WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 12, 642-645. Research Article ISSN 2277– 7105

ANTI BREAST CANCER ACTIVITY AND STUDIES OF COPPER (II) COMPLEX CONTAINING MIXED LIGANDS NITROGEN-OXYGEN DONOR SCHIFF BASE (4-BROMO-(2-CARBOXYPHENYL)-PYRIDINE-2YL ETHYLENE AMINE) AND 2,2' BIPYRIDINE

Shrimant V. Rathod*, Smita S. Giri and Shweta N. Dandekar

Chemistry Research Laboratory, Bhavan's Hazarimal Somani College, K. M. Munshi Marg, Chowpatty, Mumbai-400007, (M.S.), India.

Article Received on
07 Oct. 2016,

Revised on 27 Oct. 2016,
Accepted on 17 Nov. 2016

DOI: 10.20959/wjpr201612-7399

***Corresponding Author**
Dr. Shrimant V. Rathod
Chemistry Research Laboratory, Bhavan's Hazarimal Somani College, K. M. Munshi Marg, Chowpatty, Mumbai-400007, (M.S.), India.

ABSTRACT

Copper (II) per chlorate Schiff's base complex has been prepared by 4-bromo-(2-carboxy- phenyl)-pyridine-2-yl ethylene amine with 2,2'bipyridine and characterized. We report anti-breast cancer activity and study of copper (II) complex of mixed ligands Schiff base, 4-bromo-(2-carboxy phenyl)-pyridine-2-yl ethylene amine and 2,2'-bipyridine. It has been evaluated for anti breast cancer activity against MCF-7 cell line.

KEYWORDS: Schiff Base, 4-Bromo- (2-carboxyphenyl)-pyridine-2-yl ethylene amine, 2,2'-Bipyridine, Copper (II) Complex, Anti Breast Cancer.

INTRODUCTION

Schiff bases derived from an amino and carbonyl compound are an important class of ligands that coordinate to metal ions via azomethine nitrogen and have been studied extensively. Schiff bases are useful chelators because of their ease of preparation, structural varieties, varied denticities and subtle steric and electronic control on their framework. The biocidal effect of Schiff bases as well as its metal complexes is of interest due to their pharmacological activities.[1]

Schiff's base and their copper complexes possess remarkable properties as catalysts in various biological systems, polymers, dyes, antimicrobial activities, antifungal activities, antiviral activities insecticides, antitumor and cytotoxic activities, plant growth regulator,

enzymatic activity and pharmaceutical fields.[2-5] The role of Schiff base complexes of transition metals in chemistry and biochemistry suggest that considerable potential exists for their chelation reaction representing an exclusive beginning in this direction.[6-12]

Keeping the above facts in mind and in continuation of our recent work we studied the anti breast cancer activity of copper (II) complex of mixed ligands Schiff base, 4-bromo-(2-carboxyphenyl)-pyridine-2-yl ethylene amine and 2, 2'- bipyridine.

EXPERIMENTAL SECTION

Materials

All chemicals used were of the analytical reagents grade (AR) and of highest purity available. Copper carbonate, perchloric acid, 2-amino 5-bromo benzoic acid, 2-acetyl pyridine, 2,2'-bipyridine was purchased from the respective concerns and was used as received.

Methods

Copper was analyzed by titrimetric method. Elemental analysis (C, H and N) were performed on a Thermo Finnigan FLASH EA-112 CHNS analyzer. Infrared spectra were recorded on Perkin Elmer FT-IR spectrometer as KBr pellets in the 4000-400 cm-1 spectral range. 1H NMR spectra of ligands were recorded on Bruker 400 MHz spectrometer using DMSO as a solvent. Electronic spectra were recorded on a Shimadzu UV-visible NIR spectrophotometer. Magnetic susceptibility (μeff) was measured on Gouy balance at room temperature using Hg [Co(SCN)4] as calibrant. Molar Conductance (ΛM) was measured on the ELICO (CM-185) conductivity bridge using 10-3 M solution in DMF.

Preparation of copper (II) per chlorate

Copper per chlorate is prepared by dissolving copper carbonate (10 gm) in hot solution of concentrated perchloric acid (10ml) (50%) and then filter the solution. The filtrate was concentrated on a steam bath to get the blue needles of copper per chlorates. It was then dried under vacuum over $CaCl_2$ and used.

