

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES ON SCHIFF BASE DERIVED FROM 2-AMINO 4,6-DIHYDROXYPYRIMIDINE AND BENZALDEHYDE AND ITS COBALT COMPLEXES

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ABSTRACT:

In this work, the heterocyclic Schiff bases ligand derived from 2-amino-4,6-dihydroxypyrimidine with Benzaldehyde (L) was synthesized. The ligand used to synthesis complexes of Co(II). The synthesized compounds have been characterized by FT-IR, ¹H-NMR and UV-Vis techniques for the ligands and FT-IR, UV-Vis, all reactions monitored by TLC, molar conductivity and magnetic susceptibility measurements for the corresponding complexes. The conductance measurements in DMSO showed that the Co(II) complex was 1:2 electrolytes respectively. The ligand and its complexes were screened for their antifungal and antibacterial activity against *Aspergillus niger*, *Penicillium chrysogenum*, *Fusarium moneliforme* and *Aspergillus flavus* and *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, *B. subtilis*. The result indicated that the complexes exhibited good antifungal and antibacterial activities.

KEYWORDS: Schiff base, Metal complexes, Thermal analysis, Powder X-ray diffraction, Antibacterial studies.

1. INTRODUCTION:

Coordination chemistry is undoubtedly the most active research area in inorganic chemistry. Several thousands of coordination complexes have been synthesized and investigated during the past few decades. Ever since the importance of coordination phenomenon in biological processes

was realized, lot of metal containing macromolecules have been synthesized and studied to understand the role of these ligands in biological systems, and they also contribute to the development of new metal-based chemotherapeutic agents. These have resulted in the emergence of an important branch of inorganic chemistry viz. bioinorganic chemistry because in several cases, the metal chelates have been found to be more antimicrobial than the chelating agents themselves.[1] Schiff base ligands have been studied extensively due to synthetic flexibilities, selectivity as well as sensitivity towards the transition metal ions. The architectural beauty of these coordination complexes arises due to the interesting ligand systems containing different donor sites in heterocyclic rings. In the last decades, Schiff base have received much great interest, mainly because of their wide application in the field of synthesis and catalysis [2, 3]. Similarly heterocyclic ligands containing nitrogen atoms are drawing a great deal of attention in Coordination chemistry and homogeneous Catalysis [4-6]. Two or more potential donor centre of amino heterocycles plays an important role in the study of comparative reactivity of ambidentate ligand systems [7]. Furthermore, transition metal complexes containing pyrimidine ligands are commonly found in biological studies and play important roles in processes, such as catalysis of drug interaction with biomolecules [8-10]. A tumid number of Schiff base ligand and metal complexes are of substantial sake and attention because of their biological activity including anti-tumor, antibacterial, fungicidal and anti-carcinogenic properties [11, 12]. Several complexes coordinated through the Schiff base ONNO donors have been studied as oxygen carrier and they are useful models for bioinorganic processes [13]. The cobalt(II) and manganese(II) complexes with tetradentate Schiff base which coordinate through N_2O_2 donor atoms have been extensively studies as oxygen carriers and also as catalysts for water-splitting systems[14].

Pyrimidine is the parent heterocyclic of a very important group of compounds that occurs in living system. They are considered simple as far as their interactions with metal ion are concerned since they possess fewer coordination sites [15]. Pyrimidine derived metal ion complexes have been studied in recent years [16], owing to their numerous biological activities ranging from antimalaria, antiviral, antibacterial, antitumor and antifungal [17]. which often have been related to their chelating ability with trace metal ions. There are some literatures on metal (II) complexes of trimethoprim, pyrimethamine, various pyrimidine and pyrimidinyl Schiff base chelates [18]. However, no work has been reported on of metal(II) complexes of 2-amino-4,6-dihydropyrimidine. Thus, our aim is to synthesize, characterize and investigate the magnetic properties of these novel metal(II) complexes for possible magnetic interactions such as antiferromagnetism, and their antibacterial properties will also be investigated for potentials as broad-spectrum antibacterial agents in-vitro as a continuation of the research activities of our group on metal-based therapeutics agents [19]. In this research paper, we report the recent research on template reaction of 2-amino-4,6-dihydropyrimidine with Benzaldehyde in the presence of cobalt(II) Schiff base condensation complexes. The obtained new metal complexes was characterized by some physico-chemical techniques and antimicrobial activity.

