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Low cost green technological synthesis, spectral, antibacterial, antifungal and anti-inflammatory activities of Cr(III) and Fe(II) complexes with some bio-active ligands

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Abstract

Six coordinated Cr(III) and Fe(II) complexes have been synthesized with bio-active benzimidazole and benzoate ion and characterized by micro-analytical methods viz., elemental analysis, metal estimation, molar conductance, magnetic moments (VSM), Redox properties (cyclic voltammetry), spectral methods, UV-Visible, IR, Far-IR and bio-potential activities like antibacterial, antifungal and anti-inflammatory activities. Metal ions and ligands are in the ratio of 1:3:3 for (M: L_1: L_2) for Cr(III) and 1:4:2 (M: L_1: L_2) for Fe(II) complexes. Where L_1 is benzimidazole (neutral monodentate) and L_2 is benzoate (monodentate anionic) and formulae of the complexes were deduced from elemental analysis and metal estimation. Non-electrolyte, neutral nature of the complexes deduced from 10^{-3} M complex solution in acetonitrile. Quasi reversible one electron transfer reaction confirmed from Redox behavior (cyclic voltammetry). Magnetic moment and electronic spectra of the complexes were confirmed by its octahedral six coordinated geometry. Complexing ability and metal-chelating nature of the complexes were also confirmed by IR and Far-IR spectral data. The antibacterial and antifungal activities of the complexes comparing with those for the benzimidazole, The MIC value was measured in millimeter, the results indicated that the complexes have moderate activities than the ligand. The anti-inflammatory activities of the ligand and Cr(III) complex were carried out by protein denaturation method using Bovine serum albumin protein the concentration and IC50 values were also predicted and it indicate that the complex and benzimidazole are moderate anti-inflammatory agent.

Key words: *Benzimidazole, Cr(III) complex, Fe(II) complex, Antibacterial, Antifungal and Anti-inflammatory*

1. Introduction

Coordination complexes are interesting in the field of inorganic chemistry due to the lot of donor ('N' and 'O') site organic ligands available which are biologically and pharmaceutically active. (Vikas S. Padalkar et al., 2014) Phenyl ring fused with imidazoles ring, the compound is benzimidazole they have variety of applications in co-ordination chemistry, viz., photo physics, photochemistry and bio-inorganic chemistry because of their well known pharmaceutical applications that is antibacterial, antihelmintic, antifungal, anti-inflammatory, antiviral and analgesic properties [Aruna Sindhe M etal., 2016; Buttrus H et al., 2012; Misbah Ur Rehman et al., 2016; B. Anil Reddy, 1929; S.O.Podunavac-Kuzmanovi et al., 2007). Nitrogen based ligands are widely used as a very good donor chelate ligands which are effectively forming stable complexes with transition and post-transition metals. Microwave assisted synthetic reactions are low-cost, eco-friendly, less-time and high efficient synthesis in co-ordination chemistry. (Matangi Sunitha et al., 2012; Ramalingam Balamurugan et al., 2001; Vikas S. Padalkar et al., 2011; K. C. Rout et al.,1996). In this regards the present studies aims at low-cost, green technological synthesis, spectral, antibacterial, antifungal and anti-inflammatory activities of Cr(III) and Fe(II) complexes with bio-active benzimidazole and benzoate ion.

2. Materials and methods

2.1 Instrumental Methods

All the chemicals were purchased and used as it is without further purification. Benzimidazole: Alfa Aesar, cadmium nitrate, sodium nitrite, DMSO, methanol, ethanol and CH_3CN were used of AnalaR grade.

The elemental analysis of the complex was carried out using (Thermo Finnegan make, Flash EA1112 series) CHNS(O) analyzer instrument. The molar conductance of the complex of 10^{-3} M in acetonitrile was conducted using Systronic Conductivity Bridge at 30^0C. The magnetic moment by VSM method and the solid state UV-visible spectra of the complexes was measured by using Varian carry-5000 model UV-Visible spectrophotometer. IR spectra of the free INH (ligand) and its complexes were carried out using Schimadzu FT-IR 8400s spectroscopy at 4000-400 cm^{-1} wave number with KBr pellet technique. The antibacterial and antifungal activities of INH and its complex were done by in-vitro Agar well diffusion method using Amikacin and ketoconazole as a standard for bacterial and fungal strain respectively. The anti-inflammatory activity by protein denaturation method was also carried out and compared with those for standard.

