bottom flask, aqueous solution of $CoCl_2.6H_2O$(1.19g, 5mmol) was added and the reaction mixture was heated under reflux on a water bath for 3hr. On cooling reaction mixture to room temperature, deep red coloured complex was separated out. It was collected by filtration, washed with methanol followed by hexane and dried in vacuuo. Yield. 69%.
3) **Synthesis of $Ni(HAPINH)_2$**
   It was prepared by mixing methanolic solution of MBINH (1.27g, 5mmol) and aqueous solution of $NiCl_2.6H_2O$(1.18g, 5mmol) in a clean 100-ml round bottom flask and followed by refuxion on water bath for 1 hour. The reaction mixture was cooled to room temperature. A deep green coloured complex which separated out was collected by filtration, washed with methanol followed by hexane and dried in vacuuo. Yield. 65%.

2.4 Antimicrobial Analysis by Disc Diffusion Method

The 2-Methoxy benzaldehyde isonicotinoylhydrazone (MBINH) and its metal complexes were screened for their antimicrobial activity by disc diffusion method [10] against six bacterial strains such as *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Bacillus subtilis bacteria*. Antibacterial activity was tested by the filter paper disc diffusion technique involving the cultures of the selected organisms for 24h. Mueller Hintonagar number 2 (Hi Media, India) was used as the bacteriological medium and sterile yeast nitrogen base with 2% agar (Hi Media, India) was used as the fungal medium. The test solutions of the ligand and its metal complexes were prepared in sterile dimethyl sulfoxide (DMSO) solvent for the study. The synthesized 2-Methoxy benzaldehyde isonicotinoylhydrazone and its metal complexes were tested at different concentrations to find out the minimum concentration of the ligand and its metal complexes required for inhibiting the growth of microbes.

Ampiicillin (100 μg/mL) was taken as the standard for antibacterial activity. The organism was seeded into sterile nutrient agar medium by mixing one mL of inoculum with 20mL sterile melted nutrient agar kept at 48–50ºC in a sterile petri dish. The medium was allowed to solidify first. Then the test solutions, the standard drugs, and the blank were impregnated in Whatman filter paper discs, placed on the solidified medium in the petri dish, and left undisturbed for 2 h at room temperature. The petri dishes were then incubated at 37ºC for 24hr and the zone of inhibition for the test samples, standard, and control (DMSO) was measured.

3. Results and Discussion

3.1 Elemental analysis, molar conductivity measurements and magnetic moment

All the complexes are stable at room temperature, non-hygroscopic, slightly soluble in water, but more soluble in methanol, ethanol and readily soluble in CH_3CN, DMF and DMSO. The analytical data **(Table 1)** are consistent with the proposed molecular formulae of complexes. High molar conductivity values of present complexes suggest electrolytic nature of the complexes. The effective magnetic moment (μ_{eff}) of the metal complex of $[Fe(MBINH)_2]Cl_2.H_2O$ is 5.1B.M. The value suggest high spin octahedral geometry for the complex[11]. The effective magnetic moments (μ_{eff}) of the $[Co(MBINH)_2]Cl_2.H_2O$ is 4.28 B.M. which is consistent with three unpaired electrons and falls within the range reported for mononuclear cobalt(II) complex[12]. The magnetic moment of $[Ni(MBINH)_2]Cl_2$is 2.95 B.M. The data reveal that the observed magnetic moment values of this complex is as expected for mono nuclear nickel(II) complexes having two unpaired electrons [13]. The mass spectrum of $[Co(MBINH)_2]Cl_2.H_2O$ is shown in **Figure 2**.