2. MATERIAL AND METHODS:

2.1 Reagents and solvents :

2-amino- 4,6 dihydroxypyrimidine (Aldrich sigma) and Benzaldehyde (AR grade) were used for synthesis of ligand. AR grade metal nitrate were used for the complex preparation.

2.2 Synthesis of ligand:

The ligand was prepared by a modification of the reported methods [20]. The Schiff base ligand has been synthesized by refluxing a mixture of 0.01 mol (1.4057 g) of, Benzaldehyde and 0.01 mol (1.2710 g) of 2-amino-4, 6-dihydroxypyrimidine in 50 ml super dry ethanol refluxed for about 4h. Schiff base thus formed was cooled to room temperature and collected by filtration, followed by recrystallization in ethanol and dried in vacuo over anhydrous calcium chloride (Yield:70%).

2.3 Synthesis of metal complexes:

To a hot ethanol solution (25ml) of the ligand (2 mol) and (25ml) of metal Nitrate (1mol) was added with constant stirring. The pH of reaction mixture was adjusted to 7-8 by adding 10% alcoholic ammonia solution and refluxed for about 3 h. The precipitated solid metal complex was filtered off in hot condition and washed with hot ethanol and dried over calcium chloride in vacuum desiccators. (Yield: 60%)

2.4 Physical Measurement:

IR spectra were recorded on FTIR (ATR)-BRUKER-TENSOR37 spectrometer using KBr pellets in the range of 4000-400 cm^{-1} . $^1\text{H-NMR}$ (Varian mercury 300MHZ) spectra of ligand were measured in DMSO using TMS as internal standard. X-RD was recorded on BRUKER D8 Advance. TGA- DTA was recorded on Shimadzu. The carbon, hydrogen and nitrogen contents were determined on Elemental model vario EL-III. The UV-visible spectra of the complexes were recorded on model UV-1800, SHIMADZU spectrometer. Molar conductance of complexes was measured on Elico CM 180 conductivity meter using 10^{-4} M solution in DMSO. Magnetic susceptibility measurements of the metal chelates were done on a Guoy balance at room temperature using $\text{Hg}[\text{Co}(\text{SCN})_4]$ as a calibrant.

3. RESULTS AND DISCUSSION:

Schiff bases of 2-amino- 4,6 dihydroxypyrimidine and its complexes have a variety of applications including biological, clinical and analytical. The coordinating possibility of 2-amino- 4,6 dihydroxypyrimidine has been improved by condensing with a variety of carbonyl compounds. An attempt has been made to synthesize Schiff bases from 2-amino- 4,6

dihydroxypyrimidine with benzaldehyde. Physical characteristics, microanalytical, and molar conductance data of ligand and metal complexes are given in (Table 1 and 2) The analytical data of complexes reveals 2:1 molar ratio (ligand: metal) and corresponds well with the general formula $[ML(H_2O)_2]$ (where M= Co(II)). The magnetic susceptibilities of Co(II) complexes at room temperature are consistent with high spin octahedral structure with two water molecules coordinated to metal ion. The presence of two coordinated water molecules was confirmed by TG-DTA analysis. The metal chelate solutions in DMSO show low conductance and supports their non-electrolyte nature (Table 1).