2.2 Preparation of complex: The Cr(III) and Fe(II) complexes were synthesized by mixing benzimidazole 0.88 g (7.49 mmol), 1.38 g (11.69 mmol) in 5ml methanol with 1g (2.49 mmol and 2.92 mmol) of metal nitrate in 5ml methanol and then sodium benzoate 1.08g (7.49 mmol), 0.84 g (5.84 mmol) in ethanol respectively was mixed and the whole mixture was irradiated on a microwave oven for few seconds. The precipitated colored complexes were filtered, washed with ethanol and dried. The complexes are stable under ordinary condition and the yield is 80%.

3. Results and discussion

3.1 Micro-analytical data

Elemental analysis and metal estimation of the complexes were recorded using CHN analyzer and volumetric/ colorimetric estimation with standard procedure. The results indicating that the complexes are mononuclear with metal: ligands ratio if 1:3:3 (Cr (III): benzimidazole: benzoate) for Cr(III) complex but in Fe(II) it is 1:4:2 (Fe(II): benzimidazole: benzoate). The non-electrolytic nature (1:0 type), neutral nature of the complexes was confirmed by the molar conductance of 10-3M solution of metal complexes, these values are lie 16.80 $Ohm^{-1}cm^2mol^{-1}$ in Cr(III) and17.30 $Ohm^{-1}cm^2mol^{-1}$ Fe(II) complex.(G. H. Anuradha et al., 2012; G.H. Anuradha et al, 2015).

3.2 Cyclic voltammetry

Cyclic voltammogram of Cr(III) and Fe(II) complexes were carried out using three electrode The cyclic voltammogram of Cr(III)complex shows a Redox process corresponding to the formation of one electron transfer quasi reversible Cr(III)/Cr(II) couple. The cathodic peak potential E_{pc} = -1.339 V anodic peak potential E_{pa} = -0.250V and the peak potential separation is Δ_{Ep} = 1.089V. The ip_a/ip_c value is at -0.5V and the reduction potential (E_0) at -0.794 V also confirming the one electron transfer quasi reversible reaction. (A.H. Manikshete, et al., 2010). Cyclic voltammogram of Fe(II) complex shows E_{pc} at -1.187V, E_{pa} = -0.800V and the peak potential separation is Δ_{Ep} = 0.387V. The ip_a/ip_c value at -0.11V and the reduction potential (E_0) is at -1.987 V also confirming the one electron quasi reversible reaction (Mohamed M. Ibrahim et al., 2012). Fig.1.

3.3 Magnetic moment and electronic spectra

The electronic absorption spectra of the Cr(III) complex in the solid state diffused reflectance spectral method were recorded, it is very close to the octahedral geometry around Cr(III) with $^4A_{2g}$ ground state configuration. The complex exhibits three λ_{max} values at 577 nm (ν_1; 10Dq), 421 nm (ν_2, 18Dq), 269 nm (ν_3, 12Dq+15B) which correspond to $^4T_{2g}$ (P) ← $^4A_{2g}$, $^4T_{1g}$(F) ← $^4A_{2g}$ and $^4T_{1g}$(P) ← $^4A_{2g}$. These transitions are also confirmed by the octahedral geometry for the chromium complex. The effective magnetic moment (μ_{eff}) 3.87 BM obtained for the complex also confirming the octahedral geometry (Jyoti C. Ajbani et al., 2015). In Fe(II) complex exhibits three λ_{max} values at 680 nm, 490 nm, 266 nm which corresponds to ^5E_g ← $^5A_{1g}$, $^5B_{2g}$ ← $^5A_{1g}$ and C-T transition confirming the octahedral geometry. (Mahasin F. Alias et al., 2015).

