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Research Article

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In vitro antimicrobial evaluation of copper, palladium, ruthenium complexes derived from schiff bases

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ABSTRACT

Two Schiff bases were synthesized from raceacetophenone: 1) ADS1: 4-ethyl-6-{(E)-1-[(3-nitrophenyl) imino] ethyl} benzene-1, 3-diol and 2) ADS3: 4-ethyl- 6-{(E)-1-[(2-nitrophenyl) imino] ethyl} benzene-1, 3-diol. Then their metal complexes were formed. The metals ions selected for the synthesis of new complexes were copper, Ruthenium, palladium. Hence, in total 19 metal complexes were synthesized and screened for antibacterial activity against some clinically important bacteria, such as Pseudomonas aeruginosa, Proteus vulgaris, Proteus mirabilis, Klebsiella pneumoniae and Staphylococcus aureus. Ruthenium compounds possess more antibacterial activity when compared with the standard drug ampicillin. Copper compounds possess more antifungal activity when compared with the standard drug clotrimazole.

Keywords: Schiff bases, receacetophenone, copper, nickel, iron, zinc, antibacterial, antifungal.

INTRODUCTION

In the field of medicine, inorganic chemistry there is increasing prominence of metal base compounds offer possibilities for the design of the therapeutic agents not readily available to organic compounds. The intrinsic properties of the cationic metal ion and ligand itself offer the medicinal chemist a wide spectrum of relativities that can be exploited in a wide range of coordination number and geometries, accessible redox states thermodynamic name and kinetic characteristics. In a more or less empirical fashion metals have long been used for medicinal purposes (1)

Schiff base compounds have a major impact in modern medicine as these are used to diagnose a variety of diseases and conditions relating to cancer care, infection control[2], diabetic control[3], neurological [4], cardiovascular [5], anti-inflammatory diseases[6], ulcers inhibition [7-8] and have promising therapeutic properties [9]. Metal based fungicides inhibit a wide range of enzymes involved in various metabolic pathways and ultimately cause cell death. The mode of action of fungicides showed that these compounds inhibit cell division. The specific site of action is β-tubuline, a polymeric protein found in microtubules essential component of cytoskeleton. PDA rich in carbohydrates is utilized as the major nutrient source by the microbes with the help of various enzymes (viz., amylase, cellulase and pectinase). Phenyl and amine groups in complexes affected nucleic acid synthesis and mitochondrial electron transport. An interesting point for investigating Schiff base complexes is the antimicrobial activity. Several of the Schiff bases have been used for metal ion determination. In this work Copper, Platinum , Ruthenium derived complexes were characterized and screened for their activity.

EXPERIMENTAL SECTION

Schiff bases are synthesized in the Department of Chemistry, Kakatiya University, Warangal were primarily tested earlier for their antibacterial, antifungal activities. The bacterial and fungal cultures were obtained from the department of microbiology, Kakatiya University, Warangal.

Experimental Method: Schiff base were synthesised from the condensation of an amino acid with carbonyl compounds. Copper, Ruthenium,Pallidium metal complexes were screened for antibacterial activity against *Bacilli subtilis* and *Ecoli* using paper disc plate method and are screened for antifungal activity against *Rizoctonia, Fusarium solani, Currularia* fungal strains.

Paper Disc plate method for antibacterial activity.[10]

Flat-bottomed 90 mm pyrex petridishes were used. Fifteen milliliters of agar medium (Lucia Bertani) was pipetted into the petridish. After the agar solidified, 5 ml of warm seeded agar was applied. The seeded agar was prepared by cooling the molten agar to 40^oC and then adding the amount of bacterial suspension. The plate was titted to ensure even coverage before the agar solidifies. These dishes with tops in place are stacked in refrigerator upside down to prevent condition of moisture. The compounds were dissolved in DMSO in 250 and 500 mg concentrations. The petriplates were stored in an incubator at 28 ± 2^oC for 24 h. The zone of inhibition that formed around each disc containing the test compounds was measured accurately in mm.