Table 1. Physical characterization, analytical and molar conductance data of compounds

Compound Molecular formula	Mol.Wt.	M.P. Decomp temp. 0C	Colour	Molar Conduc. Mho. Cm^2mol^{-1}
L	214	80	Yellow	---
Co-L	522	>300	Dark Yellow	22.27

Table 2. Elemental Analysis of Co(II) Complex

Compound	% Found (Calculated)			
	C	H	N	M
L	52.5 (53.2)	3.64 (3.95)	16.75 (16.93)	----
Co-L	44.46 (44.35)	3.39 (3.29)	14.14 (14.15)	9.92 (9.88)

3.1 1H -NMR spectra of ligand:

The 1H -NMR. Spectra of free ligand at room temperature show the following signals. 5.9 δ (s, 2H, Phenolic (OH) hydrogen of pyrimidine ring), 6.66 δ (s, 1H, Hydrogen bonded to pyrimidine ring), 7.94 δ (s, 1H, hydrogen bonded to azomethine carbon), 7.69-7.28 δ (D, 4H, Aromatic Ha, Hb, protons of phenyl ring).

3.2 IR Spectra:

The IR spectrum in Fig.1 & 2 of free ligands shows characteristic bands at 3325, 1638, 1487,1207 and 1089 cm^{-1} assignable to νOH (intramolecular hydrogen bonded), $\nu\text{C}=\text{N}$ (azomethine), $\nu\text{C}=\text{C}$ (aromatic), $\nu\text{C}-\text{N}$ (aryl azomethine) and $\nu\text{C}-\text{O}$ (Enolic) stretching modes respectively [21] The absence of a weak broad band in the 3200-3400 cm^{-1} region, in the spectra of the metal complexes suggests deprotonation of the intermolecular hydrogen bonded OH group on complexation and subsequent coordination of phenolic oxygen to the metal ion. This is further supported by downward shift in $\nu\text{C}-\text{O}$ (phenolic) [22] with respect to free ligand. On complexation, the $\nu\text{C}=\text{N}$ [23] band is shifted to lower wave number with respect to free ligand, denoting that the nitrogen of azomethine group is coordinated to the metal ion. The $\nu\text{C}-\text{N}$ band is shifted to lower wave number with respect to free ligand, The IR spectra of metal chelates showed new bands in between the 500-600 and 400-500 cm^{-1} regions which can be assigned to $\nu\text{M}-\text{O}$ and $\nu\text{M}-\text{N}$ [24] vibrations respectively The IR spectra of Co(II) show a strong band in the 3050-3600 cm^{-1} region, suggesting the presence of coordinated water in these metal complexes. The presence of coordinated water is further confirmed by the appearance of non-ligand band in 830-840 cm^{-1} region, assignable to the rocking mode of water. The presence of coordinated water is also established and supported by TG/DTA analysis of these complexes. Hence it is concluded that the coordination takes place via phenolic oxygen and azomethine nitrogen of ligand molecule in below Table 3.

Table 3 Salient features of IR spectral data of ligands & Metal complex

Bond vibration l modes	O-H Free Stretching(\square)	C = N Azomethine Stretching (\square)	C = C Aromatic ring stretching (\square)	C -- N Aryl azomethine stretch (\square)	C -- O Enolic stretching (\square)	M--O	M--N
L	3325	1638	1487	1207	1089	--	--
Co-L	1635.55	1433.23	1354.21	1192.22	1210.31	500.30	450.23