3.4 IR spectra

The IR spectrum is the best tool to find out the complex forming ability and functional group present in the ligand and its metal complexes. The free nitrogen donor benzimidazole ligand exhibit ν(C=N) stretching frequency at 1587 cm^{-1}, ν(N-H) at 3115 cm^{-1} and ν(C-N) at 1200 cm^{-1} after complexation these stretching frequencies at

1599 cm^{-1}, 3357 cm^{-1} and 1271 cm^{-1} in Cr(III) complex whereas 1598 cm^{-1}, ν(N-H) at 3338 cm^{-1} and ν(C-N) at 1275 cm^{-1} in Fe(II) complex respectively confirming the complex formation. It is evident that the ν(C=N) frequency shifted to higher value in complexes shows the benzimidazole can coordinate to the metal ion through nitrogen atom, Fig.2 (freely available lone pair electrons).(Waqar Ahmad et al., 2017)

The mixed anionic ligands benzoate ion gives the ν(C=C) at 1400-1600 cm^{-1} and ν(C=O) at 1680-1750 cm^{-1}, ν(C-H) at 3000-3050 cm^{-1} and ν(C-O) at 1210-1320 cm^{-1} these are shifted to 1496 cm^{-1}, 1681 cm^{-1} 2924 cm^{-1} and 1251 cm^{-1} in Cr(III) complex but in Fe(II) these values at 1510 cm^{-1}, 1621 cm^{-1} 2930 cm^{-1} and 1254 cm^{-1} confirming the entry of mixed anionic ligand benzoate ion into the coordination sphere. (Ş. Yurdakul et al., 2003).