Radial Growth method for Antifungal Activity.[10]

Potato dextrose agar medium (glucose 20 g, starch 20 g, agar-agar 20 g and 1000 ml of H_2O) (1:1:1:5) was prepared in flask and sterilized. To this medium was added requisite amount of the compound after being dissolved in DMSO so as to get a certain final concentration. A series of concentration were prepared. The medium was then poured into the petriplates and a small disc (0.7 cm) of the fungus culture was cut with a sterile cork bores and transferred aseptically to the center of a petri dish containing the medium with a certain amount of the compound. Suitable checks were kept so that the culture discs were grown under the same conditions on potato dextroase media (PDA) without the compound. These petri dishes were wrapped in polythene bags containing a few drops of alcohol and were placed in an incubator at 25 ± 2^oC. Three replicates were used in each case. After 96h the colony diameter compared with check was taken as a measure of fungitoxicity. The amount of growth inhibition was calculated by the equation.

$$\% \text{ inhibition} = (d_c - dt) \times 100 \times d_c^{-1}$$

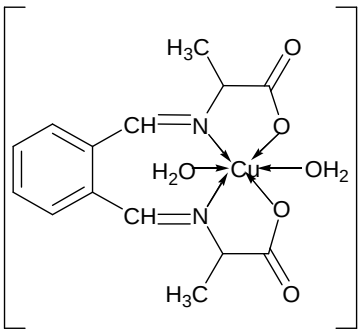
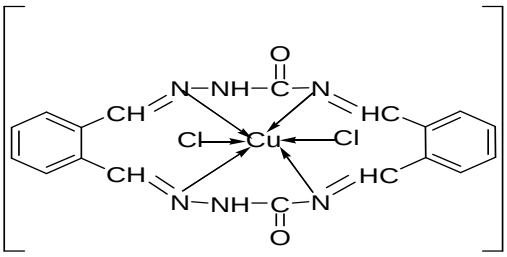
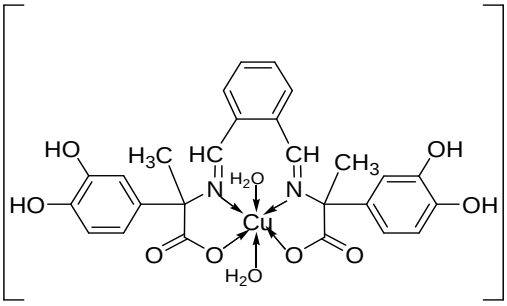
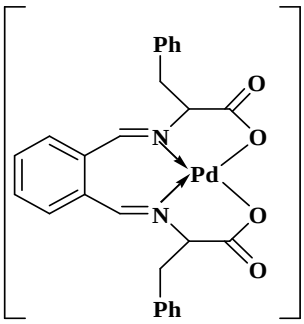
where d_c is the diameter of the fungal colony in control and dt is the diameter of fungal colony in test plate.

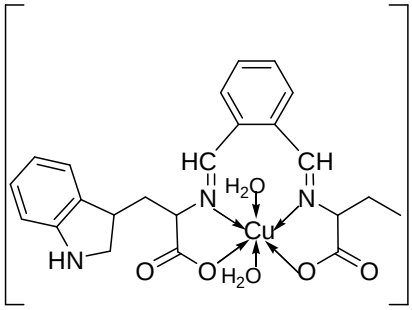
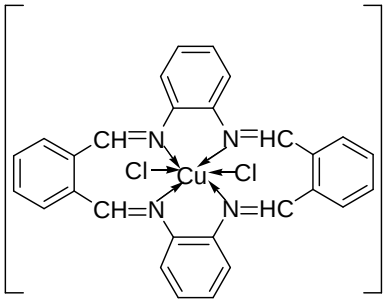
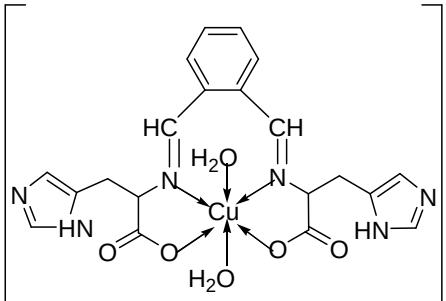
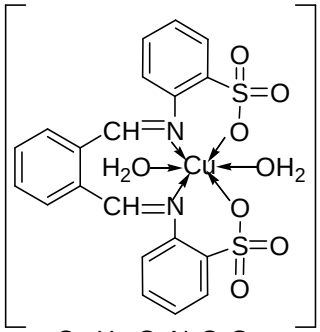
RESULTS AND DISCUSSION

Antibacterial and antifungal activity was represented in the tables Antibacterial activity: Among all the Ruthenium metal complexes, Compound $RuSP_1$ showed maximum antibacterial activity than $RuSP_4$ and $RuSP_3$ .Among the Copper metal complexes $CuPL_{14}$ and $CuPL_{45}$ showed maximum antibacterial activity.