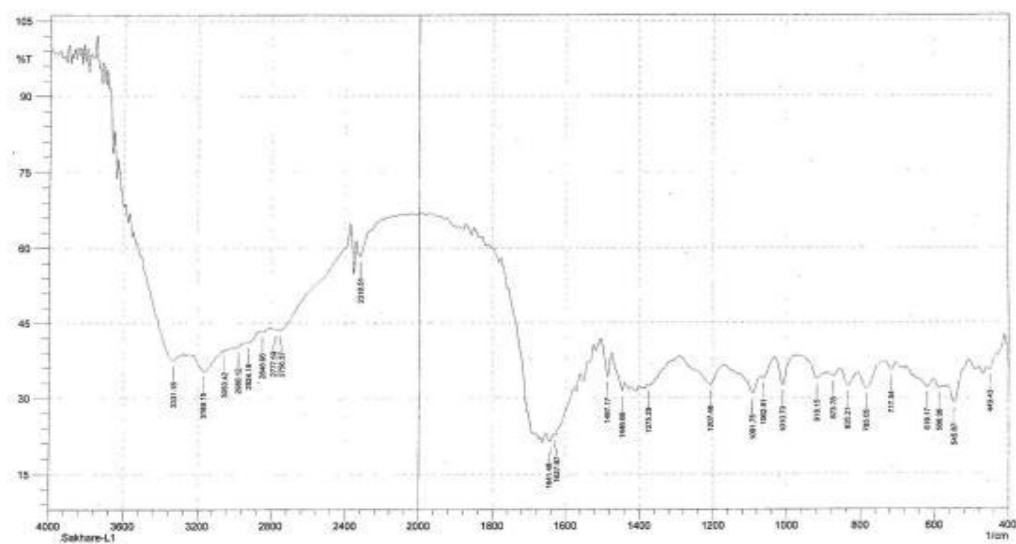


Fig. 1 Infrared Spectra of Ligand L

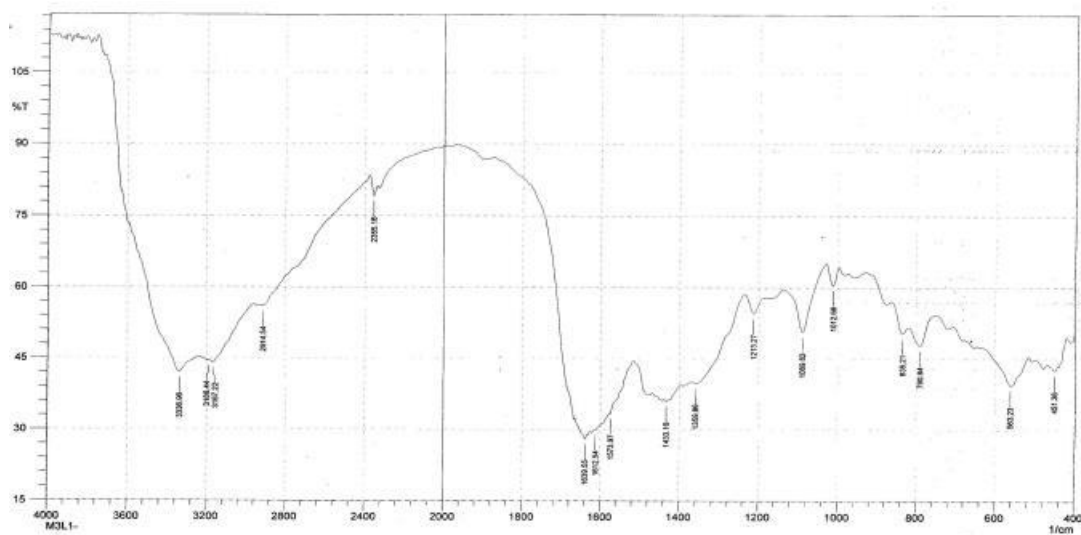


Fig. 2 Infrared Spectra of Co(II) Complex of Ligand L

3.3 Thermogravimetric analysis:

The dynamic TGA with the percentage mass loss at different steps have been recorded. The simultaneous TGA/DTA analysis of Co(II) was studied from ambient temperature to 1000 0C in nitrogen atmosphere using α -Al₂O₃ as reference. An analysis of the thermogram of the complexes indicated that Co(II) complexes shows two step decomposition. The first weight loss

