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SYNTHESIS AND BIOLOGICAL APPLICATIONS OF SOME NOVEL SCHIFF BASE TRANSITION METAL (II) COMPLEXES DERIVED FROM THIOPHENE-2-CARBOXALDEHYDE AND 4, 4' DIAMINO DIPHENYL METHANE

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ABSTRACT

Schiff bases are considered as privileged ligand in coordination chemistry as they easily form stable complexes with most transition metal complexes. In this paper, a novel Schiff base ligand derived from Thiophene-2-carboxaldehyde (TPC) and 4,4' diamino diphenyl methane (DDM) and its transition metal complexes Cu(II), Zn(II), Co(II) and Ni(II). Antimicrobial, antioxidant, anti-inflammatory, larvicidal, DNA cleavage activity against standard at variable concentrations revealed that the Cu(II), Zn(II), Co(II) and Ni(II) complexes show enhanced antimicrobial, free radical scavenging and anti-inflammatory activities as compared to TPC and DDM.

KEYWORDS: Schiff base, antimicrobial, larvicidal activity, Anticancer activity.

1. INTRODUCTION

Medicinal inorganic chemistry offers additional opportunities for the design of therapeutic agents not accessible to organic compounds [1]. The inclusion of biologically active ligands into metal complexes deals much scope for the design of novel drugs with improve targeted activity, studies on metal complexes indicate that new mechanisms of action are favorable when combining the bioactive of ligand with properties inherent to the metal leading to the possibility of overcoming current drug resistance pathway. [2]. Schiff bases form a significant class of compounds in medicinal and pharmacological chemistry due to their varied biological applications such as antimicrobial, anticancer agents. [3, 4]. Synthesis, biological evaluation of a new Schiff base ligand Thiophene-2-carboxaldehyde (TPC) and 4, 4' diamino diphenyl methane (DDM) are reported. All the Schiff bases and their metal complexes have been screen for their antibacterial activity and antifungal activity against the selected bacteria and fungi using the well diffusion method. The larvicidal activity of the Schiff base and their metal complexes have been also studied. Also anti-inflammatory activities of the synthesized compounds were carried out by protein denaturation method.

2. EXPERIMENTAL

2.1. Materials and methods: All chemicals and solvent were obtained from commercial sources and were used as received without any further purification.

2.2. Synthesis of Schiff base ligand (L): Ethanolic solution of Thiophene-2-carboxaldehyde (TPC) and 4, 4' diamino diphenyl methane (DDM) were taken in RB flask in 1:1 molar ratio and refluxed for one hour. The reaction mixture is poured into ice, a yellow compound of Schiff base ligand was obtained. The precipitate was filtered, washed with water and dried.

2.3. Synthesis of metal complexes (ML): The metal complexes were prepared by adding ethanolic solution of Zn(II) nitrate, Co(II) nitrate, Ni(II) nitrate and Cu(II) nitrate to the ligand in ethanol in 1:2 (metal:ligand) molar ratio and refluxed for about 12 hours at 80 ^{o}C. The precipitate solid were filtered and washed with ethanol and dried.

2.4. Determination of antimicrobial activity: The agar well diffusion method was used to screen the anti-microbial (20ml) was poured in to each peri plates. The plates were allowed to solidify for 5minutes and 100µl in Colum suspension was swapped uniformly and allowed to dry for15 minutes. Using sterile cork borer of 8 mm diameter, wells were bored into the seeded agar plates and these were located with a 100 µl solution of each compound in DMSO and all plates were incubated at 37^{o}C and the diameter of inhibition zone around

each disc was measured after 24 hours 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.

2.5. Larvicidal activity: The mosquito larvae were collected from water habitats of Nagercoil, Kanyakumari District using a wide mouth container. The mosquito samples were brought to the laboratory, morphologically identified using standard manual and used for larvicidal activity studies. Cleaned sterile beakers were taken and 20 early in star larvae of Culex were taken in 100 ml of tap water. To this 100 ppm of synthesized complexes was added. 20 larvae taken in tap water (without copper complex) served as control. The beakers were kept for 24 h, 48 h, 72 h and 96 h for mortality of the larvae (Culex).

