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Effect of Complexation on Antibacterial Activity of Some Cyanoacetyl Hydrazones Metal Complexes

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Some divalent metal complexes of cyanoacetyl acetic acid hydrazide (CAAH) cyanoacetyl benzalidene hydrazone (CABH) and cyanoacetyl 4-hydroxy 3-methoxy benzalidene hydrazones have been synthesized and effect of complexation on antibacterial activity have been studied. The modification in antibacterial behaviour of the ligands on complexation has revealed that some metal complexes are more potent than their corresponding ligand molecules and complexation enhances the antibacterial nature of cyanoacetyl hydrazones.

Key Words: Cyanoacetyl hydrazones, Cu(II) and Hg(II) complexes, Antibacterial activity.

INTRODUCTION

The cyano acetyl hydrazones are bidented ligands and have vast applications in chemistry and medicine[1]. The hydrazones have shown ability to form large number of metal complexes with most of the transitional metal ions[1]. The present communication is aimed to synthesis Cu(II) and Hg(II) complexes of cyanoacetyl hydrazones to determine their composition and metal ligand rato and to study the effect of complexation on antibacterial activity of the ligand molecules.

EXPERIMENTAL

All the reagents and chemicals used were of AR grade. The conductivity bridge (Elico-CM-82) was used to determine metal ligand ratios and Parkin-Elmar model 237IR spectrometer was used to get IR spectra.

Synthesis of ligand: The cyano acetyl hydrazide was prepared[2] and condensed in equimoler proportions with benzaldehyde and 4-hydroxy 3-methoxy benzaldehyde dissolved in minimum quantity of alcohol. On keeping the well stirred solutions for 4-6 h fine crystalline solid separated. They were filtered and recystallized from ethanol and dried in vaccum air over $CaCl_2$. They purity of the compounds were confirmed by elemental analysis:

S. no.	Ligand (colour)	m.f. (m.p.)	Nitrogen Calculated (found) %
1	Cyanoacetyl hydrazide (Microcrystalline needle)	$C_3H_5N_3O$ (110 ºC)	42.42 (42.40)
2	Cyanoacetyl benzalidene hydrazone (Colourless needles)	$C_{10}H_9N_3O$ (178 ºC)	22.46 (22.45)
3	Cyanoacetyl 4-hydroxy 3-methoxy benzaldehyde hydrazone (Light yellow plates)	$C_{11}H_{11}N_3O_3$ (203 ºC)	18.03 (18.04)

Synthesis of metal complexes: The solid metal complexes of the ligands were isolated by mixing aqueous ammonical solution of $CuCl_2$/$HgCl_2$ to hot alcoholic solutions of the ligands with stirrings and refluxing the mixture solutions for 1 h in a round bottom flask fitted with an air condenser[3]. The solid thus separated was filtered washed, purified and dried.

The metal ligand ratio was determined conductometrically employing Job's method[4] of continuous variation and composition of the complexes was established by elemental analysis and metal estimations of the metal complexes.

Frisk[5] has demonstrated that antibacterial activity *in vitro* and *in vivo* correspond quite well. Measurement of antibacterial activity *in vitro* consists of cultivating this bacteria in fluid medium to which drug has been added. Slide cell[6] agar cup plates[7] and agar streak method[8] have been commonly used. The microorganism against which the antimicrobial activity was determined was *Escherichia coli* and *Staphylococii* which were isolated from urine and throat swab from sore throat, respectively.

Isolation of pure culture from urine: Catheterized samples of urine in cases of females and catheterized or med-stream specimens of urine in males were collected aseptically.

The urine was centrifuged and supernatant pipetted off. From the residue at the bottom of the test tube a loopful was taken and inoculated on MacConkeys neutral red bile -salt-lactose- agar medium. A smear from the residue was them made strained with Gram's Method and examined for the presence of microorganism and cells.

After 24 h pink colonies on MacConkeys media were observed. A smear made from one of the colonies was examined for the presence of growth of pure growth of *Escherichia coli*. The remaining part of the colony was subcultured in peptone water.

Isolation of pure culture from throat swab: Koch utilized solid gelatins media for this purpose and a loopful of the material was rubbed in one segments of the streak plate. Stroke cultures were made so that well separated colonies were developed on the plate.

Preparation of drug solutions: The ligands and their metal complexes were dissolved in propylene glycol and the concentration of the solutions were adjusted to 25 mg/100 mL.

Drug sensitivity test: Lund's dise method[9] modified by Fairbrother and Martyn[10] was used 2.5 % nutrient agar plates (3" diameter) 6-8 mm thick were inoculated with 24 h broth culture. After allowing it to stand at 37 ºC for 15 min the plates were divided into radial zones on the centre of each zone was placed a filter paper dise of 6.2 mm diameter.