4.78%, in between temp. 75-1600C could be correlated with the loss of two coordinated water (calculated 5.85%). The anhydrous compound does not remain stable at higher temperature, it undergoes rapid decomposition in the range 160-650°C, with 81.30% mass loss corresponds to decomposition of the complex (calcd. 81.96%) in second step. The decomposition is completed leading to the formation of stable residue of metal oxide CoO obs. 11.95% (calcd. 12.18%). kinetic and thermodynamic viz the energy of activation (Ea), frequency factor (Z), entropy change (-ΔS) and free energy change (ΔG) for the non-isothermal decomposition of complexes have been determined by employing Horowitz-Metzger method [25] values are given in Table 4. The Calculated values of the given activation energy of the complexes are relatively low, indicating the autocatalysis effect of metal ion on the thermal decomposition of the complex. The negative value of activation entropy indicates that the activated complexes were more ordered than the reaction was slow. The more ordered nature may be due to the polarization of bonds in the activated state, which might occur through charge transfer transitions [26].

Table 4. The kinetic and thermodynamic parameters for decomposition of metal complexes

Complex	Step	Decomp. Temp. (0C)	n	Ea (kJmole-1)	Z (S-1)	ΔS (JK-1mole-1)	ΔG (kJmole-1)	Correlation coefficient
Co-L	I	431	0.9	10.41	1.26 ×10 ⁴	-174.55	25.07	0.963

3.4 Magnetic measurements and electronic absorption spectra:

The electronic spectral studies of metal complexes of Co (II) with Schiff bases were carried out in DMSO solution. The absorption spectrum of the Co(II)complex shows bands at 19920 and 29069 cm⁻¹ attributed to ⁴T_{1g}→⁴A_{2g}(F) and charge transfer in an octahedral field [27]. The Co (II) complexes was diamagnetic in nature.

3.5 Molar Conductivity Measurements:

The metal (II) complexes were dissolved in DMSO and the molar conductivity of 10⁻⁴ M of their solution at room temperature was measured. The lower conductance values of the complexes support their non-electrolytic nature of the compounds.

3.6 Powder x-ray diffraction:

The x-ray diffractogram of Cu(II), Ni(II) and Co(II) complexes of L was scanned in the range 20-80° at wavelength 1.543 Å. The diffractogram and associated data depict the 2θ value for each peak, relative intensity and interplanar spacing (d-values). The diffractogram of Co(II) complex of L had twelve reflections with maxima at 2θ = 13.18° corresponding to d value 6.70 Å. The x-ray diffraction pattern of these complexes with respect to major peaks of relative intensity greater than 10% has been indexed by using computer programme [28]. The above indexing method also yields Miller indices (hkl), unit cell parameters and unit cell volume. The unit cell of Co(II) complex of L yielded values of lattice constants, a=9.45 Å, b=9.91 Å, c = 18.99 Å and unit cell volume V=11778.40392 Å³. In concurrence with these cell parameters, the condition such as a = b = c and α = β = γ = 90° required for sample to be Orthorhombic. Hence it can be concluded Co(II) complex of L has Orthorhombic and monoclinic crystal system. The experimental density values of the complexes were determined by using specific gravity method [29] and found to be 1.08 g cm⁻³ for Co(II) complexes respectively. By using experimental density values, molecular weight of complexes, Avogadro's number and volume of the unit cell were calculated. Number of molecules per unit cell were calculated by using equation $\rho = nM/NV$ and was found Co(II) complexes respectively. With these values, theoretical density were computed and found to be 1.06 g cm⁻³ for respective complexes. Comparison of experimental and theoretical density shows good agreement within the limits of experimental error [30]

4. Antifungal Activity

Antifungal activity and Antibacterial activity of ligand and metal complexes were tested in vitro against fungal such as *Aspergillus niger*, *Penicillium chrysogenum*, *Fusarium moneliforme*, *Aspergillus flavus* and bacteria such as *E. Coli*, *B.Subtilis*, *Staphylococcus aureus* and *Bacillus subtilis* by paper disc plate method. The compounds were tested at the concentrations 1% and 2% in DMSO and compared with known antibiotics viz Griseofulvin and Penicillin. (Table 5 and 6). From Table 4 and 5, it is clear that the inhibition by metal chelates is higher than that of a ligand and results are in good agreement with previous findings with respect to comparative activity of free ligand and its complexes [31] Such enhanced activity of metal chelates is due to the increased lipophilic nature of the metal ions in complexes. The increase in activity with concentration is due to the effect of metal ions on the normal cell process. The action of compounds may involve the formation of hydrogen bond with the active centre of cell constituents, resulting in interference with the normal cell process.

