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SYNTHESIS AND BIOLOGICAL ACTIVITIES OF COBALT COMPLEX WITH SCHIFF'SBASE LIGAND DERIVED FROM 4-CHLORO-N-[(E)-PYRIDIN-2-YLMETHYLIDENE] ANILINE

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ABSTRACT

4-chloro-N-(E)-pyridin-2-ylmethylidene aniline isprepared by condensing 2-pyridine carboxaldehyde and 4-chloroanilinein ethanol. The Schiff base was reacted with cobalt chloride in acetonitrile and solution of two equivalent of triphenylphospine to obtain the corresponding Cobalt4-chloro-N-[(E)-pyridin-2-ylmethylidene]aniline complex. The synthesised Schiff base and complex were characterized on the basis of their chemical properties and spectroscopic data. These compounds were tested for anticancer,anti-inflammatory activity and antimicrobial activity against a variety of test organisms: *Escherichia coli, Staphylococcus aureus, and Candida albicans.* The compounds containing chlorogroup as substituents on the phenyl ring have been found to be very effective antimicrobial agents.

Keywords: - Schiff base, anticancer, antiinflametry, antimicrobial.etc

INTRODUCTION

The field of Schiff base complexes is fast developing because of the wide variety of possible structures for the ligands. Schiff base are organic compounds possessing azomethine group which resulted from condensation of amine with aldehyde or ketone.

Schiff base ligands are essential in the field of coordination chemistry, especially in the development of complexes of Schiff bases because these compounds are potentially capable of forming stable complexes with metal ions[1]. Such type of ligands represents vast utilized classes of new series of compounds in coordination chemistry[2]. Schiff bases are organic compounds with great utility in various fields[3], such as medicine, agriculture, cosmetic products etc. Recently, Schiff base complexes have drawn attention in biochemistry and biomedicine because of their unique properties[4,5]. Schiff bases are important precursors for the synthesis of some bioactive compounds[6,7]. Schiff bases have received considerable attention since the discovery of their antibacterial[8,9], antifungal[10] anti-HIV[11,12], anti-inflammatory[13],anticonvulsant[14,15], antiviral[16], antimalarial, anti-proliferative, and antipyretic activities[17,18] and anticancer properties[19]. The presence of the inimical grouping in these organic ligands plays an important part in manifesting these biological characteristics[20].

The aim of the resent study was to prepare, characterize and determine the anticancer, antiinflametry, antimicrobial properties of 4-chloro-*N*-[(*E*)-pyridin-2-ylmethylidene] aniline ligand and their cobalt metal complex for pharmaceutical uses.

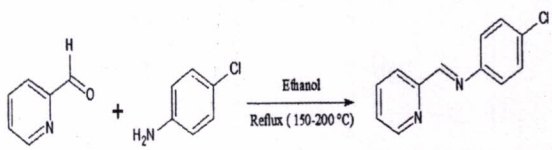
MATERIAL AND METHODS

All chemicals used in synthesis of compounds were of synthetic grade and were procured from Sigma-Aldrich, Hi-media. All melting points were taken on Veego model VMP-DS with ± 0.5ºC accuracy and are uncorrected. The purity of compounds was checked by TLC.IR spectra were recorded on SHIMADZU-FTIR-8400 spectrophotometer in frequency range of 4000-400 cm^{-1} using KBr pallet.^{1}HNMR spectra were recorded on BRUKER spectrometer (400 MHz) using $CDCl_3$ as a solvent and TMS as an internal reference.

Synthesis of 4-chloro-N-[(E)-pyridin-2-ylmethylidene]aniline (Schiff Base-1):

A reaction mixture of 2-pyridine carboxyaldehyde(0.01mol) and 4-chloroaniline(0.01mol), and ethanol (10ml) was refluxed at 150-200°C in oil bath for 3-4 Hrs, reaction was monitored through TLC. Recrystallized in ethanol to obtained compound **(SB-1)**[21].