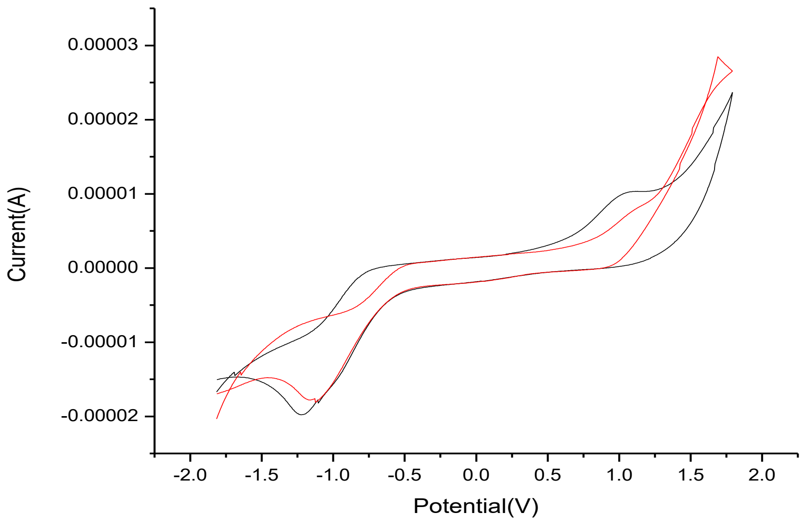

Fig- 1

Cyclic voltammogram of **Cr(III)** and **Fe(II)** complexes

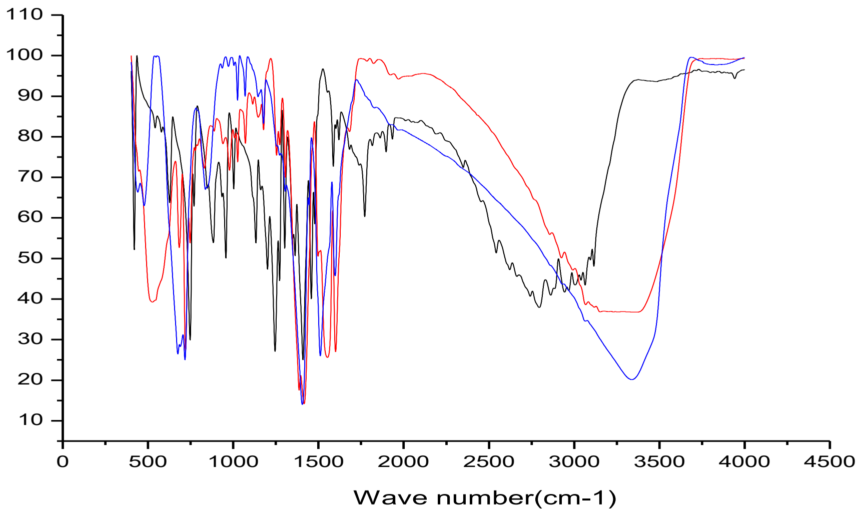

Fig-2

IR Spectra of Benzimidazole, Cr(III) complex and Fe(II) complex

3.5 Far-IR spectra

Far-IR spectra of the complexes confirming the metal linked atom capability. Obviously the far IR spectra of the complex shows the stretching frequencies at 435 cm^{-1} 427 cm^{-1} for ν(M-N) and 419 cm^{-1} 406 cm^{-1} is ascribed to the ν(M-O) linkage of benzimidazole nitrogen and benzoate ion oxygen donor site. (S. O. Podunavac-Kuzmanovic et al., 2008).

3.6 Antibacterial and antifungal activities

All the complexes were evaluated by in-vitro antibacterial activities against three gram negative bacteria (*Pseudomonas, Proteus and Klebsiella pneumonia*) and one gram positive bacterium (*Bacillus*) and antifungal activity against pathogenic yeast *C.albicance* by Agar well diffusion method. (Fig-3), According to MICs of complexes and ligand, they are moderately active against tested microorganism on comparing standards (Amikacin & Ketoconazole) because of the ligands are unsubstituted only electron donor nitrogen and oxygen present and these are coordinated to metal ions. After complexation the lipophilicity is the major factor to enhance the biological activities. (ÖzdenTar et al., 2017)

3.7 Anti-inflammatory activities

The reaction mixture (5ml) consisting of 2 mL of different concentrations of *samples* (100,200,300,400and 500 µg/ml) and 2.8 mL of phosphate buffered saline (pH 6.4) was mixed with 0.2 mL of Bovine serum albumin and incubated at (37±1)°C for 15 min. Denaturation was induced by keeping the reaction mixture at 70°C in a water bath for 10 min. After cooling, the absorbance was measured at 660 nm by using double distilled water as blank. Diclofenac sodium (100,200,300,400and 500 µg/ml) used as reference drug and similarly for determination of absorbance. Each experiment was done in triplicate and the average was taken. The percentage inhibition of protein denaturation can be calculated as:

% of Inhibition = [100 - (OD of test solution - OD of control)] × 100

The in-vitro anti-inflammatory activities of benzimidazole and Cr(III) complex were studied by using protein (bovine serum albumin) denaturation method with different concentration (100, 200, 300, 400 & 500 µg/ml), diclofenacsodium used as a references drug. The percentage inhibition of protein denaturation calculated and compared with reference. Three separate experiments were carried out and inhibition concentration IC50 were also found out.(Fig-4 & Table-1). The results indicating the benzimidazole (57.93%) and Cr(III) complex (56.95%) are moderate anti-inflammatory agent on comparing reference (82.89%) but the IC50 values also increases from standard to benzimidazole and Cr(III) complex (Figure-). Due to presence of donor site in the ligand ('N' donor) and additional ligand benzoate ('O' donor) present in the complex which shows the moderate activity of the complexes. (Xia-BingFu et al., 2015; Gajendra Kumar et al., 2018)

