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METAL BASED SCHIFF BASES AS ANTICANCER AGENTS.

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ABSTRACT
In the present work Ruthenium and copper complex schiff bases were synthesized and they were evaluated for anticancer activity of Rusp1, Rusp 2, Rusp 3, CuAl 5, CuAl 6, and CuAl 7 were studied. Anticancer activity of given compounds were evaluated against the HeLa cell.3 by MTT assay. The IC_{50} values (the concentration of test compound needed to inhibit 50% of cells) of given compounds were determined.

KEYWORDS: Ruthenium, Copper, Schiff bases, MTT assay.

INTRODUCTION

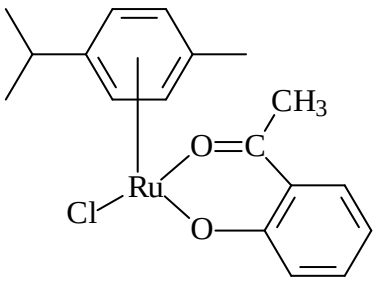
Cancer is a group of diseases in which cells are aggressive (grow and divide without respect to normal limits), invasive (invade and destroy adjacent tissues), and sometimes ***metastatic*** (spread to other locations in the body). Nearly, all cancers are caused by abnormalities in the genetic material of the transformed cells. These abnormalities may be due to the effects of carcinogens, such as tobacco smoke, radiation, chemicals, or infectious agents. Other cancer-promoting genetic abnormalities may be randomly acquired through errors in DNA replication or are inherited, and thus present in all cells from birth.

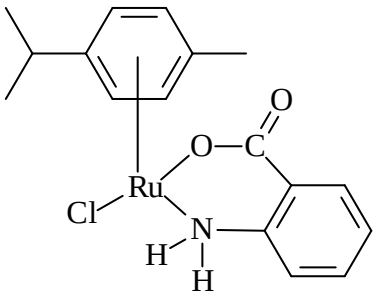
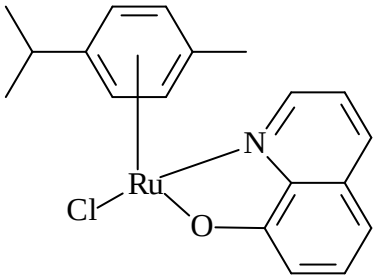
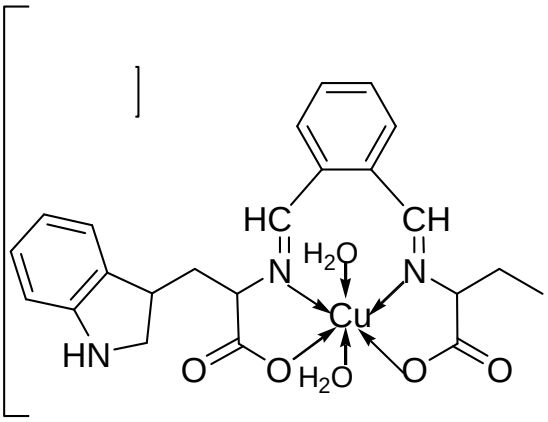
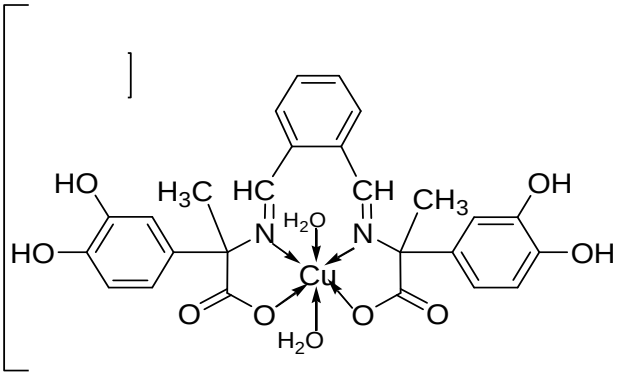
Schiff bases are aldehydes - or ketone - like compounds in which the carbonyl group is replaced by an imines or azomethine group. They are widely used for industrial purposes and also exhibit a broad range of biological activities. Schiff bases are biologically active compounds and have been reported to possess various important pharmacological properties like antifungal, anticancer, anticonvulsant and diuretic activities. Metal based Ruthenium and Copper complex Schiff base compounds were examined for Anticancer activity.