Table 1: Physico-chemical properties of metal complexes

S.NO	Complex	M.P ºC	Mol.Wt	Elemental analysis found (cal.)%				μ_{eff}	ΛM^a
				C	H	N	M		
1	$[Fe(MBINH)_2]Cl_2.H_2O$	>300	654	51.42 (51.37)	4.34 (4.28)	12.89 (12.84)	8.59 (8.53)	5.3	36
2	$[Co(MBINH)_2]Cl_2.H_2O$	287	657	51.15 (51.14)	4.29 (4.26)	12.73 (12.78)	8.94 (8.98)	4.31	67
3	$[Ni(MBINH)_2]Cl_2$	>300	638	52.49 (52.66)	4.36 (4.38)	13.21 (13.16)	9.07 (9.09)	2.91	45

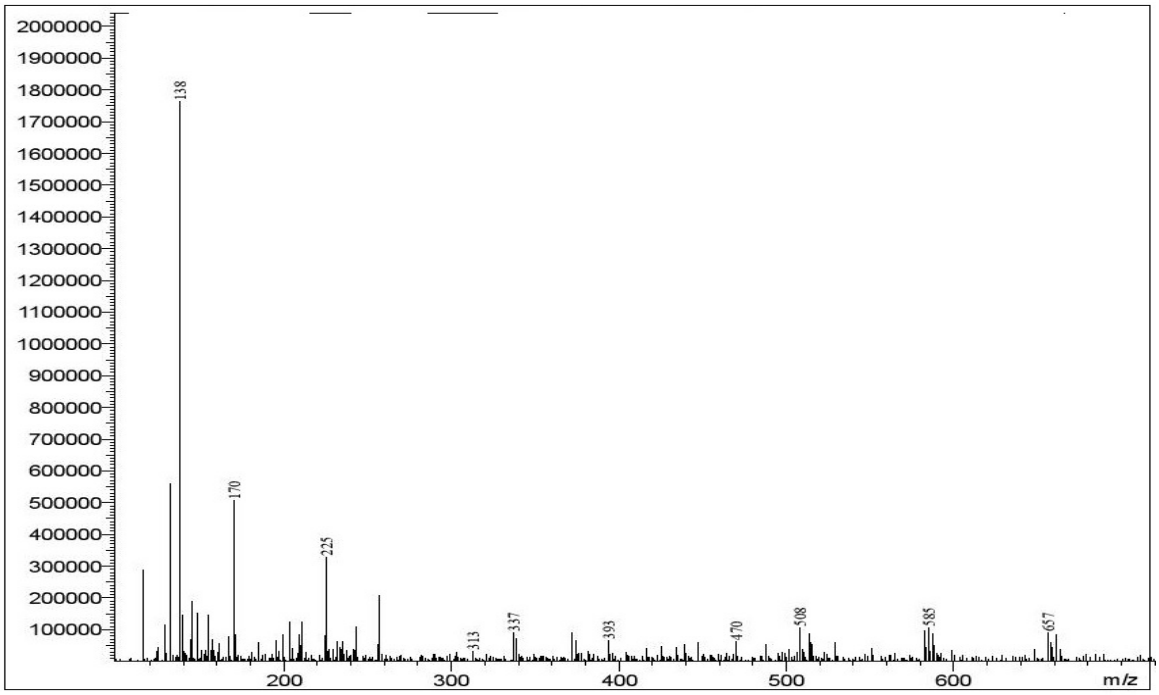

Figure 2: Mass spectrum of $[Co(MBINH)_2]Cl_2.H_2O$

3.2 Electronic spectra

Electronic absorption spectra of metal complexes were recorded in DMSO. The important electronic spectral data of metal complexes are presented in **Table 2**. The electronic spectrum of $[Fe(MBINH)_2]Cl_2.H_2O$ is shown in **Figure 3**. The study of magnetic and electronic spectra data is quite informative in characterizing the geometry of the complexes. The UV-visible spectrum of the ligands and their complexes were recorded in DMSO. In common transition metal complexes, the colour consequences of light absorption is due to the transfer of electrons from an orbital primarily on the ligand to one primarily located on the metal ions, such as ligand-to-metal charge transfer (LMCT) or *vice versa*, metal-to-ligand charge transfer (MLCT).