Antifungal activity: Among all the metal complexes, Copper metal complexes $CuBl_5$,$CuBL_{14}$,$CuPL_4$ showed maximum activity. Among Ruthenium metal complexes $RuSP_4$ showed maximum activity when compared with the standard clotrimazole.

Table 1: Structure of metal complexes (copper and Palladium)

S.No.	Metal Complex	Structure
1-	$CuAL_1$	 $C_{14}H_{18}CuN_2O_6$ Mol. Wt.: 373.85 2,2'-{benzene-1,2-diylbis[(*E*)methylylidene(*E*)azanylylidene]}-dipropanoic acid
2-	$CuPL_2$	 $C_{18}H_{14}Cl_2CuN_6O_2$ Mol. Wt.: 480.79
3-	$CuAL_4$	 $C_{26}H_{26}CuN_2O_{10}$ Mol. Wt.: 590.04
4.	$PdAL_5$	 $C_{26}H_{22}N_2O_4Pd$ Mol. Wt.: 532.88

5-	$CuAL_6$	 $C_{23}H_{27}CuN_3O_6$ Mol. Wt.: 505.02
6	$CuPL_6$	 $C_{28}H_{20}Cl_2CuN_4$ Mol. Wt.: 546.94
7-	CuAL7	 $C_{20}H_{22}CuN_6O_6$ Mol. Wt.: 505.97
8.	$CuPL_{14}$	 $C_{20}H_{18}CuN_2O_8S_2$ Mol. Wt.: 542.04

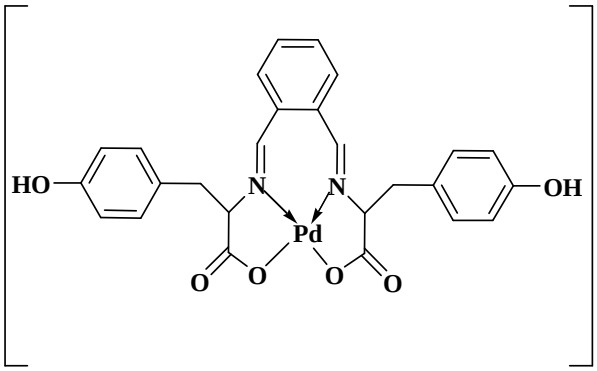
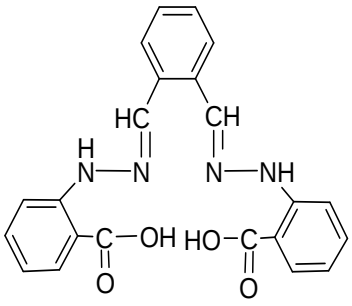
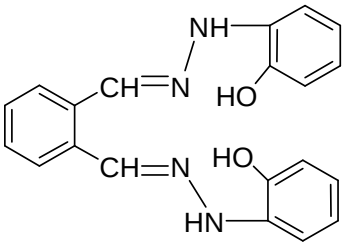
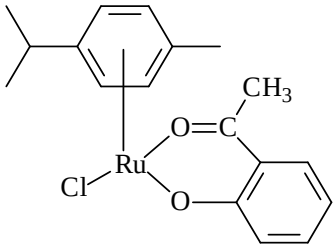
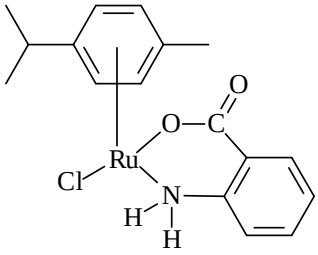
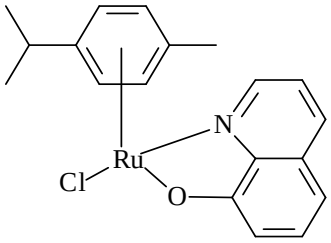
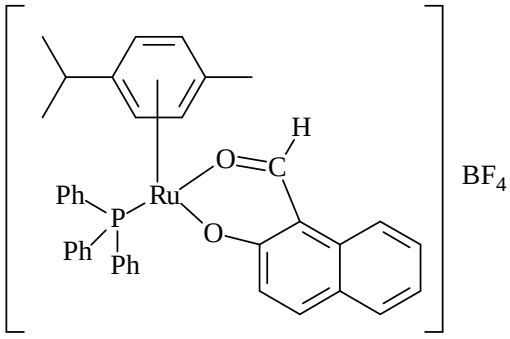
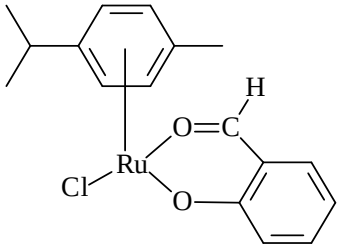
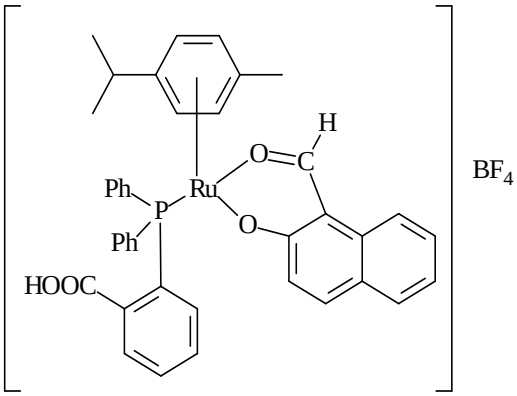
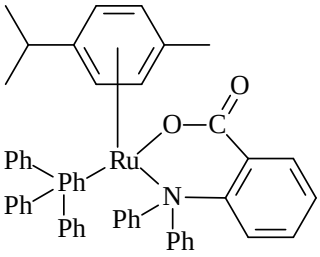
9.	$PdPL_{21}$	 $C_{26}H_{22}N_2O_6Pd$ Mol. Wt.: 564.88
10.	$CuPL_{45}$	 $C_{22}H_{18}N_4O_4$ Mol. Wt.: 402.4
11.	$CuPL_{50}$	 $C_{20}H_{18}N_4O_2$ Mol. Wt.: 346.38