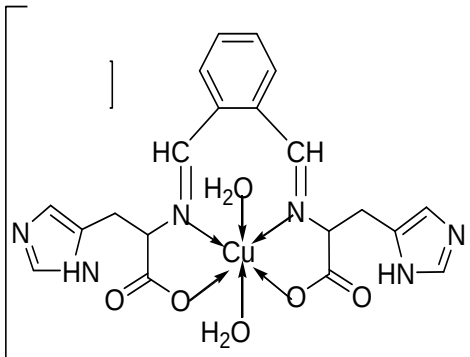
METHODS AND MATERIALS: Schiff bases are synthesized in the Department of Chemistry, Kakatiya University, Warangal were primarily tested for anticancer activity. Cell culture: HeLa (Cervical cancer) / IMR-32(Neuroblastoma) were obtained from the department of microbiology, Kakatiya University, Warangal.

EXPERIMENTAL METHOD: Schiffbase were synthesised from the condensation of an amino acid with carbonyl compounds. These compounds and their metal complexes are very important as catalysts in various biological systems, polymers, dyes and medicinal and pharmaceutical fields.

Table 1: Code and corresponding complex structures.

S.No.	Ligand	Corresponding Ru(II) complex
1-$RuSP_1$	2-Hydroxy acetophenone	 [(n^6-p-cymene)Ru(2-hydroxyacetophenone)

2-RuSP$_2$	Anthranilic acid	 [(n^6-p-cymene)Ru(aa)Cl]
3-RuSP$_3$	8-Quinolinol	 [(n^6-p-cymene)Ru(quin-8-O)Cl]
4-CuAL$_6$	2E)-2-(2-((E)-(1-carboxy-2-(indolin-3-yl)ethylimino)-methyl)benzylideneamino)butanoic acid	 $C_{23}H_{27}CuN_3O_6$ Mol. Wt.: 505.02
5-CuAL$_5$	2-{[(E)-1-(2-{[(1-carboxy-2-carboxyphenylethylimino]methyl}-phenyl)methylidene]amino}-3-phenylpropanoic acid	 $C_{26}H_{26}CuN_2O_{10}$ Mol. Wt.: 590.04

6-	CuAL7	2,2'-{benzene-1,2-diylbis[(*E*)methylylidene(*E*)azanylylidene]}-bis[3-(1*H*-imidazol-5-yl)propanoic acid]	 $C_{20}H_{22}CuN_6O_6$ Mol. Wt.: 505.97

Evaluation of in vitro anticancer activity against HeLa, IMR-32 cancer cell lines

In vitro anticancer activity of all the title compounds was evaluated against HeLa, IMR-32 and MCF-7 cancer cell lines using MTT assay16,17. The cell suspension of 1 × 105 cells/ml was prepared in complete growth medium.Stock solutions of synthetic compounds were prepared in DMSO. The stock solutions were serially diluted with complete growth medium containing 50 mg/ml of gentamycin to obtain working test solution of required concentrations (having <1% DMSO). The 100 µl of cell suspension was added to each well of the 96-well tissue culture plates.The cells were allowed to grow in CO2 incubator (37°C, 5% CO2, 90% relative humidity) for 24 hr. The test materials in complete growth medium (100 µl) were added after 24 hr incubation to the wells containing cell suspension. After 48 hr of treatment with different concentrations of test compounds, the cells were incubated with MTT (2.5 mg/ml) for 2 hr. The medium was then removed and 100 µl of DMSO were added into each well to dissolve formazan crystals, the metabolite of MTT. After thorough mixing,the plate was read at 490 nm for optical density that is directly correlated with cell quantity.

RESULTS AND DISCUSSION

The anticancer activity of the below Schiff base compounds was investigated by MTT assay method from the observations, Copper and Ruthenium complexes $CuAL_5$ and $RuSP_3$ compounds showed potent anticancer activity. The data shows the compounds activity in the range of $CuAl_5$> $RuSP_3$> $RuSP_1$> $RuSP_2$> $CuAl_6$> $CuAl_7$

Table 2: ANTICANCER SCREENING DATA OF THE SCHIFF BASE COMPLEXES

Sample	Concentration/ % Inhibition		
	30 mg/ml	100 mg/ml	300 mg/ml
Code 1	7.28	18.54	44.85
Code 2	9.63	22.62	51.25
Code 3	12.19	27.51	44.69
Code 4	10.27	24.58	40.31
Code 5	18.67	40.57	56.56
Code 6	15.13	33.81	42.18