The complex $[Fe(MBINH)_2]Cl_2.H_2O$ shows strong intense band at 34129 cm^{-1} assigned due to intraligand and π-π* aromatic ring. Another sharp peak shows at the region of 28089 cm^{-1} is due to n-π* transition, corresponding to the nonbonding electron pairs of the azomethine bond. One medium intensity band observed in the range 21786 cm^{-1} is due to metal to ligand charge transfer transition (MLCT). A weak band is observed in the region of 10152 cm^{-1} is due to d-d transition which is assigned to the $^5T_{2g} \rightarrow {}^5E_g$ transition in octahedral field.

The $[Co(MBINH)_2]Cl_2 . H_2O$ shows strong band at 33172 cm^{-1} is due to intraligand and π-π* aromatic ring. The Co(II) complexes generally give rise to three absorption bands in the visible region under the influence of the octahedral field by the excitation of the electron from the ground state $^4T_{1g}(F)$ to the excited states $^4T_{2g}$ (F), $^4A_{2g}$ (F) and $^4T_{1g}$ (P). In $[Co(MBINH)_2]Cl_2 . H_2O$, the three bands are observed at the range of 11891 cm^{-1}, 16013 cm^{-1} and 25741 cm^{-1} corresponding to $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ (F) (υ_1), $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ (υ_2) and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (υ_3) transitions, respectively, characteristic of octahedral of geometry [14-16].

The electronic spectra of $[Ni(MBINH)_2]Cl_2$ complex displayed three absorption bands in the region of 16782, 21428, and 26154cm^{-1}. Thus, these bands may be assigned to the three spin allowed transitions $^3A_{2g}$ (F) $\rightarrow {}^3T_{2g}$ (F), $^3A_{2g}$ (F) $\rightarrow {}^3T_{1g}$ (F), and $^3A_{2g}$ (F) $\rightarrow {}^3T_{1g}$ (P), respectively, characteristic of octahedral geometry [17].

Table 2: Electronic Spectral data (cm^{-1}) of metal complexes

Complex	*Bands*	*Assignments*
$[Fe(MBINH)_2]Cl_2.H_2O$	34129	π-π*
	28089	n-π*
	21786	MLCT
	10152	$^5T_{2g} \rightarrow {}^5E_g$
$[Co(MBINH)2]Cl_2 . H_2O$	33172	π-π*
	25741	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$
	16013	$^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$
	11891	$^4T_{1g}(F) \rightarrow {}^4T_{2g}$ (F)
$[Ni(MBINH)_2]Cl_2$	32435	π-π*
	26154	$^3A_{2g}$ (F) $\rightarrow {}^3T_{1g}$ (P)
	21428	$^3A_{2g}$ (F) $\rightarrow {}^3T_{1g}$ (F)
	16782	$^3A_{2g}$ (F) $\rightarrow {}^3T_{2g}$ (F)

