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Synthesis, Characterization and Biological Activity of a Schiff Base Derived From Curcumin and 2-Aminophenol and Its Transition Metal Complexes

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ABSTRACT

Schiff bases are important intermediates for the synthesis of various bioactive compounds. However, various studies have shown that schiff bases derived from biologically active ingredients present in medicinal plants are more effective in biological and medicinal activity than in its pure form. In this paper Zn(II), Cu(II), Ni(II), Co(II) and Mn(II) complexes were synthesized from schiff bases derived from curcumin (a yellow bioactive component extracted from curcuma longa) and 2-Aminophenol. The ligand and their complexes were characterized by powder XRD, SEM-EDAX, and Antioxidant studies. Also the synthesized ligand and metal complexes have been screened for their antimicrobial activity against E.coli, S.aureus, B.subtilis, P.aeruginosa, K.pneumoniae and against various fungi like C.albicans and A.niger. Results revealed that the complexes showed enhanced activity than their corresponding ligand.

Keywords :- Curcumin, 2-Aminophenol, Transition metal complexes, Antioxidant activity, antimicrobial activity.

I. INTRODUCTION

The chemistry of co-ordination compounds with heterocyclic ligands containing oxygen and nitrogen as donor atoms has attracted the attention of chemists in recent years[1]. Schiff bases derived from an amino and carbonyl groups are an important class of compounds that contains azo-methine nitrogen ie; > C = N linkage which is essential for biological activity[2]. Several azomethines were reported to posess remarkable antibacterial[3]-[5], antifungal[6]-[7], anticancer[8] and diuretic activities[9]. According to scientific research, Curcumin or 1, 7-bis (4-hydroxy-3 methoxyphenyl)-1, 6-heptadiene-3, 5-dione or Feruloyl methane, the main bioactive component of turmeric (Curcuma longa) has been known to have the medicinal activity, since ancient times and this molecule has been the object of several investigations in the field of biological medicine such as antioxygenation, antibiosis, anti-tumour, anti-inflammatory, anti-carcinogenic[10], herbicidal activities and Alzheimer's prevention[11]. Curcumin has a highly conjugated β-diketone moiety and can be a powerful natural chelating agent. Complexition of curcumin with metals has attracted much interest over the past years as it is one of the useful requirements for the treatment of alzheimer's diseases and in-vitro antioxidant activity[12]. Transition metal complexes of 2-Aminophenol based Schiff bases have been the subject of extensive investigation because of their wide use in various fields like antidepressants, antimicrobial, antitumour, nematocide, antiphlogogistic etc[13]. The present investigation deals with the synthesis of metal complexes of Zn(II), Cu(II), Ni(II), Co(II), and Mn(II) with the schiff base derived from Curcumin and 2-Aminophenol. The synthesized ligand and their metal complexes were characterized by SEM-EDAX and powder XRD. The synthesized compounds were studied for their antioxidant activity by DPPH method. Also the ligand and their metal complexes have been screened for their antimicrobial activities against the selected bacteria and fungi using the well diffusion method.

II. EXPERIMENTAL

2.1 Materials and Methods

All the chemicals and solvents used in the preparation of ligands and their metal complexes were of A.R grade. Curcumin and 2-Aminophenol were purchased from Sigma-Aldrich. Metal salts like Zn(II), Cu(II), Ni(II), Co(II) and Mn(II) chlorides and the solvents were purchased from Merck.

2.2 Synthesis of Schiff base ligand [4,4'-(1E,3Z,5Z,6E)-3-hydroxy-5-(2-hydroxyphenyl)imino)hepta-1,3,6-triene-1,7-diyl) bis (2-(methyl peroxy) phenol)]

Curcumin (0.005 mol, 1.8445g) was dissolved in 20 ml methanol and stirred well at room temperature. Then methanolic solution of 2-Aminophenol (0.005 mol, 0.5456g) was added to the prepared curcumin solution. The obtained orange coloured mixture was stirred and refluxed at 60^0C in presence of catalytic amount of glacial acetic acid (1-2 drops) for about 6 hrs. After cooling, the resulting orange fine precipitate was filtered and washed well with distilled ethanol repeatedly to remove any unreacted chemicals. The obtained orange crystals were then dried at room temperature.