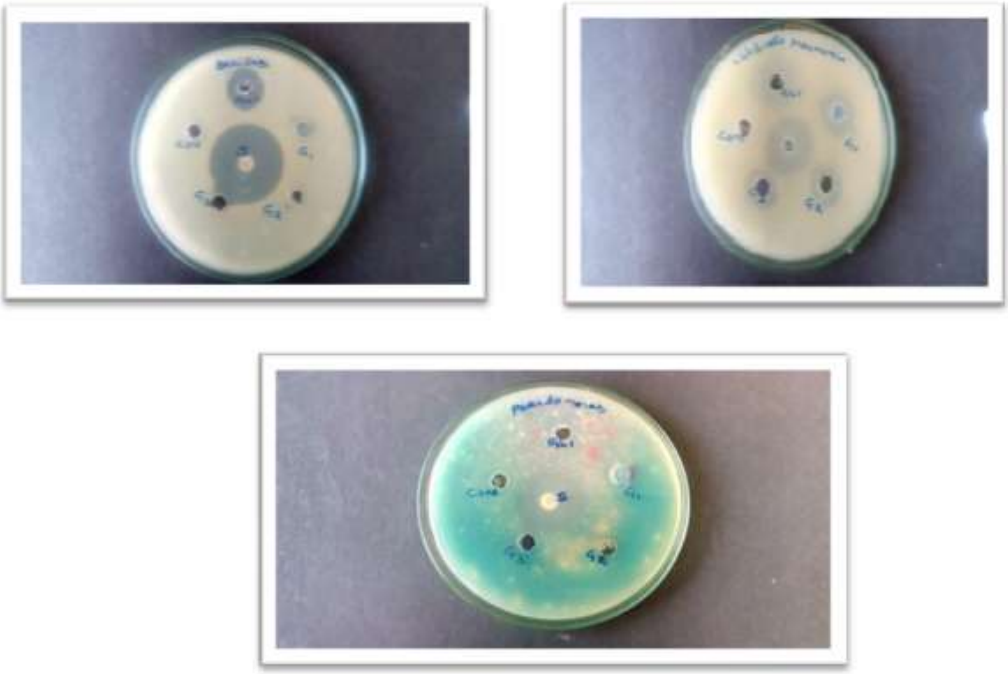

Fig-3 Bio-potential activities of Benzimidazole, Cr(III) complex and Fe(II) complex

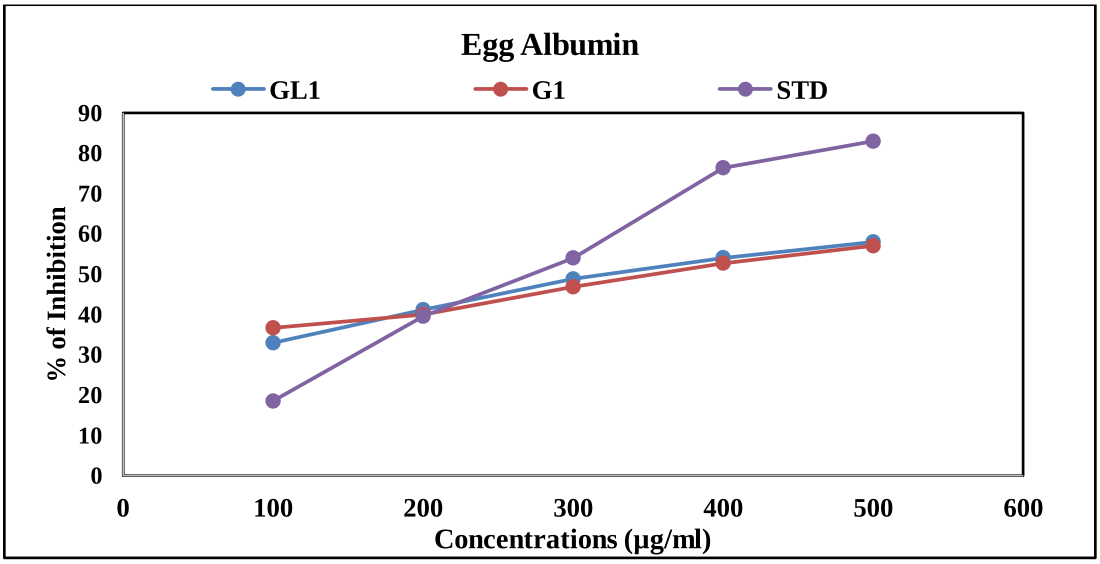

Fig-4 Anti-inflammatory activity of Benzimidazole, Cr(III) complex and standard

Table.1: Anti-inflammatory activity of samples using protein (Bovine serum albumin) denaturation method