2.6. Anti-inflammatory activity: The reaction mixture (0.5 ml) consisted of 0.45 ml bovine serum albumin (3% aqueous solution) and varying concentration of compound (25, 50, 75,100 µg/ml of final volume), pH was adjusted to 6.3 using small amount of 1N hydrochloric acid. The samples were incubated at 37ºC for 20 min and then heated at 80ºC for 2min. After cooling the samples, 2.5 ml phosphate buffer saline (pH 6.3) was added to each tube. The absorbance was measured using spectrophotometer at 416nm. The percentage inhibition of protein denaturation was calculated as follows:

Percentage inhibition = [(Abs Control – Abs Sample) / Abs control)] x100

2.7. Anti-oxidant activity by dpph radical scavenging assay: Ascorbic acid was used as a reference standard and dissolved in distilled water to make the stock solution with the concentration (1mg/1000µl). The solution of DPPH in methanol 60µM was prepared fresh daily before UV measurements.

%Inhibition =(Absorbance of control at 0 minute-Absorbance of Test)/Absorbance of control at 15 minutes x 100

3. RESULT AND DISCUSSION

3.1. Antimicrobial activity: The antibacterial activity of synthesized Schiff bases and their metal (II) complexes was tested against gram positive and gram negative micro-organism using disc diffusion method. The micro-organism used in the present investigations included Pseudomonas, S.Aureus and Klebsiella. Amikacin was used as standard antibiotics.

The results shows that both the Schiff base ligand have moderate activity in the antibacterial species. In Pseudomonas organism have highly active in L_2Cu and L_2Zn complex. In L2Ni and L2 Co have moderate activity. In zone of inhibition in L_2Cu and L_2Zn have 16mm. [6]. Research has shown that the structural components possessing additional (C=N) bond with nitrogen and oxygen donor systems inhibit enzyme activity due to their deactivation by metal coordination.[9,10].

Table 1: Anti-microbial activity of Schiff base Ligand and their metal complexes

Samples	Zone of inhibition (mm)					
	Pseudomonas	S.Aureus	Klebsiella	C.Albican	A.Niger	Penicillium
L_2	10	9	16	7	11	8
L_2Co	12	6	14	12	9	10
L_2Zn	16	8	18	11	14	13
L_2Ni	11	10	19	17	12	20
L_2Cu	16	12	22	16	19	24

In antifungal activities the microorganism used in the present investigations included C.Albican, A.Niger and penicillium. In L_2Cu complex have better antifungal activity than L_2Ni and L_2Zn. In L_2Co have moderate activities in A. Niger and Penicillium. All the Schiff base metal (II) complex have highly active than ligand. The enhances of delocalization of the Pi electrons over the entire complex ring thereby promoting the lipophilicity character of the central metal ion, hence increasing the hydrophobic character and liposolubility of the complex

3.2. Larvicidal activity: The Larvicidal activity of synthesized ligand (L2) and metal complexes were tested

against culex mosquito. The values are shown in the table 2.The highest mortality values was obtained from Cu(II) complexes. The moderate mortality value was obtained in other metal complexes.

3.3. Anti-inflammatory activity: The newly synthesized Schiff base ligand (L2) and its Cu(II), Co(II), Ni(II) and Zn(II) Transition metal complexes that have been investigated for anti-inflammatory values in Table 3 and the graphical representation in figure 3. A common strategy that has been employed is the coordination of anti-inflammatory compounds or other bioactive molecules to metal ions, resulting in enhanced activity. In these series metal complexes were superior to those of the ligand L2. Cu (II) complex is better activity than other metal complexes. Ni (II) and Zn (II) metal complexes have moderate activity and Zn (ii) metal complex have low activity.

3.4. Anti-oxidant activity by dpph radical scavenging assay: The antioxidant activities of ligand and metal complexes with control were assessed Table.4 on the basis of the free radical scavenging effect on the stable DPPH free radical effect of the stable DPPH free radical efficiency (Breca.A2002). The examined changes in the free radical scavenging ability of the test sample on the basis of percent inhibition are presented in figure 4. In these series the results obviously showed that metal complexes are better activity than ligand. The Cu (II) metal complex exhibited best scavenging activity among the examined complexes, while Ni (II) and Zn (II) complexes have shown moderate activity in comparison with Co (II).

4. CONCLUSION

Zn (II), Co (II), Ni (II) and Cu (II) Schiff base metal complexes are derived from ethanolic solution of Thiophene-2-carboxaldehyde (TPC) and 4, 4’ diamino diphenyl methane (DDM) were synthesized and characterized. In antimicrobial screening the Cu (II) possess high bacterial and fungal activity. All the metal complexes are the higher active than the ligand. The anti-oxidant activity results shows due to the redox properties. Comparatively Cu (II) complex shows higher antimicrobial activity than all other complex which is due to its higher lipid solubility and can be used as drug after in vivo studies. Furthermore, copper complex appears to be an excellent candidate possessing anti-inflammatory and larvicidal activity.

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