2.3 Synthesis of Schiff base metal complexes.

To the hot solution of schiff base ligand (0.005 mol) in methanol (20ml) was added a hot methanolic solution (10ml) of respective metal chlorides (0.005 mol) drop by drop in 1:1 (ligand: metal) molar ratio. P^H of the solution was maintained just below the value of hydrolysis of the metal ion using alcoholic ammonia. The reaction mixture was magnetically stirred and refluxed for 4 hrs at 60^0C. The coloured precipitate was filtered and washed by cold ethanol to remove the residue reactants. Finally the obtained powder was dried to get the complex.

2.4 Determination of antimicrobial Activity

2.4.1. Test organisms:

The in-vitro biological activity of the schiff base and its metal complexes in DMSO were tested against the bacterial species such as Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacillus subtilis and fungal species like Candida albicans and Aspergillus niger by Muller Hinton well diffusion method using nutrient agar as medium.

2.4.2. Experimental methods:

The agar well diffusion method was used to screen the antimicrobial activity. Muller Hinton agar medium (20ml) was poured into each petri plates. The plates were allowed to solidify for 5min and 100µl inoculum suspension was swabbed uniformly and allowed to dry for 15 min. Using sterile cork borer of 8mm diameter, wells were bored into the seeded agar plates and these were located with a 100µl solution of each compound in DMSO and all the plates were incubated at 37^0C and the diameter of inhibition zone around each disc was measured after 24hr for bacterial and fungal species. The inhibition zone was developed at which the concentration was noted and the results were recorded. From the results, the activity index was calculated using the formulae.

2.5 Antioxidant assay (DPPH scavenging activity)

The antioxidant activity of the synthesized curcumin derivatives was evaluated using the DPPH (1,1-Diphenyl-2-picryl-hydrazyl) free radical scavenging assay[14]. DPPH scavenging is considered as a good in-vitro model and is widely used to assess antioxidant efficacy[15]. 100µg/ml of the test sample solution was added to 4ml of 100M methanolic DPPH at various concentrations (20, 40, 60, 80 µg). After stirring, the mixture was incubated for 20 min at room temperature and the absorbance at 517 nm was measured. Ascorbic acid (100 µg/ml) was used as the standard. A blank was prepared without adding standard or test compound (95% methanol). Lower the absorbance of the reaction indicates higher the free radical scavenging activity. The capability to scavenge the DPPH radical were calculated using the equation,

$$\% \text{ of inhibition} = \frac{A_{control} - A_{sample}}{A_{control}} \times 100$$

where $A_{control}$ is the absorbance of the control reaction and A_{sample} is the absorbance in the presence of test compounds[16].

III. RESULTS AND DISCUSSIONS

The condensation of curcumin with 2-aminophenol give the schiff base 4,4'-(1E, 3Z, 5Z, 6E) -3- hydroxy-5-{(2-hydroxyphenyl)imino) hepta-1, 3, 6-triene-1,7-diyl) bis (2-methyl peroxy) phenol}. The ligand L_2 which coordinated with Zn^{2+}, Cu^{2+}, Ni^{2+}, Co^{2+} and Mn^{2+} ions separately to give coloured complexes N_1, N_2, N_3, N_4 and N_5 respectively. The schiff base ligand L_2 and its metal complexes are stable at room temperature and soluble in almost all organic solvents like DMSO and DMF.

3.1. X-Ray Diffraction analysis

X-ray diffraction studies of curcumin were investigated from the angle of 10^0 to 80^0. The powder XRD patterns of ligand (L_2) and Cu complex (N_2) are recorded in the range 2θ = 0-80 A^0 were shown in fig: 1.

The average crystalline size d_{XRD} of the complexes was calculated using Scherrer's formula[17],

$$d = 0.89\lambda/\beta\cos\theta),$$

where 'd' is the average crystalline size of the phase under investigation. 'λ' is the wavelength of X-ray beam used. 'β' is the full width at half maximum of diffraction and 'θ' is the Bragg's angle. From the observed XRD patterns, the average crystalline size for the ligand L_2 and N_2 are found to be 71.1nm and 59.9nm respectively. After complexetion, the particle size decreases. This suggests that the ligand and the complexes are nanocrystalline in nature.