Samples	Concentrations (µg/ml)					IC_{50} (µg/ml)
	100	200	300	400	500	
benzimidazole	32.88 ±0.86	41.1 ±0.44	48.73 ±0.66	54.01 ±0.50	57.93 ±0.97	348.77
Cr(III) complex	36.59 ±0.66	39.92 ±0.71	46.77 ±1.04	52.64 ±0.57	56.95 ±1.00	364.38
Standard (Diclofenac sodium)	18.42 ± 1.18	39.47 ± 0.72	53.95 ± 0.73	76.31 ± 1.11	82.89 ± 0.55	274.58

Values are expressed as Mean ± SD for triplicates

4. Conclusion

The present studies confirmed by the low-cost, green technological synthesis, spectral, antibacterial, antifungal and anti-inflammatory activities of Cr(III) and Fe(II) complexes with bio-active benzimidazole and benzoate ion. From the results of micro-analytical, spectral, Redox and biological activities, the complexes are octahedral geometry; they are non-electrolyte, neutral complexes and also mononuclear, potent bioactive and moderate anti-inflammatory agent. They show very good Redox properties.

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References

[1] Vikas S. Padalkar, Vinod D. Gupta, Kiran R. Phatangare, Vikas S. Patil, Prashant G. Umape, N. Sekar, Synthesis of novel dipodal-benzimidazole, benzoxazole and benzothiazole from cyanuric Chloride: Structural, photophysical and antimicrobial studies. Journal of Saudi Chemical Society,18: 262-268. (2014)

[2] Aruna Sindhe M., Yadav D. Bodke, Kenchappa R., Sandeep Telkar, Chandrashekar A., and Vinoda B.M., Catalytic assemble of 2-amino-5,6-dimethyl-1H-benzimidazole with carboxylic acids and evaluation of their antimicrobial and antioxidant activities. Journal of Taibah University Medical Sciences, 11(5): 418-426. (2016)

[3] Buttrus H. Nabeel and Saeed T. Farah, Synthesis and Structural Studies on Some Transition metal complexes of Bis-(benzimidazole-2-thio) ethane, propane and butane ligands. Research Journal of Chemical Sciences, 2(6): 43-49. (2012)

[4] Misbah Ur Rehman, Muhammad Arif, Muhammad Imran, Muhammad Farooq, Synthesis, Characterization and Antimicrobial Properties of Mannich Base Cyclization Derivatives of Benzimidazole and Their Metal Complexes. American Journal of Chemistry, 4(1): 10-21. (2014)

[5] Anil Reddy B, Synthesis, Characterization and Biological Evaluation of 1, 2-Disubstituted Benzimidazole Derivatives using Mannich Bases. E-Journal of Chemistry, 7(1): 222-226. (1929)

[6] Podunavac-Kuzmanovi S.O and Cvetkovi D.M, Antibacterial evaluation of some benzimidazole derivatives and their zinc(II) complexes. J. Serb. Chem. Soc., 72 (5): 459–466. (2007)

[7] Matangi Sunitha, Pragathi Jogi, Bathini Ushaiah and C. Gyana Kumari, Synthesis, Characterization and Antimicrobial Activity of Transition Metal Complexes of Schiff Base Ligand Derived from 3-Ethoxy Salicylaldehyde and 2-(2-Aminophenyl) 1-H-benzimidazole. E-Journal of Chemistry, 9(4):2516-2523.(2012)

[8] Ramalingam Balamurugan and Mallayan Palaniandavar, Trigonal Planar Copper(I) Complex: Synthesis, Structure, and Spectra of a Redox Pair of Novel Copper(II/I) Complexes of Tridentate Bis(benzimidazol-2-yl) Ligand

Framework as Models for Electron-Transfer Copper Proteins. Inorg. Chem., 40:2246-2255.(2001)

[9] Vikas S. Padalkar, Vikas S. Patil, Vinod D. Gupta, Kiran R. Phatangare, Prashant G. Umape, and N. Sekar, Synthesis, Characterization, Thermal Properties, and Antimicrobial Activities of 5 (Diethylamino)-2-(5-nitro-1H-benzimidazol-2-yl)phenol and Its Transition Metal Complexes. ISRN Organic Chemistry, 2011: 7 pages. (2011)