One drop of each sample solution was placed on the respective dise with help of no. 1 gauze needle filted to a syringe. The concentration of the sample was adjusted to 25 µg/disc. After 24 h incubation at 37 ºC the diameter of the inhibition zone was measured in millimeters. During experiment all precautions were taken to keep the conditions uniform regarding pH thickness of the medium time of incubation inoculum and quantity of the drug used.

RESULTS AND DISCUSSION

The antibacterial activity of cyano acetyl benzalidene hydrozone and cyanoacetyl 4-hydroxy 3-methoxy benzalidene hydrozone and their copper and mercury metal complexes have been studied on *Escherichia coli, Staphylococii albus*, *Staphylococii aurius* and *Staphylococii citrius* and the results are given in Table-1.

TABLE-1
ANTIBACTERIAL ACTIVITY OF CYANOACETYL BENZALIDENE HYDRAZONE AND ITS Cu(II) AND Hg(II) COMPLEXES

Escherichia coli	Cu-CABH Sensitive	Hg-CABH Resistant, CABH Resistant
Staphylococii albus	Cu-CABH Sensitive	Hg-CABH Resistant, CABH Resistant
Staphylococii aurius		CABH Resistant, Cu-CABH Resistant, Hg-CABH Resistant
Staphylococii citrius	CABH Sensitive	Cu-CABH Resistant, Hg-CABH Resistant

The antibacterial activity study with *Escherichia coli, Staphylococii albus, Staphylococii aureus* and *Staphylococii citrius* reveal that Cu-CABH complexes are sensitive and its Hg-CABH complex and the ligand CABH are resistant. This indicates that complexation enhance the antibacterial activity of the CABH ligand.

The antibacterial activity study with *Staphylococii albus, Staphylococii aureus* and *Staphylococii citrius* reveals that Cu-CABH complex is sensitive but CABH ligand and Hg-CABH are resistant. The study with *Staphylococii aurius* shows that CABH ligand and its Cu-CABH and Hg-CABH complexes are resistant. The CHBH ligand shows potent nature only with *Staphylococii citrius* strain.

The antibacterial activity studies of cyanoacetyl 4-hydroxy-3-methoxy benzalidene hydrazone and its Cu(II) and Hg(II) complexes revealed that although its Hg(II) complex and the ligand itself are resistant to *Staphylococii albus, Staphylococii aureus* and *Staphylococii citrius* strains but its Cu(II) and Hg(II) complexes show marked potent nature with *Escherichia coli* and *Staphylococii albus* and the ligand itself also is sensitive to *Escherichia coli* strain (Table-2). Therefore the present studies of antibacterial activity establish beyond doubt that complexation with metal ions enhances antibacterial nature of the ligand and make then potent.

TABLE-2
ANTIBACTERIAL ACTIVITY OF 4-HYDROXY 3-METHOXY BENZALIDENE HYDRAZONE AND ITS COPPER(II) AND MERCURY(II) COMPLEXES

Escherichia coli	CA 4-Hydroxy-3-methoxy BH sensitive Cu-CA 4-Hydroxy-3-methoxy BH sensitive	Hg-CA_4h-$_3$mBH Resistant
Staphylococii albus	Cu-CA 4-Hydroxy-3-methoxy BH highly Sensitive, Hg-CA4-hydroxy-3-methoxy BH highly sensitive	CA_4h-$_3$mBH Resistant
Staphylococii aureus		CA_4h-$_3$mBH Resistant
Staphylococii citrius		CA_4h-$_3$mBH Resistant

REFERENCES

1. Y.P. Kitaev and B.I. Buzykin, *Russ. Chem. Rev.*, **41**, 495 (1972).
2. D. Chakravosty, A. Bose and S. Bose, *J. Pharm. Sci*., **535**, 1036 (1964).
3. S.K. Mukherjee, J. Naha, S. Raymahasaya, S.L. Lashkar and P.R. Gupta, *J. Pharm. Pharmacol*., **7**, 35 (1955).
4. P. Job, *Ann. Chim. (Paris)*, **9**, 113 (1928).
5. A.R. Frisk, *Acta Med. Scandinav.*, **142S**, 1 (1943).
6. R. Brand, *South M. J*., **34**, 941 (1941).
7. D.S. Damrosch, *J. A.M.A*., **136**, 124 (1946).
8. W.W. Spink, *Arch. Int. Med*., **77**, 260 (1946).
9. E. Moerch-Lund, *Acta Path. Microbiol. Scand.*, **26**, 821 (1946).
10. R.W. Fairbrother and G. Martyn, *J. Clin. Path*., **4**, 374 (1951).

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