3.2 SEM – EDAX Analysis

Morphology of synthesized ligand and complexes were characterized by SEM analysis. SEM images of ligand (L_2) and Cu complex (N_2) were shown in fig:2. SEM picture of the metal complexes shows that the particles are agglomerated with controlled morphological structure and the presence of small grains in non-uniform size. After agglomeration, SEM image of compounds shows irregular shaped grains with elongated morphology and increased particle size. The SEM-EDAX images of L_2 and N_2 were shown in Fig: 3. The results of Energy Dispersive X-ray analysis (EDAX) data reveals the purity of the complex which indicates that there is no elemental contamination present in the complex. The % content of elements in the complex is C (71.80), O (24.60), Cl(2.70) and Cu (1.53) respectively.

3.3 Antioxidant activity

Antioxidant activity evaluation of ligand and its complexes was measured in terms of decreases in absorbance at 517 nm of DPPH methanolic solution (0.1 mmol) produced by the effect of each compound as a result of their ability to donate

a hydrogen giving to the reduced form of DPPH radical. The reducing abilities of the synthesized compounds were determined by their interaction with the free radical DPPH at 20µg concentrations for 15 min. This investigation indicates that there is a greatest possibility of finding potent antioxidants. The antioxidant activity of ligand and metal complexes are given in table 1. The ligand (L_2) and its Cu complex (N_2) have exhibited very good free radical scavenging activity. N_3, N_4 and N_5 complexes were shown moderate activity. N_1 showed less activity compared to standard. This study determined the antagonistic activity of the complexes when compared to ligand. The bar graph representation of percentage of free radical scavenging activity is shown in fig: 4.

3.4 Antimicrobial activity

The in-vitro biological screening effects of the investigated compounds were tested against various bacterial species like E.coli, S.aureus, K.pneumoniae, P. aeruginosa, B.subtilis and fungal species like C.albicans and A.niger. Amikacin is used as +ve standard for antibacterial and Nistatin for antifungal studies. The presence of clear zones noted that the compounds were active.

The antimicrobial activities of ligand and its metal complexes are shown in fig.5-6. Antimicrobial results showed that all the synthesized compounds possess biological activity[18].The increased activity of metal complexes may be considered due to chelation of metal ions with schiff base which enhanced lipophilicity due to delocalization of pi-electrons over the whole chelate ring[19]. These increased lipophilicity enhances the penetration of complexes into the lipid membranes and blocks the meta binding sites in enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts the growth of organisms. This data revealed that the activity of the ligand enhanced on complexetion but less than the standard used [20]. Comparative study of ligand and its metal complexes showed moderate to their better antibacterial activty. Mn complex (N_5) showed 22mm zone of inhibition against Staphylococcus aureus, 20mm zone of inhibition against E.coli and 20mm zone of inhibition against K.pneumoniae. Cu complex(N_2) showed good activity against S.aureus but no activity against P.aeruginosa. All other complexes show moderate activity against all other bacterial species. Overall comparison of the observed data reveals that Mn complex, N_5 shows excellent antibacterial activity and can be tested for further in-vivo studies and can be used as drug. The orders of activity of synthesized compounds are as follows.

Mn(II) > Cu(II) > Co(II) > Ni(II) > Zn(II).

Also Co complex (N_4) and Mn complex (N_5) showed moderate antifungal activity against Candida albicans but no activity against Aspergillus niger. Ni complex (N_3) shows moderate activity against A.niger but no activity against C.albicans when compared with standard nistatin.