REACTION SCHEME



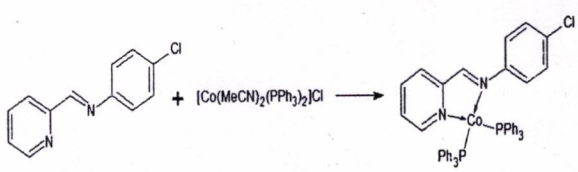
4-chloro-*N*-[(*E*)-pyridin-2-ylmethylidene] aniline (SB-1)

IR spectrum (KBr pellets), υ (cm^{-1}): 1651.63 (C=N str.), 1495.03 (C=C str.), 1304.07 (C-N str.) and 737.92 (C-Cl).^{1}HNMR spectrum (δ ppm): 7.210-7.347 (2H, m, Cl-Ar-H); 7.785-8.184 (4H, m, pyridine-H) and 8.577 (1H, s, H). C^{13}NMR spectrum (δ ppm): 122.01-122.46,129.08-129.35 (Cl-Ar-CH), 136 (Cl-Ar-CH), 149.37, 149.74, 154.23 (Pyridine CH), 160.91 (HC=N).

Synthesis of Cobalt 4-chloro-N-[(E)-pyridin-2-ylmethylidene]aniline complex:

To a solution of cobalt chloride (1mmol) in a 10 ml acetonitrile a solution of two equivalent of triphenylphosphine was added. The reaction mixture was stirred for 30 min at room temperature and allowed to evaporate slowly. The crystalline product obtained was subsequently added to a stirred solution of 4-chloro-*N*-[(*E*)-pyridin-2-ylmethylidene]anilineligand(1 mmol) in 10 ml dichloromethane for 2 Hrs and solution was evaporated to small volume under vacuum. The yellow coloured complex were developed by diffusion of diethyl ether into the solution

REACTION SCHEME



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RESULT AND DISCUSSION

Sr.No	Sample	ABS T1	ABS T2	ABS T3	Mean O.D	%of Cell Viability	%of Cell Inhibition on	IC.50
1.	Control	0.312	0.311	0.313	0.312	------	------	--------
2.	200 µg/ml	0.000	0.000	0.000	0.000	0.000	0.000	
3.	400µg/ml	0.143	0.144	0.145	0.144	46.16	53.84	
4.	600 µg/ml	0.128	0.128	0.131	0.129	41.35	58.65	390.83
5.	800 µg/ml	0.109	0.110	0.108	0.109	34.94	65.06	
6.	1000µg/ml	0.048	0.046	0.053	0.049	15.71	84.29	

Anti-Cancer:4-Chloro-N-[(E)-pyridin-2-ylmethylidene] aniline[Schiff Base]

Anti-Cancer: $[Co(SBL_1)\ (PPh_3)_2\ Cl_2]$

Sr. no.	Sample	ABS T1	ABS T2	ABS T3	Mean O.D.	% of cell viability	% of cell inhibition	IC 50
1	Control	0.312	0.311	0.313	0.312	--	--	--
2	200 µg/ml	0.305	0.305	0.296	0.302	96.08	3.20	
3	400 µg/ml	0.214	0.211	0.220	0.215	68.92	31.08	
4	600 µg/ml	0.190	0.192	0.191	0.191	61.22	38.78	665.91
5	800 µg/ml	0.177	0.182	0.175	0.178	57.06	42.94	
6	1000 µg/ml	0.108	0.109	0.104	0.107	34.30	65.70	

The test results indicated significant differences in Schiff base ligand and metal complex.

Anti-Inflammatory

Concentration (µg/ ml)	Diclofenac Sodium(Abs)	% inhibition
200	0.13	88.07
400	0.11	89.90
600	0.07	93.57
800	0.05	95.41
1000	0.04	96.33

$[Co(SBL_1)\ (PPh_3)_2\ Cl_2]$ MW793.5

Concentration (µg/ ml)	Observed Value of % inhibition	% inhibition
200	0.68	37.61
400	0.14	87.15
600	0.07	93.57
800	0.04	96.33
1000	---	--

Anti-Inflammatory Test for:4-Chloro-N-[(E)-pyridin-2-ylmethylidene] aniline

Concentration (µg/ ml)	Schiff Base	Inhibition%
200	0.17	84.40
400	0.15	86.23
600	0.14	87.15
800	0.08	92.66
1000	--	--

As above table indicated that the compounds 4-Chloro-N-[(E)-pyridin-2-ylmethylidene]

anilineand $[Co(SBL_1)\ (PPh_3)_2\ Cl_2]$showed strong inhibition of protein denaturation which indicated anti-inflammatory activity.

Anti- Microbial:

The antimicrobial activity is estimated by comparing the inhibition of growth of sensitive micro-organisms produced by known concentrations of the isolated substance to be examined against a reference substance.

