

Synthesis, characterization and antimicrobial activities of some transition metal complexes of biologically active bidentate ligands

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ABSTRACT

A new solid complexes of Mn(II) and Fe(III) complexes with bidentate Schiff base ligand derived from 2-amino 4,6 dihydroxypyrimidine and P-chlorobenzaldehyde, P-nitrobenzaldehyde have been reported. The complexes have been characterized by elemental analysis, magnetic susceptibility measurements, conductometry, electronic and infrared spectra, X-ray diffraction, ¹H-NMR spectra and thermogravimetric analysis. 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*, *Salmonellatyphi*, *Staphylococcus aurious*, *B.subtilis*. The result indicated that the complexes exhibited good antifungal and antibacterial activities. The Schiff base commonly coordinates through the oxygen atom of phenolic OH group and the nitrogen atom of azomethine group, which is confirmed by IR spectral data. Further conclusive evidence of the co-ordination of the Schiff bases with the metal ions was shown by the appearance of new bands due to $\nu(M-N)$ and $\nu(M-O)$ in the metal complexes.

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KEYWORDS

Schiff bases;
Transition metal complexes;
Powder X-ray diffraction;
Antimicrobial activity.

INTRODUCTION

Compounds containing pyrimidine and purine play a significant role in many biological systems^[1], where both exist in nucleic acids, several vitamins, coenzymes, and antibiotics. Pyrimidine-derived metal ion complexes have been extensively investigated because of their biological activity^[2-7]. Moreover, recent studies^[8] showed that introduction of substituent groups at C₅ and C₆ positions of pyrimidine can increase the biological activity. Addition-

ally, metal pyrimidine derivative complexes are also biologically active materials. The variety of biological applications of those compounds was correlated with the chelating property of the pyrimidine derivatives toward traces of metal ions. These provide potential binding sites for metal ions, and information on their coordination properties is important in understanding the role of the metal ions in biological systems. Many compounds of therapeutic importance contain pyrimidine ring system. Pyrimidine compounds are also used as hypnotic drugs^[8,9].

Pyrimidine nucleus is imbedded in a large number of compounds with diverse pharmacological activities, such as antitumor^[10], antiviral^[11], anti-inflammatory^[12], antibacterial^[13], and antifungal^[14]. Here, we present the synthesis and properties of a new heterocyclic ligand containing pyrimidine ring and their Mn(II) and Fe(III) complexes. All the synthesized compounds were investigated for physicochemical properties and antimicrobial activities. The aim of present investigation is to synthesize transition metal complexes of Schiff base condensed from 2-amino-4,6 dihydroxypyrimidine and p-chlorobenzaldehyde, P-nitrobenzaldehyde.

MATERIALS AND METHODS

Reagents and solvents

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

Synthesis of ligand

The ligand L₁, L₂ was prepared by a modification of the reported methods^[15-17]. The Schiff base ligand L₁ has been synthesized by refluxing a mixture of 0.01 mol (1.4057 g) of, P-chlorobenzaldehyde and 0.01 mol (1.2710 g) of 2-amino-4,6-dihydroxypyrimidine and ligand L₂ has been synthesized by refluxing a mixture of 0.01 mol (1.5110g) of, P-nitrobenzaldehyde 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% and 72%).

Synthesis of metal complexes

To a hot ethanol solution (25ml) of the ligand L₁

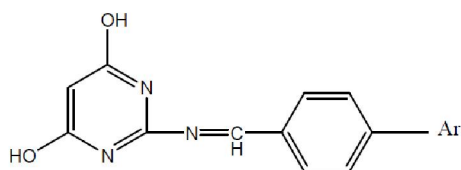


Figure 1 : Structure of ligand; When Ar = Cl, NO₂

(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%). To a hot ethanol solution (25ml) of the ligand L₂ (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: 65%).

Physical measurement

IR spectra were recorded on FTIR (ATR)-BRUKER -TENSOR37 spectrometer using KBr pellets in the range of 4000-400 cm⁻¹. ¹H-NMR (varian mercury 300MHZ) spectra of ligand were measured in CDCl₃ 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 Elementar 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 Hg [Co (SCN)₄] as a calibrant.