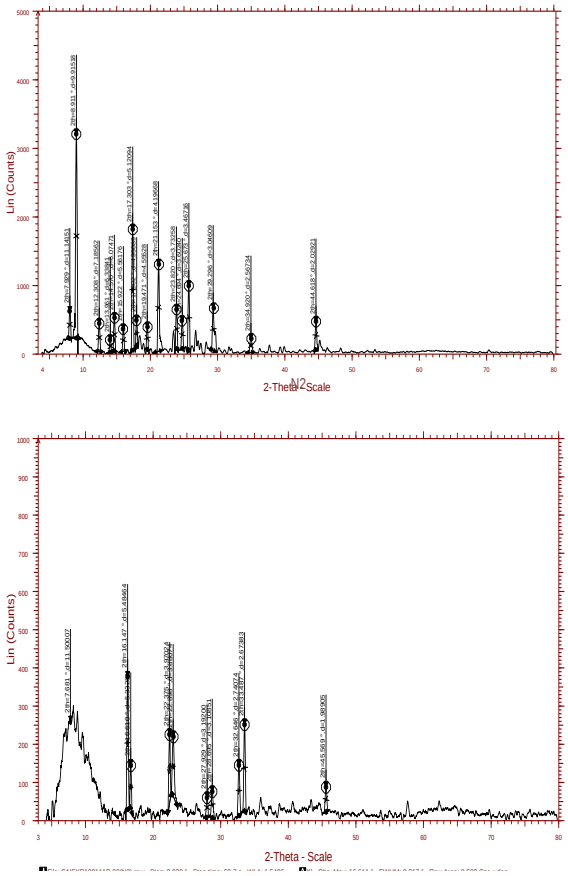


Fig.1 Powder XRD pattern of ligand of L_2 and N_2 complex

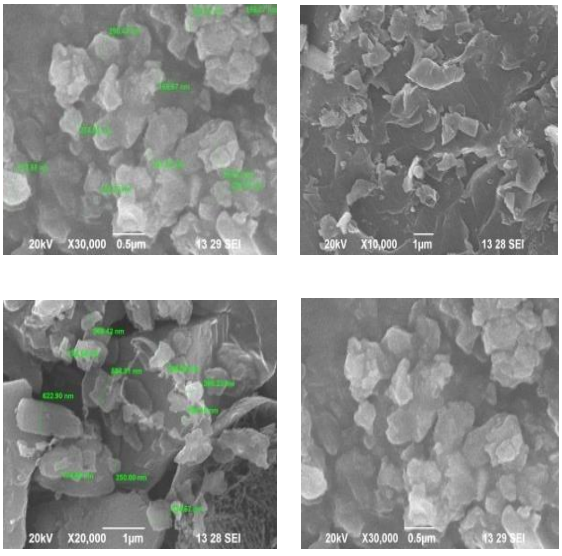
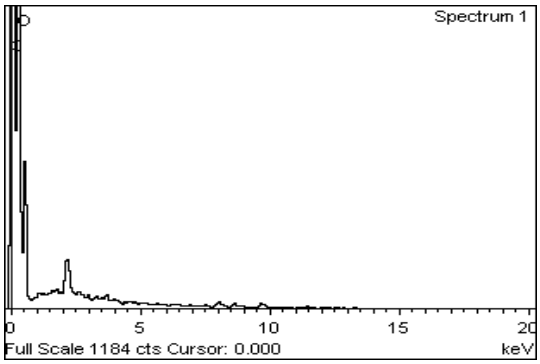


Fig.2 SEM images of L_2 and N_2 complex



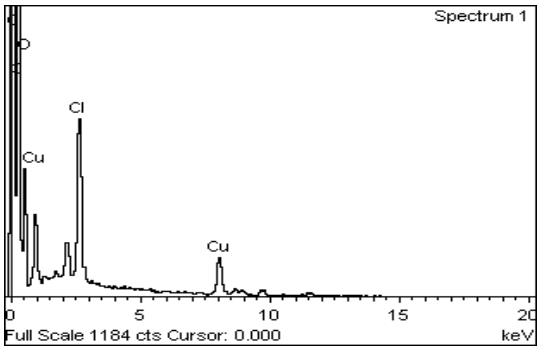


Fig.3 EDAX specrum of L_2 and their metal complex

S.No.	Compounds	% of Inhibition (mg/ml)
Control	-	100
1	L_2	91
2	N_1	14.7
3	N_2	91.4
4	N_3	74.2
5	N_4	50.0
6	N_5	64.7