During the study it has been found that some drug isolates inhibiting the growth of test organisms because of its antimicrobial property. Based on the results following is conclusion

Plate ID.5-4-chloro-N-[(E)-pyridin-2-ylmethylidene]aniline

Plate ID.15-Complex $[Co(SBL_1)\ (PPh_3)_2\ Cl_2]$

Plate ID	Sample ID	E. coli (Zone in mm)	S.aureus (Zone in mm)	Candida albicans (Zone in mm)
17	*Standard*	23.42 Antimicrobial	32.17 Antimicrobial	13.16 No Antimicrobial
5	*(Schiff Base)*	14.33 Significant Antimicrobial	14.90 Significant Antimicrobial	12.53 No antimicrobial
15	Complex	15.73 Significant Antimicrobial	12.20 No antimicrobial	12.82 No antimicrobial

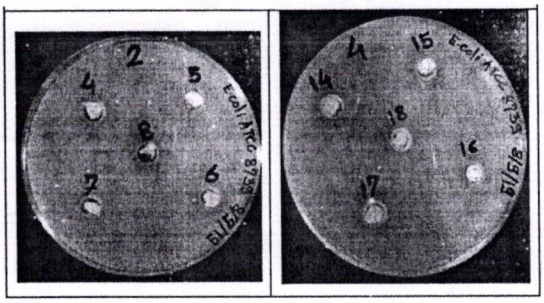
Weak significant – zone above 12 mm and below 14, Significant antimicrobial- zone above 14 mm based on diameter of agar cup and diluents interference

Remark –

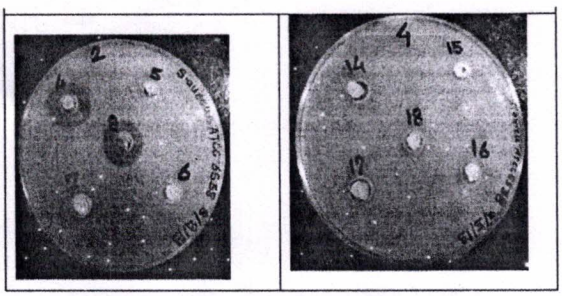
1. Gram Negative antibacterial complexes Bacterial (E. coli) – Indicated by GREEN

2. Gram positive antibacterial complexes Bacterial (S. aureus) – Indicated by BLUE

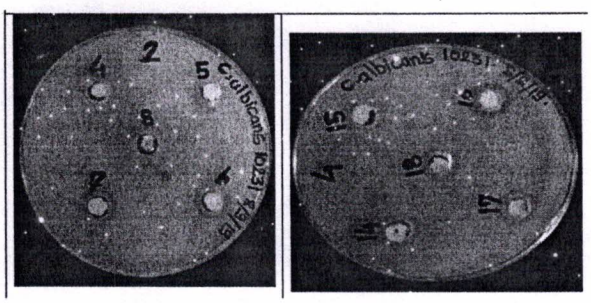
3. Antifungal complexes (Candida albicans) - Indicated by YELLOW



Echerchia coli ATCC no. 8739.



Staphylococcus aureus Slant ATCC no.6538



Candida albicans Slant ATCC no. 10231

CONCLUSION

Schiff bases possess a high potential toinhibit carcinoma cells which enhanced with complexation but the mechanism of their anticancer activity is not confirmed.

From results of anti-inflammatory studies it was observed that all synthetic compound exerts steady and significant antiinflammatory actions. This results is also recommended that antiinflammatory actions of synthetic compounds is due to attached groups.

The results of the antimicrobial screening of the Schiff bases against all bacteria have been found. The inhibition zones were measured in mm and results are shown in Table. The results of antimicrobial screening, indicate that Schiff bases show significant activity against Staphylococcus aureus, Escherichia coli, Candida *albicans*.Schiff base 4-Chloro-N-[(E)-pyridin-2-ylmethylidene]anilinewere found to be weak significant against Candida *albicans* and more active against Staphylococcus aureus, Escherichia coli bacterial strains because of the presence of chloro group which itself is active against microbes. Complex of Schiff base **[Co(SBL$_1$) (PPh$_3$)$_2$ Cl$_2$]** show SignificantAntibacterial activity against Escherichia coli, and No antimicrobial activity against Staphylococcus aureus, Candida *albicans*.

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