RESULTS AND DISCUSSION

Physical characteristics, micro analytical, 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(H₂O)₂] (where M= Mn(II) and Fe(III). The magnetic susceptibilities of Mn(II) and Fe(III) complexes at room temperature are consistent with two water molecules coordinated to metal

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TABLE 1 : Physical characterization, analytical and molar conductance data of compounds

Compound	Molecular formula	Mol.Wt.	M.P. Decomp temp. °C	Colour	Molar Conduc Mho. Cm ² mol ⁻¹
L ₁		249.66	82	Yellow	----
L ₂		260.21	110	Yellow	----
MnL ₁		590.28	>300	Dark Brown	31.36
FeL ₁		591.18	>300	Brown	82.26
Mn L ₂		611.38	>300	Faint Brown	44.59
Fe L ₂		612.29	>300	Brown	42.79

TABLE 2 : Elemental analysis of Mn (II) and Fe(III) complex

Compound	Found (Calculated)			
	C	H	N	M
L ₁	52.92 (43.20)	3.23 (3.95)	16.83 (16.93)	-
L ₂	50.78 (39.29)	3.10 (3.67)	21.53 (17.55)	-
MnL ₁	44.76 (55.83)	3.41 (3.35)	14.23 (14.12)	9.30 (9.15)
FeL ₁	44.69 (44.55)	3.40 (3.35)	14.21 (14.10)	9.44 (9.30)
MnL ₂	43.22 (43.12)	3.29 (3.15)	18.32 (18.12)	8.98 (8.85)
FeL ₂	43.15 (43.09)	3.29 (3.15)	18.30 (18.20)	9.12 (9.00)

TABLE 3 : Characteristic IR frequencies (cm⁻¹) of the ligands and their complexes

Compound	ν (C=N)	ν (C=C)	ν (C-N)	ν (C-O)	ν (M-O)	ν (M-N)
L ₁	1641	1487	1207	1091	--	--
L ₂	1672	1516	1346	1197	--	--
Mn-L ₁	1615.10	1440.87	1346.36	1209.41	503.10	426.28
Fe-L ₁	1627.97	1408.08	1227.48	1161.19	543.94	459.22
Mn-L ₂	1604.83	1450.15	1348.29	1213.27	508.15	450.00
Fe-L ₂	1615.47	1460.16	1348.29	1224.10	542.02	426.28

ion. The metal chelate solutions in DMSO show low conductance and supports their non-electrolyte nature.

¹H-NMR spectra of ligand

The ¹H-NMR. Spectra of free ligand L₁ at room temperature shows 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 H_a, H_b, protons of phenyl ring). The ¹H-NMR. Spectra of free ligand L₂ at room temperature shows the following signals. 3.79 δ (s, 2H, Phenolic (OH) hydrogen of pyrimidine ring), 6.07 δ (s, 1H, Hydrogen bonded to pyrimidine ring), 8.07 δ (s, 1H, hydrogen bonded to azomethine carbon), 7.369-8.18 δ (D,4H, Aromatic H_a, H_b, protons of phenyl ring).

IR spectra

The characteristic IR frequencies (cm⁻¹) of the ligand L₁ and L₂ and their metal complexes are shown in TABLE 3. The IR spectrum of the free ligands shows a broad weak band 3331 cm⁻¹ and 3327 cm⁻¹ attributed to intramolecular bonding ν (OH). The bands 1641-1091 cm⁻¹ and 1672-1197 cm⁻¹ are assigned to ν (C=N) (azomethine), ν (C=C) (Aromatic double bond), ν (C-N) (aryl azomethine) and ν (C-O) (enolic) stretching modes, respectively. The disappearance of IR band at 3100-3300 cm⁻¹ (intramolecular hydrogen bonding) in the spectra of all the complexes indicates deprotonation of enolic oxygen and azomethine nitrogen in coordination to the metal ion. It is further supported by a downward shift in ν (C-O) by 52-61 cm⁻¹ in all complexes^[18]. An upward shift in ν (C=N) by 6-31 cm⁻¹ indicates participation of azomethine nitrogen in complex formation^[19]. The IR spectra of the metal complexes showed new bands in the 503-543 cm⁻¹, 408-542 cm⁻¹

TABLE 4 : 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 ₁	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
L ₂	+ve	RG	RG	-ve	RG	-ve	+ve	+ve
Mn- L ₁	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Fe- L ₁	-ve	+ve	-ve	-ve	-ve	-ve	-ve	-ve
Mn- L ₂	+ve	RG	+ve	-ve	RG	RG	+ve	+ve
Fe -L ₂	-ve	+ve	RG	RG	RG	RG	-ve	RG
+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)

¹ and 426-459 cm⁻¹, 426-450 cm⁻¹ region, which can be assigned to ν (M-O) and ν (M-N) vibrations respectively^[20-22].