Table. 1 DPPH assay of L_2 and its complexes

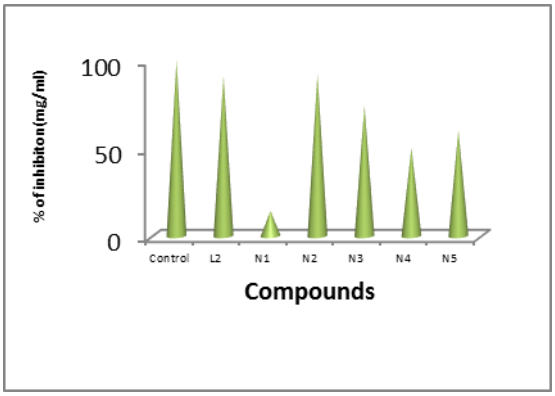


Fig.4 Bar diagram representation of antioxidant activity

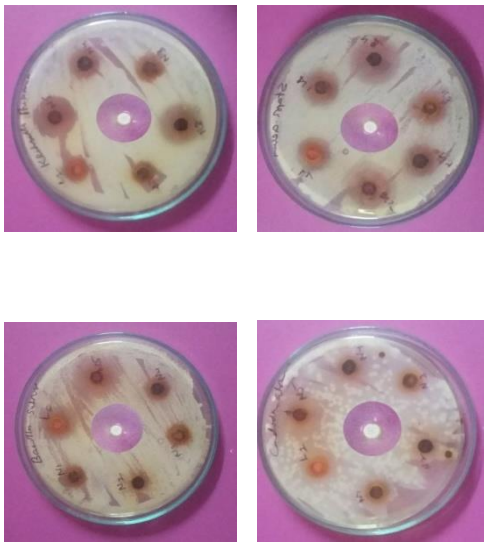


Fig.5 Inhibition zone against screened bacteria and fungi by the ligand and complexes

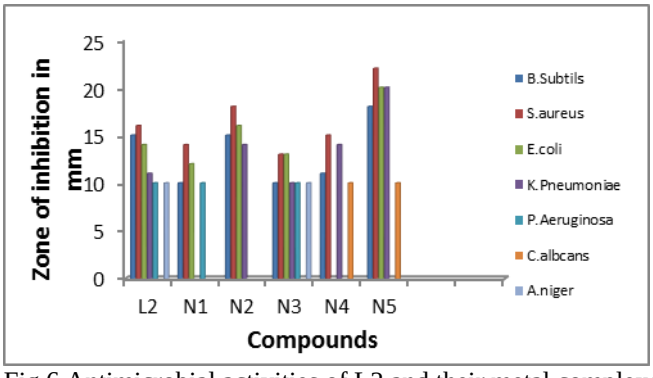


Fig.6 Antimicrobial activities of L2 and their metal complexes

Ligand/ Complexes	Antibacterial activity					Antifungal activity	
	B. Subtilis	S. aureus	E.Coil	K. Pneumoniae	P.aeuroginosa	C. albicans	A.niger
L_2	15	16	14	11	10	-	10
N_1	10	14	12	-	10	-	-
N_2	15	16	10	14	-	-	-
N_3	10	13	13	10	10	-	10
N_4	11	15	-	14	-	10	-
N_5	18	22	20	20	-	10	-
Amikacin	21	22	21	22	23		
Nistatin						15	17

Table 2: antimicrobial activity of L_2 and their metal complexes

IV. CONCLUSION

In this study, a schiff base ligand (Curcumin and 2-Aminophenol) was synthesized. They formed stable complexes (1:1) with transition metal ions such as Zn(II), Cu(II), Ni(II), Co(II) and Mn(II). The ligand and its complexes were stable at room temperature and are completely soluble in almost all organic solvents. The synthesized compounds were characterized by XRD and SEM-EDAX analysis. They are also tested for antioxidant and antimicrobial activities. The XRD and SEM analysis explains the nanocrystalline nature of the compounds. EDAX studies gives information about metal purity and elemental composition. Antioxidant studies reveal that most of the synthesized compounds have potential antioxidant activity. Antimicrobial study showed that all the complexes were moderately active against the tested organisms. Comparatively Mn complex (N_5) shows higher antibacterial activity than all other complex which is due to its higher lipid solubility and can be used as drugs after invivo studies.

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