Synthesis of Schiff base ligand (4-bromo(2-carboxyphenyl)-pyridine-2-ylethyleneamine (L)

4- Bromo(2-carboxyphenyl)-pyridine-2-ylethyleneamine (L_1) is synthesized by mixing a solution of 2-Acetyl-pyridine (0.121 g, 1 mmol) in 10 ml of ethanol with solution of 2-amino 5-bromo benzoic acid (0.137 g, 1mmol) dissolved in 10 ml of absolute ethanol. The resulting mixture was refluxed at 80°C until the completion of reaction (checked by TLC). The

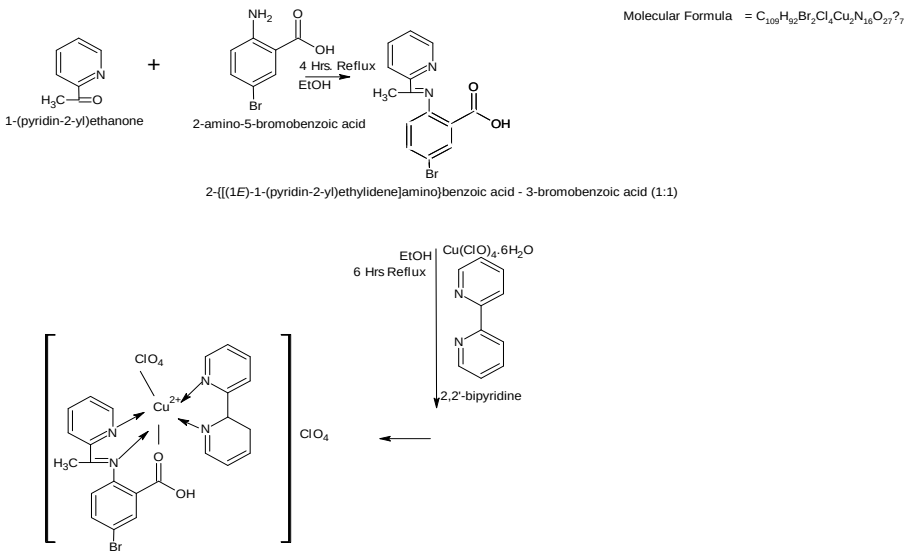
resultant brown colored liquid was concentrated to give dark brown colored solid and purified by crystallization to give product. (Yield: 70%; M.P.: 173^{0}C).[4]

Synthesis of copper (II) complex [CuL(bipy)ClO4]ClO4

To ethanolic solution of the appropriate metal per chlorate (1 mmol, 0.370 g, Cu $(ClO_4)_2$. $6H_2O$ and a ethanolic solution of L **(**1 mmol, 0.319 g) was added followed by addition of 2,2'-Bipyridine (1 mmol, 0.156 g) as secondary ligand with stirring. The resultant mixture was stirred for 1 h and refluxed for 4 h. The pale green product obtained was filtered, washed with ethanol and dried under vacuum over $CaCl_2$ gives green colored solid. (Yield: 62%; M.P.: 300^{0}C).[4]

RESULTS AND DISCUSSION

Analytical data for Copper (II) complex conform to $C_{24}H_{19}N_4O_{10}$ Cl_2 Br Cu. The Complex is soluble in DMF and DMSO. The spectroscopic evaluation of the synthesized complex involved elemental analysis, IR, UV-Visible spectral investigations and the results are matched the proposed structure. Copper (II) complex was obtained by the reaction of the ligands Schiff base 4-bromo(2-carboxyphenyl)-pyridine-2-ylethyleneamine and 2,2'-bipyridine with $CuClO_4.6H_2O$ in ethanol (Scheme 1).



Scheme 1: Synthesis of [CuL(bipy)ClO4]ClO4.

Following table shows the results of anti Breast cancer MCF-7 cell line. Cancer activity of the synthesized compounds against MCF-7 cell line. These results are expressed in terms of present growth in the presence of the test compounds. The IC_{50} values are shown in table.

Compound no.	MCF 7 (Breast carcinoma) IC_{50} (ug)
a[L_{1b}ByCu(ClO_4)$_2$]	5.95
cyclophosphamide	18.97

CONCLUSION

In the present research work, we synthesized Cu(II) complex of 4-bromo-(2-carboxyphenyl)-pyridine-2-yl ethylene amine, with 2,2'bipyridine and studied its anti brest cancer activity**.** Thus Complex [LBipy Cu (ClO_4)] ClO_4 shows promising anti breast cancer cell activity against MCF-7 cell line.

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