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## ANTIMICROBIAL ACTIVITY OF THE LIGANDS, METAL COMPLEXES AND THEIR ADDUCTS WITH BASES AGAINST PHYTOPATHOGENIC FUNGI

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### Abstract

The ligands, metal complexes and their adducts with bases namely, pyridine, 2-methylpyridine and 4-methyl-pyridine were evaluated for their antimicrobial activity against three phytopathogenic fungi viz., *Alternaria alternata*, *Fusarium lycopersici* and *Rhizoctonia bataticola* and two bacteria viz., *Escherichia coli* and *Xanthomonas compestris* Pv. *compestris*. Stock solutions were prepared by dissolving the compounds in dry DMSO and two fold serial dilution technique (Donald and Williams, 1955) was employed to evaluate the antimicrobial activity. The results obtained were expressed in terms of minimum inhibitory concentration (MIC) values.

The concentration at which complete growth inhibition occurred, was taken as the minimum inhibitory concentration (MIC) value expressed in perimeters.

The results were plotted (concentration vs. compounds) for comparing the activity pattern of different ligands, metal complexes and their adducts and are given in figures

### Introduction

Macrocyclic compounds derived from biguanide viz., cyclo(1,2)-dibiguanidiny] bis[ 2-hydroxy-w+(benzoyl/4-chlore benzoyl /3-nit robenzoyl/3 ,5-dinitrobenzoyl )acetophenone] (Ly-Lyy) exhibited promising activity against all the test organisms. The compounds could control the growth of microorganism at concentrations ranging from  $>100 \text{ ug ml}^{-1}$  to  $12.5 \text{ pe ml}^{-1}$ .

Among the fungi, *Fusarium lycopersici* was the most affected organism as evidenced by the lowest MIC value of  $12.5 \text{ ug ml}^{-1}$  in this case. 'The ligands were found to be more active against the fungi than the bacteria since the MIC values for the latter varied from  $>100$  to  $100 \text{ ug ml}^{-1}$ .

Cyclo(1,2)-dibiguanidinyl bis[2-hydroxy-w (benzoyl) acetophenone] (Ly) was most active against *Rhizoctonia bataticola* with MIC value of  $25 \text{ ug ml}^{-1}$ , The MIC. values against *Alternaria alternata* and *Fusarium lycopersici* were,  $50$  and  $100 \text{ ug ml}^{-1}$ , respectively, whereas the same against bacteria *Escherichia coli* and *Xanthomonas compestris* Pv. *compestris* were  $>100 \text{ ug ml}^{-1}$  each.

Cyclo (1,2)-dibiguanid-inyl bis[ 2-hydroxy-w-(4-chlorobenzoyl) acetophenone] (Ly y) was most active against *Fusarium lycopersici* having minimum inhibitory concentration value of  $12.5 \text{ ug ml}^{-1}$  moderately active against *Rhizoctonia bataticola* with MIC values of  $25 \text{ ug ml}^{-1}$  and least active against *Alternaria alternate* (MIC  $50 \text{ ug ml}^{-1}$ ), The compound exhibited MIC value of  $100 \text{ ug ml}^{-1}$  against *Escherichia coli* and *Xanthomonas compestris* Py. *compestris*.

Cyclo(1,2)-dibiguanidinyl bis [ 2-hydroxy-wW-3-nitrobenzoyl) acetophenone] (Lyyy) and cyclo (1,2)-dibiguanidinyl — bisl 2-hydroxy-wW=(3,5-dinitrobenzoylL )

acetophenone) (Lyy) exhibited MIC value of  $25 \text{ ug ml}^{-1}$  against *Alternaria alternata* and *Rhizoctonia bataticola* while the same against *Fusarium lycopersici* was  $50$  and  $25 \text{ ug ml}^{-1}$  in case of  $L_{III}$  and  $L_{IV}$  respectively.

The compounds  $L_{III}$  and  $L_{IV}$  were found to be active at  $100 \text{ ug ml}^{-1}$  against *Escherichia coli* and *Xanthomonas compestris* Py. *compestris*.

The side chain length and the presence of various substituent's on the main nucleus and on the side chain(s) have pronounced impact on the nature and the magnitude of the biological activities (Mitchinson, 1983). Consequently substituting various nuclei of biological importance has emerged as one of the important aspects in the development of new compounds with potential antimicrobial activity.

In the present investigation the macrocyclic ligands were obtained by the condensation of biguanide with diketones substituted at phenyl ring.