Table 2: Structure of ruthenium complexes

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-RuSP$_4$	2-Hydroxcy-1-naphthaldehyde+PPh$_3$	 [(n^6-p-cymene)Ru(2-hna)(PPh$_3$)]BF$_4$
5-RuSP$_5$	Salicylaldehyde	 [(n^6-p-cymene)Ru(sal)Cl]
6-RuSP$_6$	2-Hydroxy-1-naphthaldehyde+o-PPh$_3$COOH+PPh$_3$	 [(n^6-p-cymene)Ru(2-hna)(o-PPh$_3$COOH)]BF$_4$

7-RuSP$_7$	2-Carboxyphenyl-diphenylphosphine + PPh_3	

[(n^6-p-cymene)Ru(2-carboxylphenyl-diphenyphosphine)PPh_3]BF_4

Table 3: BACTERIAL SCREENING DATA OF THE SCHIFF BASE COMPLEXES

Sl. No.	Compound Name	Bacterial Strains					
		Bacillus subtilis (G+ve)			Escherichia coli (G-ve)		
		Diameter of Growt zone of Inhibition (mm)					
		250 mg	500 mg	750 mg	250 mg	500 mg	750 mg
1	*CuAL$_1$*	6mm	7mm	9mm	6mm	6mm	9mm
2	*CuPL$_2$*	3mm	4mm	6mm	6mm	9mm	11mm
3	*CuAl$_4$*	5mm	5mm	6mm	5mm	6mm	7mm
4	*CuAl$_5$*	8mm	9mm	11mm	4mm	8mm	8mm
5	*CuBl$_5$*	7mm	8mm	9mm	4mm	6mm	8mm
6	*CuAl$_6$*	5mm	5mm	6mm	7mm	8mm	10mm
7	*CuPl$_6$*	8mm	9mm	14mm	4mm	8mm	15mm
8	*CuAl$_7$*	6mm	7mm	9mm	5mm	6mm	7mm
9	*CuPL$_{14}$*	11mm	12mm	16mm	10mm	11mm	12mm
10	*CuPL$_{21}$*	5mm	6mm	8mm	3mm	4mm	5mm
11	*CuPL$_{45}$*	8mm	13mm	14mm	4mm	8mm	15mm
12	*CuPL$_{50}$*	7mm	8mm	10mm	5mm	6mm	8mm
13	Standard Drug Ampicillin	8mm	9mm	10mm	7mm	11mm	14mm

