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SYNTHESIS AND MICROBIAL ACTIVITY OF TRANSITION METAL COMPLEXES OF *p*-DIMETHYLAMINOBENZYLIDINE RHODANINE

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ABSTRACT

p-Dimethylaminobenzylidine rhodanine has been known as sensitive spectrophotometric reagent for the determination of traces of copper, silver and gold. Synthesised rhodanine with aryl/benzyl group at 5-position have been studied and found to be exhibit fungitoxic and bacteristatic activity. It is found that some drugs have increased activity, when administered as metal complexes. Antimicrobial activity of p-dimethylaminobenzylidine rhodanine and its metal complexes in dimethylformamide was studied. Dilution method was used to determine minimum inhibitory concentration based on dilution series 400 µg/mL, 200 µg/mL, 100 µg/mL, 50 µg/mL, 25 µg/mL, 12.5 µg/mL.

Key words: Transition metal, Complexes, *p*-Dimethylaminobenzylidine rhodanine, Microbial acitivity.

INTRODUCTION

Heterocycles with rhodanine template are perspective class of biological active[1-7] compounds with a broad range in the field of chemistry and pharmacology. Over views of their synthesis, properties and applications have been published[8,9] and therefore, the preparation of this heterocyclic core unit has attracted the attention of many organic chemists.

Rhodanine and substituted rhodanine, which contains toxiphoric dithiocarbamate chromophore –NCSS– has been the subject of scrutiny as fungicides and mildew proofing agents[10-12]. It has been shown that 3-substituted rhodanines posses pronounced antimicrobial activity.[13-15] Condensation products of rhodanine with aldehyde and ketones exhibit mildew proofing activity.[16] Mildew-proofing agents contain the structure –NCSS–, present in many

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plant fungicides. Rhodanine also has some fungicidal property. Phthalsulphathiazole[17], sulphathiazole[18] and sulphamethizole[19], have antibacterial activity. The antitubercular activity of some benzylidine derivatives of sulphathiazole and sulphaphenazole have been studied[20]. *p*-Dimethylaminobenzylidine rhodanine has been known as a sensitive reagent for silver, copper and mercury. This reagent is used in determination of cyanides and argentometric titration in high acidic solution.

Transition metals have property to form complex ions. A complex ion consists of a metal ion, surrounded by non-metallic ions or molecules called ligands. The ligands are bonded by dative covalent bonds by donating lone pairs of electrons to the metal ion. Many transition elements have been extensively investigated with regard to their potential quality as anticancer agents. The chief donor in most of the complexing agents are N, O and S and it has been found that some drugs have increased activity, when administered as metal complex.

In present paper we report the synthesis of complex and these were screened for microbial activity.

EXPERIMENTAL

Synthesis of *p*-dimethylaminobenzylidine rhodanine

p-Dimethylaminobenzylidine rhodanine has been prepared as reported in literature[21]. All the chemicals used were analytical grade reagent. Melting points were taken in open capillary and were uncorrected. Infra-red spectra were recorded as KBR pellets on Shimadzu PC FTIR.

Synthesis of metal complexes

Metal acetates (Cu, Fe and Zn) were treated with 50% dimethylformamide with ethanol separately and *p*-dimethylaminobenzylidine rhodanine with 50% dimethyl-formamide with ethanol in 1 : 2 molar ratio and then refluxed on water bath for 3.0-8.0 hrs. The solid complexes were separated out by filtration, washed with ethanol; followed by ether and dried in vaccuo. The colour of Cu, Fe and Zn complex is black/grey, brown and reddish brown, respectively.

All the complexes are amorphous having high melting point and are insoluble in water and common organic solvents. They are soluble in dimethylformamide, dioxane and 40%, 50% dimethylformamide in alcohol.

Low conductance value observed in dimethylformamide for all the complexes indicates that they are non-electrolyte. They are not attacked by acid and undergo decomposition.

Microbial activity

Microbial activity of *p*-dimethylaminobenzylidine rhodanine and its metal complexes in dimethylformamide was studied. The stock solution of compound and complexes were prepared by dissolving 10-40 mg/mL in appropriate solvent viz, 50% v/v solution of dimethylformamide. For antibacterial and antifungal activity, different concentrations i.e. 12.5 µg, 25 µg, 50 µg, 100 µg, 200 µg and 400 µg per disc were screened.

Table 1: Antibacterial activity of ρ-dimethylaminobenzylidine rhodanine and their copper, iron, zinc complexes

Abb.	Gram positive bacteria												Gram negative bacteria											
	S. epidermides						*B. subtilis*						*E. coli*						*P. aruginosa*					
	Concentration of compounds/ complexes in µg/mL						Concentration of compounds/ complexes in µg/mL						Concentration of compounds/ complexes in µg/mL						Concentration of compounds/ complexes in µg/mL					
	12.5	25	50	100	200	400	12.5	25	50	100	200	400	12.5	25	50	100	200	400	12.5	25	50	100	200	400
5P DARH	+	+	+	+	-	- -	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-
5P DARH +Cu	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
5P DARH + Fe	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-
5P DARH + Zn	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

(+) : Growth) i.e No inhibition, (−) : 7-8 mm inhibition, (−−) : 8-10 mm inhibition, (−−−) : 10-12 mm inhibition; 5P DARH = Ligand

The sterile 6 mm diameter filter paper discs were thouroghly moistened in the drug sample to be tested and placed on the solidify agar plates. Simultaneously, effect of control was also run by placing discs of filter paper moisten thoroughly in the solution of controlled compound i.e. Cefotaxime sodium and fluconazole were used for antibacterial, and

antifungal activity, respectively in dimethylformamide. The inhibitory effect of the sample was noted against each organism. The measured zone of inhibition was compared with those caused by controlled compound under identical conditions. All the tests were conducted in three replicates.

All the compounds and complexes have been evaluated for their *in vitro* – growth inhibitory activity against the organism like *S. epidermides, P. aruginosa, S. aureus, E. coli* and Fungi *C. albicans*.

Table 2: Antifungal activity of ρ-dimethylaminobenzylidine rhodanine and their copper, iron, zinc complexes

Antifungal study with *C. albicance*						
Abb.	**Concentration of compounds/Complexes in µg/ml**					
	12.5	**25**	**50**	**100**	**200**	**400**
5P DARH	+	+	+	+	+	−
5P DARH + Cu	+	+	+	+	+	+
5P DARH + Fe	+	+	+	+	+	−
5P DARH + Zn	+	+	+	+	+	+

(+) : Growth) i.e No inhibition, (−) : 7-8 mm inhibition, (−−) : 8-10 mm inhibition, (−−−) : 10-12 mm inhibition; 5P DARH = Ligand

RESULTS AND DISCUSSION

An overall representation of antibacterial and antifungal behavior reveals that the synthesized compound and complexes exhibit effect over the control drug i.e. Cefotaxime sodium and fluconazole for antibacterial and antifungal activity, respectively. The synthesized compound and complexes were purified before screening. Compound and their metal complexes are less active upto 200 µg concentration and as a general rule, inhibition increases with increasing concentration of compound or complexes. It shows activity upto 400 µg concentration while zinc complex have no activity.

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