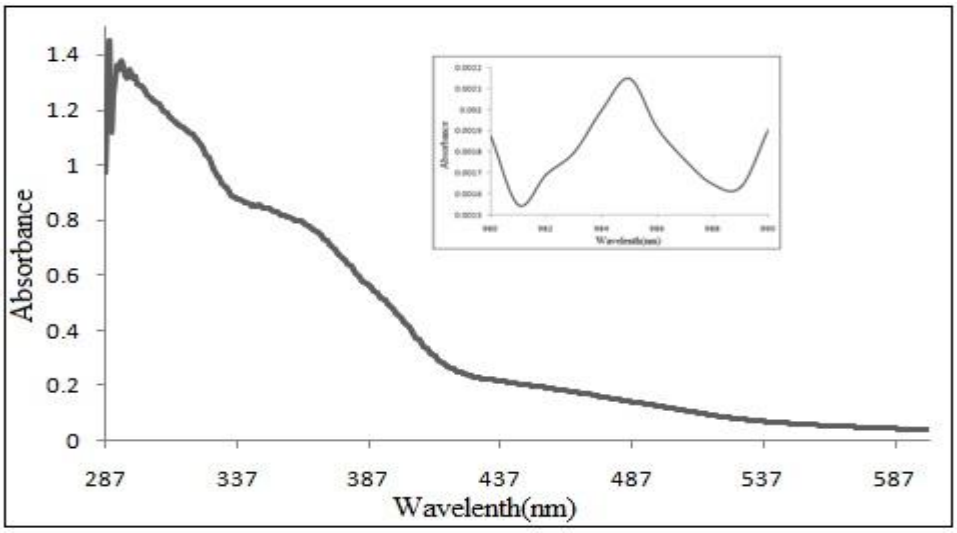

Figure 3: The electronic spectrum of $[Fe(MBINH)_2]Cl_2 .H_2O$

3.3 IR spectra

The important bands in infrared spectra of the ligand and it's metal complexes are discussed. Important IR spectral bands of complexes are presented in **Table 3**. A strong band is observed in the range of 3495-3521 cm^{-1} is observed and it is assigned to O-H strtching vibrations. In the IR spectrum of ligand a strong band is observed in the region of 1678 cm^{-1} which is assigned to ν(C=O)group. In the IR spectra of complexes this peak is shifted to lower wave numbers suggesting the involvement of >C=O group in chelation. The non-ligand absorption bands occurring in the regions 531-515cm^{-1} are assigned to $\nu_{(M-O)}$ and vibrations respectively [18]. The C=N (imine) vibration is observed in 1603 cm^{-1} range in the IR spectra of ligand. This band is shifted to lower or higher wave number in IR spectra of all the complexes suggesting the participation of azomethine nitrogen atom in complexation with metal ion. This was further supported by the appearance of a new band in the region 423-405 cm^{-1} in the complexes due to metal ligand M-N bonding [19]. A band is observed at 932 cm^{-1} in the ligand and corresponding to C-O-Me group. This band is shifted to higher wave number in IR spectra of all the complexes suggesting the participation of (C-OMe) with with M(II) ion[20].

Table 3: Important IR spectral bands of complexes & ligand

Compound	ν(O-H) cm^{-1}	ν(N-H) cm^{-1}	ν(C=O) cm^{-1}	ν(C=N) cm^{-1}	ν (OCH_3) cm^{-1}	ν(M-O) cm^{-1}
MBINH	-	3023	1678	1586	932	-
$[Fe(MBINH)_2]Cl_2 .H_2O$	3521	3012	1669	1573	953	515
$[Co(MBINH)2]Cl_2 . H_2O$	3495	3007	1656	1578	967	526
$[Ni(MBINH)_2]Cl_2$	-	3019	1672	1581	964	531

Based on the above spectral data we suggest general structure of the metal complexes. It is shown in **Figure 4**.

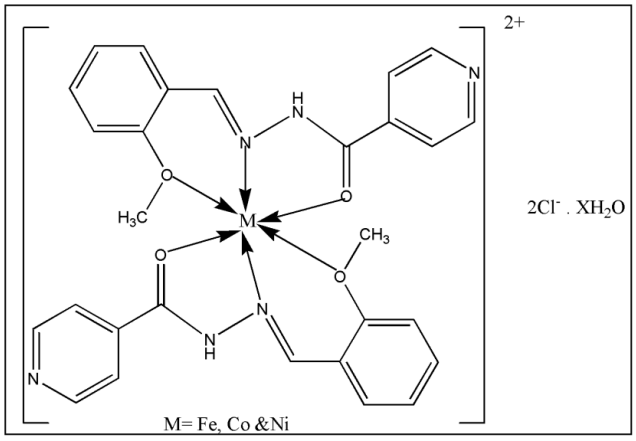

Figure 4: The Structure of metal complexes

3.4. Antibacterial activity

To determine the antibacterial activity of MBINH ligand and its Fe^{2+}, $Co^{2+,}$ and Ni^{2+} complexes, the disc diffusion method was used, with ampiciillin as the standard antibiotic. The prepared compounds were tested against *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Bacillus Subtilis bacteria species* microorganisms. The compounds are found to show low bactericidal behavior against most of the bacterial culture and resistance towards the other. In general the results reveal that the activity of the ligand was found to enhance on complexation with metal. The inhibition effect of the ligand and its metal complexes on the growth of various bacteria is summarized in **Table 4**.