[10] Rout K. C, Mohanty R.R , Jena S and Dash K.C ,Dioxouranium(VI) and thorium(IV) complexes with 2(2′-pyridyl)1-methylbenzimidazole and reaction of dioxouranium(VI) complex with mercury(II), cobalt(II) and nickel(II). Polyhedron, 15(5–6):1023-1029.(1996)

[11] Anuradha G.H and Chandrapal A.V, Synthesis and Structural Studies of Cr(III), Mn(II) and Fe(III) Complexes of N(2-Benzimidazolyl)acetylacetohydrazone. E-Journal of Chemistry, 8(1): 421-426. (2011)

[12] Anuradha G.H and Neelamma M, Synthesis and Characterization of Cr (III), Mn (II), Fe (III), Co (II), Ni (II), Cu (II) and Zn (II) Complexes of 2(α-mercaptoacylhydrazonyl) benzimidazole. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 6(4): 507-513.(2015)

[13] Manikshete A.H , Kamble V.N , Sanjay Sarsamkar and Doedware S, Synthesis, spectral and biological studies of Cr(III), Mn(II) and Fe(II) complexes with diacetylmonoxime. Oriental Journal of Chemistry 26(2): 573-580.(2010)

[14] Mohamed M. Ibrahim, Gaber A. M. Mersal, Samir A. El-Shazly and Abdel-Motaleb M. Ramadan, Synthesis, Characterization, and Electrochemical Properties of Bis(2-benzimidazolylmethyl-6-sulfonate)amine-based zinc(II), copper(II), and oxidovanadium(IV) Complexes: SOD Scavenging, DNA binding, and Anticancer Activities. Int. J. Electrochem. Sci.,7: 7526 – 7546. (2012)

[15] Jyoti C. Ajbani, D. Smita Revankar, Mita Revankar, M. Revanasiddappa, Veerabhadra Swamy and S. Shankar, Microwave synthesis, spectroscopic, thermal and biological studies of some transition metal complexes containing heterocyclic ligands. Int. J. Chem. Sci., 13(4): 1673-1692.(2015)

[16] Mahasin F. Alias , Maysoon M. Abdul Hassan , Sameaa J. Khammas, Synthesis, Characterization of Some Metal Complexes With Mixed Ligands Derived from Sulfamethoxazole and 4, 4' -dimethyl-2, 2' –bipyridyl. International Journal of Science and Research, 4(7): (2015)

[17] Waqar Ahmad, Shakeel Ahmad Khan, Khurram Shahzad Munawar and Asma Khalid, and Sadia Kawanl, Synthesis, characterization and pharmacological evaluation of mixed ligand-metal complexes containing omeprazole and 8-hydroxyquinoline. Tropical Journal of Pharmaceutical Research, 16 (5): 1137-1146.(2017)

[18] Yurdakul S and Kurt M, Vibrational spectroscopic studies of metal(II) halide benzimidazole, Journal of Molecular Structure. 650(1–3):181-190. (2003)

[19] S. O. Podunavac-Kuzmanovic, V.M. Leovac and D. D. Cvetkovic, Antibacterial activity of cobalt(II) complexes with some benzimidazole derivatives. J. Serb. Chem. Soc. 73 (12): 1153–1160. (2008)

[20] ÖzdenTarı, FatmaGümüş, LeylaAçık and BetülAydın, Synthesis, characterization and DNA binding studies of platinum(II) complexes with benzimidazole derivative ligands, Bioorganic Chemistry, 74: 272-283. (2017)

[21] Xia-BingFu, Jia-JiaZhang, Dan- DanLiu, QianGan, Hong-WeiGao, Zong-WanMao and Xue-YiLe, Cu(II)–dipeptide complexes of 2-(4′-thiazolyl)benzimidazole: Synthesis, DNA oxidative damage, antioxidant and in vitro antitumor activity. Journal of Inorganic Biochemistry,143: 77-87. (2015)

[22] Gajendra Kumar, Vidhi Singh, Preeti Sharma, Synthesis, characterization of biologically active Schiff base 14-membered M (III) macrocyclic complexes derive from 1 H-indol and diethyl oxalate and thiocarbonohydrazide. International Journal of Biology Research, 3(1):188-194.(2018)