Table 3: ANTICANCER SCREENING DATA OF THE SCHIFF BASE COMPLEXES

S. No.	Compound Name	Sample	IC 50 (mg/ml)
1	*Rusp1*	Code 1	335.62
2	*Rusp3*	Code 2	289.47
3	*Rusp2*	Code 3	337.47
4	*CuAL7*	Code 4	382.92
5	*CuAL5*	Code 5	233.1
6	*CuAL6*	Code 6	368.17

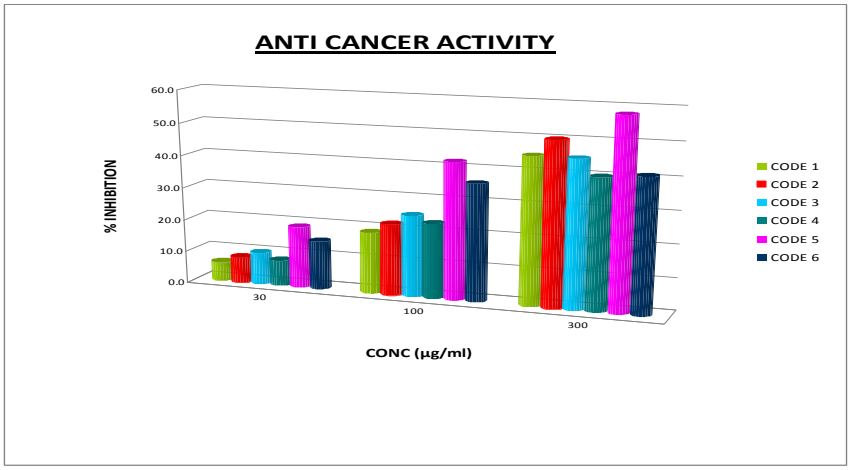


Fig.6: ANTI CANCER ACTIVITY

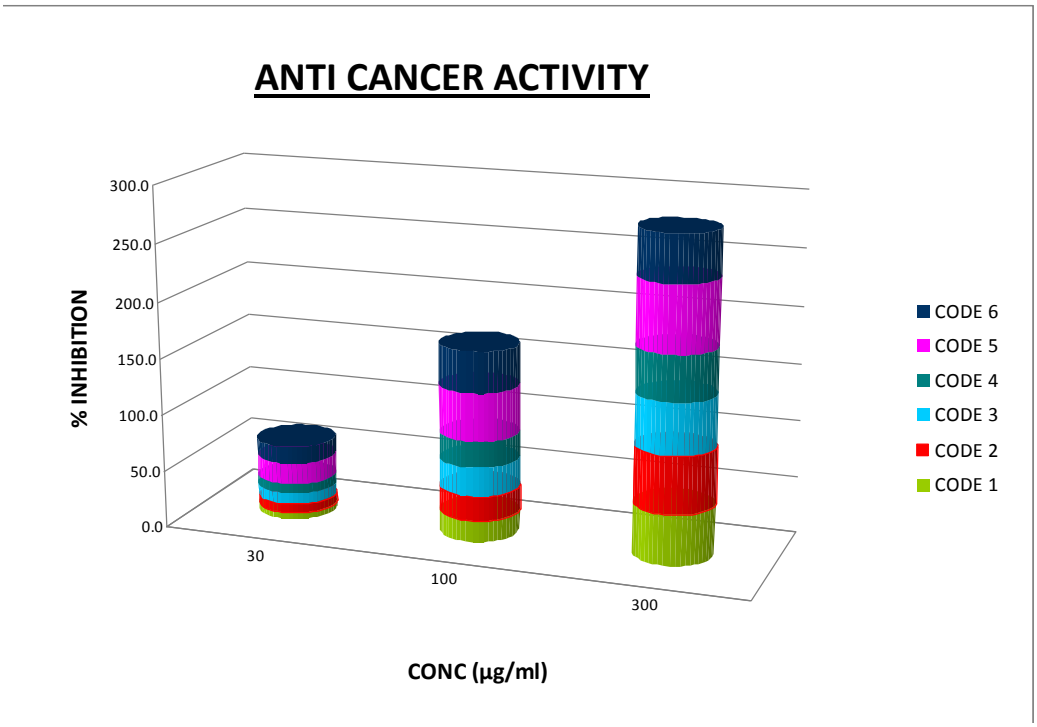


Fig.7 ANTI CANCER ACTIVITY

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