Magnetic measurements and electronic absorption spectra

The electronic absorption spectrum of the L₁ Mn(II) complexes shows bands at 13368 cm⁻¹ and 24875 cm⁻¹ are assigned to ${}^6A_{1g} \rightarrow {}^4T_{2g}$ and charge transfer transitions. All Mn(II) complexes were paramagnetic in nature indicates octahedral geometry²³. L₁ Fe(III) complexes shows bands at 29239 cm⁻¹. These transitions may be assigned to charge transfer transitions. All Fe(III) complexes were paramagnetic in nature indicates octahedral geometry²⁴. L₂ Mn(II) complex exhibits electronic spectral bands at 13966 and 24875 cm⁻¹ attributed to ${}^6A_{1g} \rightarrow {}^4T_{2g}$ (G) which can be assigned to charge transfer in an octahedral field^[25]. L₂ Fe (III) complex exhibits electronic spectral bands at 29239 cm⁻¹ which can be assigned to charge transfer in an octahedral field^[26,27]. All the Mn (II) and Fe (III) complexes were paramagnetic in nature.

Antibacterial 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*, *S. Aurious* And *Bacillus subtilis* by paper disc plate method^[28-31]. The compounds were tested at the con-

centrations 1% and 2% in DMSO and compared with known antibiotics *viz* *Griseofulvin* and *Penicillin*. (TABLE 4 and 5). 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 complexes³² 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

Powder x-ray diffraction

The X-ray diffractogram of Mn(II) and Fe(III) complexes of L₁ 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 inter-planar spacing (d-values). The diffractogram of Mn(II) complex of L₁ had fifteen reflections with maxima at $2\theta = 13.34^\circ$ corresponding to d value 6.63Å. The diffractogram of Fe(III) complex of L₁ had thirteen reflections with maxima at $2\theta = 6.63^\circ$ corresponding to d value 6.66Å. The diffractogram of Mn(II) complex of L₂ had eleven reflections with maxima at $2\theta = 6.65^\circ$ corresponding to d value 6.64Å. The diffractogram of Fe(III) complex of L₂ had ten reflections with maxima at $2\theta = 6.64^\circ$ corresponding to d value

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TABLE 5 : 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 ₁	-ve	12mm	-ve	11mm	-ve	17mm	-ve	15mm
L ₂	-ve	14mm	-ve	15mm	-ve	19mm	-ve	19mm
Mn- L ₁	-ve	-ve	-ve	-ve	14mm	18mm	18mm	18mm
Fe- L ₁	-ve	-ve	-ve	-ve	13mm	18mm	16mm	18mm
Mn- L ₂	-ve	-ve	-ve	-ve	19mm	21mm	18mm	18mm
Fe -L ₂	11mm	11mm	-ve	11mm	17mm	19mm	14mm	17mm
DMSO	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Penicillin	14mm	14mm	17mm	17mm	30mm	30mm	19mm	19mm

Ligand & Metal: - ve - No Antibacterial Activity; Zone of inhibition - —mm

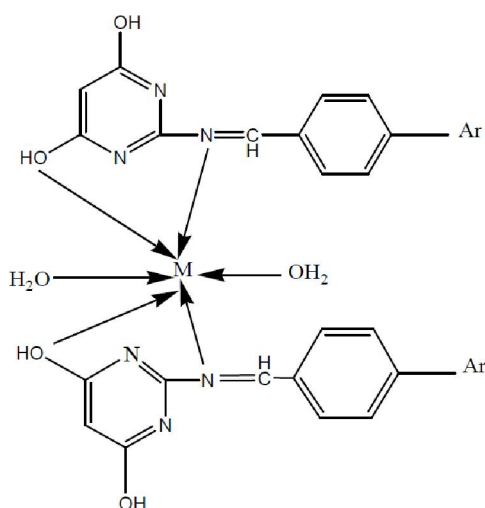


Figure 2 : The proposed Structure of the complexes; When M= Mn(II) and Fe(III), Ar = Cl, NO₂