Table 4: Antibacterial activity of metal complexes and ligand

Compound	Bacterial growth inhibition zone (in mm)											
	S. Aureus			*B. Subtilis*			*K. Pneumonia*			*E. Coli*		
	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)
MBINH	9	10	11	8	10	13	11	12	14	7	9	12
$[Fe(MBINH)_2]Cl_2.H_2O$	14	18	15	14	18	21	14	16	18	10	12	15
$[Co(MBINH)2]Cl_2.H_2O$	16	18	20	16	18	19	12	14	19	13	16	18
$[Ni(MBINH)_2]Cl_2$	12	17	18	15	16	18	11	14	16	15	17	19
Standard	16	18	21	17	18	22	15	17	20	18	20	22
Control	-	-	-	-	-	-	-	-	-	-	-	-

Standard: Ampicillin; Control:DMSO

4. Conclusions

2-Methoxy benzaldehyde isonicotinoylhydrazone has been synthesized and characterized based on elemental analysis, Mass, IR and NMR spectral studies. Fe(II), Co(II) and Ni(II) complexes of 2-Methoxy benzaldehyde isonicotinoylhydrazone have been synthesized and characterized based on various physicochemical and spectral techniques. These studies revealed that the complexes have general formula ML_2 (where L = hydrazone). The hydrazones act as neutral tridentate ligand. Electronic spectral data suggest that the complexes have octahedral geometry. Antibacterial activity of metal complexes have been studied. Among three complexes $[Co(MBINH)2]Cl_2.H_2O$ shows better activity.

References

[1] R. M. Issa, S. A. Abdel-Latif, H. A. Abdel-Salam, " Syntheis and characterization of new Cu(II) complexes derived from Benzilic and mandelic hydrazones" Synthesis and Reactivity in Inorganic and Metal Organic Chemistry, pp. 31**,** pp. 95-105, 2001.

[2] D.P. Singh, K. Kumar, C. Sharma, New 14-membered octaazamacrocyclic complexes: Synthesis, spectral, antibacterial and antifungal studies, European Journal of Medicinal chemistry, 45, pp. 1230-1236, 2010.

[3] S.M. Abdallah, G.G. Mohamed, M.A. Zayed,M.S. Abou El-Ela, "Spectroscopic study of molecular structures of novel Schiff base derived from o-phthaldehyde and 2-aminophenol and its coordination compounds togetherwith their biological activity", Spectrochimica Acta, 73A, pp. 833-840, 2009.

[4] B. N. Sivasankar and S. Gavindaragam., " Synthesis, characterization and Thermal Reactivity of Mixed Metal Hydrazidocarboxylate Hydrazinates", Synthesis and Reactivity in Inorganic and Metal Organic Chemistry, 25, pp. 127-138, 1995.

[5] P. M. Gurubasavaraj and P. M. Veeresha, "Synthesis, Characterization, Electrochemistry and Biological Activities of Ni(II) and Cu(II) Complexes of Schiff Bases", Asian Journal of Chemistry, 20, pp. 2841-2846,2008.

[6] N. Nawar and N. M. Hosny, " Syntheis, spectral and antimicrobial studies of o-aminoacetophenone o-hydroxybenzoylhydrazone complexes", Transition Metal Chemistry, 25, pp.1-8, 2000.

[7] B. Zdzislaw. Acta Pol. Pharm. 54, 1997, 49.