TABLE-4: BACTERIAL SCREENING DATA OF THE SCHIFF BASE COMPLEXES

Sl. No.	Compound Name	Bacterial Strains					
		Bacillus subtilis (G+ve)			Escherichiacoli (G-ve)		
		Diameter of Growth zone of Inhibition (mm)					
		250 mg	500 mg	750 mg	250 mg	500 mg	750 mg
1	*Rusp$_1$*	4mm	5mm	6mm	16mm	18mm	19mm
2	*Rusp$_2$*	5mm	8mm	10mm	5mm	10mm	11mm
3	*Rusp$_3$*	8mm	10mm	11mm	9mm	11mm	15mm
4	*Rusp$_4$*	10mm	12mm	17mm	7mm	8mm	11mm
5	*Rusp$_5$*	4mm	5mm	7mm	7mm	9mm	12mm
6	*Rusp$_6$*	6mm	7mm	10mm	5mm	9mm	10mm
7	*Rusp$_7$*	8mm	9mm	10mm	7mm	11mm	15mm
8	Standard Drug Ampicillin	8mm	9mm	10mm	7mm	11mm	14mm

TABLE – 5: ANTIFUNGAL SCREENING DATA OF THE SCHIFF BASE COMPLEXES

Sl. No.	Compound Name	Fungal Strains					
		Fusarium Oxysporum		Rhizoctonia		Curricularia	
		500mg	750mg	500mg	750mg	500mg	750mg
1	*CuAl$_1$*	2mm	3mm	9mm	12mm	4mm	4mm
2	*CuPl$_2$*	3mm	5mm	2mm	3mm	3mm	5mm
3	*CuAl$_4$*	3mm	8mm	8mm	11mm	2mm	6mm
4	*CuAl$_5$*	3mm	4mm	7mm	8mm	3mm	4mm
5	*CuBl$_5$*	6mm	8mm	4mm	7mm	5mm	6mm
6	*CuAl$_6$*	4mm	6mm	3mm	5mm	4mm	4mm
7	*CuPl$_6$*	2mm	3mm	5mm	10mm	3mm	5mm
8	*CuAl$_7$*	2mm	4mm	4mm	15mm	4mm	6mm
9	*CuPL$_{14}$*	4mm	6mm	3mm	5mm	4mm	5mm
10	*CuPL$_{21}$*	3mm	3mm	2mm	4mm	4mm	6mm
11	*CuPL$_{45}$*	3mm	4mm	6mm	12mm	3mm	5mm
12	*CuPL$_{50}$*	2mm	4mm	3mm	6mm	2mm	3mm
13	Standard Drug Clotrimazole	2mm	3mm	2mm	3mm	2mm	3mm

Table 6: ANTIFUNGAL SCREENING DATA OF THE SCHIFF BASE COMPLEXES

Sl. No.	Compound Name	Fungal Strains		Rhizoctonia		Curricularia	
		Fusarium Oxysporum					
		500mg	750mg	500mg	750mg	500mg	750mg
1	$Rusp_1$	3mm	4mm	3mm	4mm	5mm	5mm
2	$Rusp_2$	3mm	5mm	5mm	10mm	3mm	4mm
3	$Rusp_3$	2mm	3mm	7mm	9mm	4mm	3mm
4	$Rusp_4$	4mm	6mm	5mm	8mm	4mm	3mm
5	$Rusp_5$	3mm	3mm	5mm	11mm	3mm	4mm
6	$Rusp_6$	3mm	4mm	6mm	7mm	4mm	5mm
7	$Rusp_7$	3mm	4mm	4mm	10mm	2mm	5mm
8	Standard Drug Clotrimazole	2mm	3mm	2mm	3mm	2mm	3mm

CONCLUSION

Among all the synthesised derivatives, Ruthenium compounds possess more antibacterial activity when compared with the standard drug ampicillin. Copper compounds possess more antifungal activity when compared with the standard drug clotrimazole.

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