Table 5. Antifungal activity of ligands

Test Compound	Antifungal Growth							
	<i>Aspergillus niger</i>		<i>Penicillium chrysogenum</i>		<i>Fusarium moneliforme</i>		<i>Aspergillus flavus</i>	
	1%	2%	1%	2%	1%	2%	1%	2%
L	-ve	RG	-ve	-ve	-ve	-ve	-ve	-ve
Co-L	-ve	-ve	-ve	-ve	-ve	-ve	RG	+ve
+ve control	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
-ve control (Griseofulvin)	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve

Ligand & Metal : +ve – Growth (Antifungal Activity absent)

-ve - Growth (Antifungal Activity present)

RG - Reduced Growth (More than 50% reduction in growth observed)

Table 6. Antibacterial activity of ligands and their metal complexes

Test Compound	Diameter of inhibition zone (mm)							
	<i>E. coli</i>		<i>Salmonella typhi</i>		<i>Staphylococcus aureus</i>		<i>Bacillus subtilis</i>	
	1%	2%	1%	2%	1%	2%	1%	2%
L	-ve	12mm	-ve	14mm	-ve	18mm	-ve	19mm
Co-L	12mm	14mm	13mm	15mm	18mm	21mm	11mm	14mm
DMSO	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Penicillin	14mm	14mm	18mm	18mm	31mm	31mm	19mm	19mm

Ligand & Metal: - ve - No Antibacterial Activity

Zone of inhibition - --mm

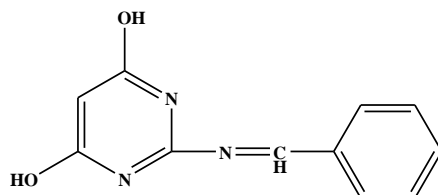


Fig. 1 Infrared Spectra of Ligand L

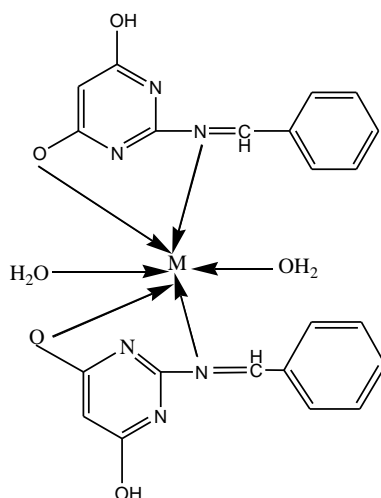


Fig. 6. The proposed Structure of the complexes. [When M= Co (II)]

5. CONCLUSION:

In the light of above discussion we have proposed octahedral geometry for Co(II) complexes. On the basis of the physico-chemical and spectral data discussed above, one can assume that the ligand behave as dibasic, NNO bidentate, coordinating via phenolic oxygen and imino nitrogen as illustrated in Fig.6. The complexes are biologically active and show enhanced antimicrobial activities compared to free ligand. Thermal study reveals thermal stability of complexes. The X-ray study suggests monoclinic crystal system for Co(II) complexes.