[8] C. Wang, Y. Wu, Y. Qu, K. Zhao, J. Xu, X. Xia and H. Wu, "Synthesis, structure and antioxidant properties of manganese(II), zinc(II) and cobalt(II) complexes with bis(benzimidazol-2-ylmethyl)allylamine", Transition metal chemistry, 45, pp. 523-529, 2020.

[9] P. P. T. Sah, S. A. Peoples, " Isonicotinyl Hydrazones as Antitubercular Agents and Derivatives for Identification of Aldehydes and Ketones", Journal of the American Pharmaceutical Association, 43, pp. 513-524, 1954.

[10] B. Mounyr, M. Sadiki and S. K. Ibnsouda, "Methods for *in vitro* evaluating Antimicrobial Activity" Journal of Pharmaceutical Analysis, 6(2), pp. 71-79, 2016.

[11] R. Castarlenas and Dixneuf, Chem. Int 42, 2003,23.

[12] R.L. Dutta and A. Syamal. Elements of Magnetochemistry. 2nd ed. New Delhi: Affiliated East- West Press Pvt. Ltd; 1993.

[13] C.M. Harris, and E.D. Mckenzie, " Nitrogenous Chelate Complexes of Transition metals-III: bis-chelate complexes of nickel(II) with 1,10-phenanthroline,2,2'-bipyridyl and analogous ligands", Journal of Inorganic and Nuclear Chemistry, 29, pp.1047-1068, 1967.

[14] V. P. Singh and A. Katiyar, "Synthesis, spectral characterization and antimicrobial activity of some transition metal(II) complexes with acetone p-amino acetophenone benzoylhydrazone", Pesticide Biochemistry and Physiology, 92, pp. 8-14, 2008.

[15] S. Chandra and S. Sharma, " Chromium(III), manganese(II), cobalt(II), nickel(II), copper(II) and palladium(II) complexes of a 12-membered tetraaza[N_4] macrocyclic ligand, Transition metal Chemistry, 27, pp.732-735, 2002.

[16] B. S. Grag, P. K. Singh and S. K. Grag, " Synthesis and Spectral Characterisation of Complexes of Acenaphthaquinonemono (Lepidyl)Hydrazone with various salts of Cobalt(II), Synthesis and Reactivity in Inorganic and Metal Organic Chemistry, 23, pp.17-28, 1993.

[17] A. B. P. Lever. Inorganic Electronic Spectroscopy. Amsterdam, New York Elsevier 1968.

[18] S. G. Teoh, G. Y. Yeap, C. C. Loh, L. W. Foong, B. Teo and H. K. Fun, "Inner Coordination Sphere Tin(IV) Complexes with some O, N, N-Tetradentate{N-(2-hydroxybenzaldehyde)-1-amino-2-phenyleneimine and N-(2-hdroxy-7-naphthaldehyde)1-amino-2-phenyleneimine}andO,N,N,O-Quadriedntate{N,N'-bis(2hydroxybenzaldehyde) enylene-1,2-phenylenediimine and N,N'-bis(2-hydroxy-1-naphaldehyde)-1,2-phenylenediimine}Schiff bases" Polyhedron, 16, pp. 2213-2221, 1997.

[19] M. Das and S. Chattopadhyay, Control of molecular architecture by hydrogeonding: mononuclear versus

dinuclear copper(II) complexes with tridentate N_2O donor Schiff base isomers", T ransition Metal Chemistry, 38 , pp.191-197. 2013.

[20] H. Ayman Ahmed , A.M. Hassan, H. A. Gumaa , B. H. Mohamed ,A. M. Eraky and A. A. Omran, "Copper(II)-oxaloyldihydrazone complexes: Physico-chemical studies: Energy band gap and inhibition evaluation of free oxaloyldihydrazones toward the corrosion of copper metal in acidic medium", Arabian Journal of Chemistry, 12, pp.4287-4302, 2019, 4287.

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