6.66Å. 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^[33] The above indexing method also yields Miller indices (hkl), unit cell parameters and unit cell volume. The unit cell of Mn(II) complex of L₁ yielded values of lattice constants, a=9.23 Å, b=10.23 Å, c = 18.95Å and unit cell volume V=1789.31386Å³. In concurrence with these cell parameters, the condition such as a = b = c and $\alpha = \beta = \gamma = 90^\circ$ required for sample to be Orthorhombic. The unit cell of Fe(III) complex of L₁ yielded values of lattice constants, a=9.345 Å, b=8.345 Å, c = 17.456Å and unit cell volume V=1178.91101Å³. In concurrence with these cell parameters, the condition such as a ≠ b ≠ c and $\alpha = \beta = 90^\circ \neq \gamma$ required for sample to be monoclinic were tested

and found to be satisfactory. The unit cell of Mn(II) complex of L₂ yielded values of lattice constants, a=9.345 Å, b=7.789 Å, c = 16.567Å and unit cell volume V=1044.32461Å³. In concurrence with these cell parameters, the condition such as a ≠ b ≠ c and $\alpha = \beta = 90^\circ \neq \gamma$ required for sample to be monoclinic. The unit cell of Fe(III) complex of L₂ yielded values of lattice constants, a=9.898 Å, b=7.895Å, c = 14.678Å and unit cell volume V=994.04065Å³. In concurrence with these cell parameters, the condition such as a ≠ b ≠ c and $\alpha = \beta = 90^\circ \neq \gamma$ required for sample to be monoclinic. Hence it can be concluded Mn(II) and Fe(III) complex of L₁ and L₂ has monoclinic crystal system. The experimental density values of the complexes were determined by using specific gravity method^[34] and found to be 1.11, 1.05, 1.08, 1.10 gcm⁻³ for Mn(II) and Fe(III) 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 Mn(II) and Fe(III) complexes respectively. With these values, theoretical density were computed and found to be 1.10, 1.03, 1.06, 1.08 gcm⁻³ for respective complexes. Comparison of experimental and theoretical density shows good agreement within the limits of experimental error^[35].

CONCLUSION

Based on the physicochemical and spectral data

discussed above octahedral geometry for the

Mn(II) and Fe(III) complexes are proposed. The ligand behave as bidentate, coordinating through phenolic oxygen and imino nitrogen as illustrated in Figure 2. The complexes are biologically active and show enhanced antimicrobial activities compared to free ligand. The X-RD study suggests monoclinic crystal system for Mn(II) and Fe(III) complexes.