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7. REFERENCES:

1. D.T. Sakhare, *Advances in Applied Science Research*, 2015; **6**(6):10-16.
2. G Hoshina; M Tsuchimoto; S Ohba; K Nakajima. *Inorg. Chem.*, 1998; **37**: 142.
3. L Canali; DC Sherrington. *Chem. Soc. Rev.*, 1999; **28**: 52.
4. J Vargas; J Costamagna; R Latorre; A Alvarado; G Mena. *Coord. Chem. Rev.*, 1992; **67**: 119.
5. A Togni; LM Venanzi. *Angew. Chem.*, 1994; **33**: 497.
6. F Fache; E Schulz; ML Tommasino; ML Emaire. *Chem. Rev.*, 2000, **100**: 2159.
7. D.A Garnovskii; MFC Guedes da Silva; MN Kopylovich; AD Granovskii; JJR Frausto da Silva; AJL Pombeiro. *Polyhedron*. **2003**, 22, 1335.
8. M Hussain; A Al-Afaj; L Hossain. *Trans. Met. Chem.*, 1990, **13**, 264.
9. Y Nagel; W Beck; Z Naturforsch; B Anorg. *Chem. Org. Chem.*, 1986, **4**, 1447.
10. J M Salas; MA Romero; MP Sanchez; M Quiros. *Coord. Chem. Rev.*, 1995, **1119**, 193-195.
11. S Ren; R Wang; K Komatsu; P Bonaz-Krause; Y Zyrianov; CE Mckenna; C Csipke; ZA Tokes; EJ Lien. *J. Med. Chem.*, 2002, **45**, 410.
12. N Raman; A Thangaraja; C Kulandaisamy. *Trans. Met. Chem.*, 2003, **28**, 29.
13. BG Jeong; CP Rim; HN Chae; KH Chio; KC Nam; YK Chol. *Bull Korean Chem. Soc.*, 1996, **17**, 688.
14. M Watkinson; M Fondo; M Bermejo; A Sousa; CA McAuliffe; RG Pritchard; N Jaiboon; N Aurangzab; M Naeem. *J. Chem. Soc. Dalton Trans.*, 1999, 31.
15. P R Reddy, A M Reddy. *Indian Academy of Sciences (Chem. Sci.)* 2000; **112**(6): 593-600.
16. M Gulcan , M Sonmez , I Berber . *Turkey Journal of Chemistry*. 2012;**36**: 189-200.
17. D Sakthilatha , R Rajavel . *J. Chem. Pharm. Res.* 2013;**5**(1): 57-63.

18. A A Osowole , E J Akpan . *European Journal of Applied Sciences*. 2012; **4**(1): 14-20.
19. A A Osowole , I Ott . . *International Research Journal of Pure and Applied Chemistry*. 2012; **2**(2): 156-169.
20. D.T. Sakhare, *Der Chemica Sinica*, 2015, **6**(6):1-6.
21. A A Osowole¹, R Kempe , R Schobert and S A Balogun , *Candian journal of pure and applied sciences* ,2010; **4**(2) 1169-1178.
22. A A Osowole . and R O Yoade , *Scientific Journal Of Applied Research* . 2013; **4**: 101-106
23. D. T. Sakhare , *Journal of Chemical and Pharmaceutical Research*, 2015; **7**(6):198-204
24. M Usharani. E Akila, And R Rajavel. *International Journal of Recent Scientific Research* ,2013; **4**(9): 1385- 1390.
25. K Arora , *Indian J. Chem*, 1997; **74**:589.
26. P G Avaji , B N Reddy and S A Patil , *Trans. Met. Chem*, 2006; **31**: 842.
27. E Akila , M Usharani , S Vimala and R Rajavel , *Che.Sci.Rev.Lett.*, 2012; **1**(4):181- 194
29. J R Carvajal. T Roisnel, A Winplotr , *Graphic Tool for Powder Diffraction*, Laboratories Leon brillouin (ceal /enrs) 91191 gif suryvette cedex, France, 2004.
29. K C Bhattacharya, “An Elementary Physics for Indian School” The Indian Press Ltd. Allahabad, 1934,105.
30. D.T. Sakhare, *Our Heritage*, 2020,Vol-68, Special Issue-38, 840-851.
31. D.T. Sakhare, *Current Pharma Research*, 2019; **9**(4): 3335-3344.