REFERENCES

- [1] F.Hueso, N.A.Illan, M.N.Moreno, J.M.Martinez, M.J.Ramirez; *J.Inorg.Biochem.*, **94**, 326 (2003).
- [2] M.Sonmez, M.C. elebi, A.Levent, I.Berber, Z.S. enturk; *J.Coord.Chem.*, **63**, 848 (2010).
- [3] S.Roy, T.N.Mandal, A.K.Barik, S.Pal, S.Gupta, A.Hazra, R.J.Butcher, A.D.Hunter, M.Zeller, S.K.Kar; *Polyhedron*, **26**, 2603 (2007).
- [4] M.Sonmez, A.Levent, M.S. ekerci; *Russian J.Coord.Chem.*, **30**, 695 (2004).
- [5] M.A.Girasolo, C.Di Salvo, D.Schillaci, G.Barone, A.Silvestri, G.J.Ruisci; *J.Organomet.Chem.*, **690**, 4773 (2005).
- [6] N.Agarwal, P.Srivastava, S.K.Raghuwanshi, D.N.Upadhyay, S.Sinha, P.K.Shulka, V.J.Ram; *Bioorg.Med.Chem.*, **10**, 869 (2002).
- [7] B.G.Tweedy; *Phytopathology*, **55**, 910 (1964).
- [8] A.Colorado, J.Brodbelt; *J.Mass Spectrom.*, **31**, 403 (1996).
- [9] N.Raman, A.Kulandaisamy, C.Thangaraja, P.Manisankar, S.Viswanathan, C.Vedhi; *Transition Met.Chem.*, **29**, 129 (2004).
- [10] P.G.Baraldi, M.G.Pavani, N.Nunes, P.Brigidi, B.Vitali, R.Gambari, R.Romagnoli; *Arch.Pharm.*, **10**, 449 (2002).
- [11] S.M.Sondhi, M.Johar, S.Rajvanshi, S.G.Dastidar, R.Shukla, R.Raghubir, J.W.Lown; *Aust.J.Chem.*, **54**, 69 (2001).
- [12] M.N.Nasr, M.M.Gineinah; *Arch.Pharm.*, **335**, 289 (2002).
- [13] N.Kumar, G.Singh, A.K.Yadav; *Heteroat.Chem.*, **12**, 52 (2001).
- [14] G.Mangalagiu, M.Ungureanu, G.Grosu, L.Mangalagiu, M.Petrovanu; *Ann.Pharm.Fr.*, **59**, 139 (2001).
- [15] A.A.Osowole, R.Kempe, R.Schobert, S.A.Balogun; *Candian journal of pure and applied sciences*, **4(2)**, 1169-1178 (2010).
- [16] A.A.Osowole, R.Kempe, R.Schobert, K.Effenberger; *Synth.React.Inorg.Met.Org.Chem. and Nano-Met.Chem.*, **41**, 825-833 (2011).
- [17] A.A.Osowole, E.J.Akpan; *J.European Journal of Applied Sciences*, **4(1)**, 14-20 (2012).
- [18] P.S.Mane, S.M.Salunke, B.S.More; *E-J.of Chem.*, **8(S1)**, S245-S252 (2011).
- [19] L.Gouta, W.N.Chong, L.Bin, M.Kunyal; *Polyhedron*, **9**, 2019 (1990).
- [20] S.F.Tan, K.P.Ang, H.L.Jatachandran; *Transition metal chem.*, **9**, 390-395 (1984).
- [21] S.G.Shirodakar, P.S.Mane, T.K.Chondhekar; *Indian J.Chem.*, **40A(10)**, 1114-1117 (2001).
- [22] A.Symal, O.P.Singhal; *Transition Met.Chem.*, **4**, 179-182 (1979).
- [23] N.Sharada, M.C.Ganorkar; *Indian J.Chem.*, **27A**, 542 (1988).
- [24] Sen S.K.Gupta, S.K.Sahani, R.N.Kapoor; *Indian J.Chem.*, **19A(7)**, 703 (1980).
- [25] V.S.Shrivastav, G.C.Saxena; *J.Indian Chem.Soc.*, **63**, 578(1986).
- [26] P.S.Mane, S.M.Salunke, B.S.More, *E-J.of Chem.*, **8(S1)**, S245-S252 (2011).
- [27] R.L.Martin, A.H.White; *Inorg.Chem.*, **6**, 12 (1967).
- [28] H.H.Thornberry; *Phytopathology*, **40**, 419 (1950).
- [29] V.G.Deshpande, S.Shaha, M.M.Deshpande, S.I.Habib, P.A.Kulkarni; *Asian Journal of Biochemical Pharmaceutical Research*, **1(3)**, 63-70 (2013).
- [30] M.V.Lokhande; *Asian Journal of Chemistry*, **18(4)**, 2662-2668 (2006).
- [31] Shastri Ranjana; *World Journal of Pharmacy and Pharmaceutical Sciences*, **3(7)**, 1814-1823 (2014).
- [32] A.K.Madhure, A.S.Aswar; *Am.J.Pharm.Tech.Res.*, **3(6)**, 462-484 (2013).
- [33] J.R.Carvajal, T.Roisnel, Winplotr; A graphic tool for powder diffraction, Laboratoire Leon Brillouin (cea/enr)91191 gif suryvette cedex, France, (2004).
- [34] K.C.Bhattacharya; "An Elementary Physics for Indian School" The Indian Press Ltd.Allahabad, 105 (1934).
- [35] M.B.Deshmukh, S.Dhongade, S.Dasai, S.S.Chavan; **44**, 1659 (2005).