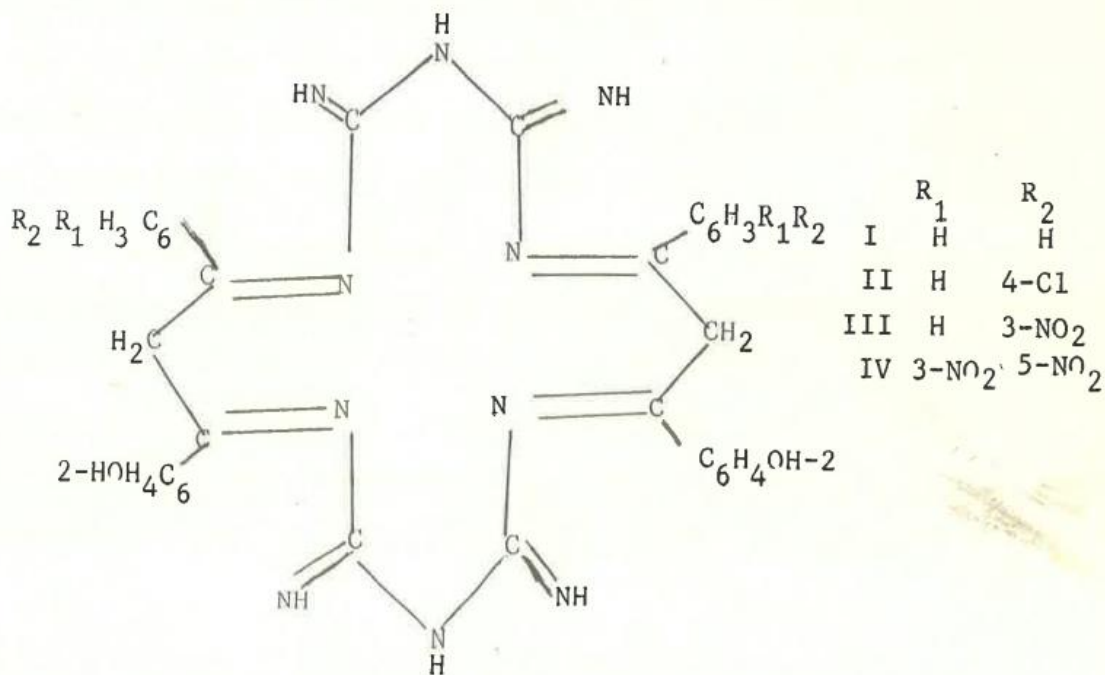


Fig. a

As an outcome, the ligands proved to be quite Promising antimicrobials. However, a comparative study on the effect of substitutions at the phenyl ring did not reveal any significant alteration in the biological activity of the compounds L<sub>I</sub>-L<sub>IV</sub>. No definite structure-activity relationship could, therefore, be established for these compounds.

In addition to the structural modifications, coordination of the bioactive ligands with suitable metal ions significantly alters their activity' pattern (Theorell et al, 1969, Lumme et al., 1984).

### ANTIMICROBIAL ACTIVITY OF THE LIGANDS, METAL COMPLEXES AND THEIR ADDUCTS WITH BASES AGAINST PHYTOPATHOGENIC FUNGI

The present investigation was aimed at preparing and screening the antimicrobial activity of the ligands, their complexes with oxovanadium(IV), manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II) and their respective base adducts.

The transition metal complexes of L<sub>I</sub>-L<sub>IV</sub> exhibited MIC values ranging from >100 to 25 ug ml<sup>-1</sup> against *Alternaria alternata* as compared to the free ligands for which the MIG values ranged from 50 to 25 ug ml<sup>-1</sup>.

The activity of ligand L<sub>I</sub> against *Alternaria* with nickel(II) and copper(II) but no significant alteration was observed on its complexation with oxovanadium(IV), manganese(II), cobalt(II) and zinc(II).

No enhancement in activity of ligand L<sub>III</sub> and L<sub>IV</sub> was observed on coordination with transition metal ions. Adducts of the transition metal complexes of ligands showed MIC values in the PES of >100 to 25 ug ml<sup>-1</sup>.

The pyridine adducts of some of the complexes of cobalt (II), Nickel(II) and zinc(II) exhibited increased antifungal activity as compared to the free ligands whereas there was no enhancement in the activity of the adducts of oxovanadium(IV), manganese(II) and copper(II) complexes.

The 2-methylpyridine and 4-methylpyridine adducts of cobalt(II) and zinc(II) complexes with cyclo(1,2)-dibiguanidinyl bis[ 2-hydroxy-W- (benzoyl) acetophenone exhibited higher activity than the parent ligand.

The Transition metal complexes of ligand L<sub>I</sub>-L<sub>IV</sub> exhibited MIC values varying from >100 to 12.5 mg against *Fusarium lycopersici*. The activity of ligands L<sub>I</sub> and L<sub>III</sub> was enhanced on coordination with oxovanadium(IV) , manganese(II) and copper(II).

There was no increase in the activity pattern of L<sub>II</sub> and L<sub>IV</sub> on coordination with metal ions. Base adducts of oxovanadium(IV), manganese(II);cobalt(II), nickel(II), copper(II) and zinc(II) complexes of ligands L<sub>I</sub>-L<sub>IV</sub>

exhibited minimum inhibitory concentration values in the range >100 to 12.5 ug ml<sup>-1</sup> against *Fusarium lycopersici*.

There was a significant increase in the activity of pyridine and 2-methylpyridine adducts of nickel(II) complexes of cyclo(1,2)-dibiguanidinylbis[2-hydroxy-w-(benzoyl) acetophenone and cyclo(1,2) dibiguanidinyl bis[ 2-hydroxy-w-(3-nitrobenzoyl) acetophenone(L<sub>III</sub>) as compared to L<sub>I</sub> and L<sub>III</sub>.

The complexes of cyclo(1,2)-dibiguanidinyl bis[2-hydroxy -w- benzoyl /4~chlorobenzoyl/3-nitrobenzoyl/3,5-dinitrobenzoyl) acetophenone] with oxovanadium(IV), manganese(II), cobalt(II) nickel(II), copper(II) and zinc(II) gave minimum inhibitory

concentration values in range  $> 100$  to  $12.5 \text{ ug ml}^{-1}$  against *Rhizoctonia bataticola*. The activity of  $L_I$  and  $L_{II}$  was significantly enhanced on coordination with manganese(II).

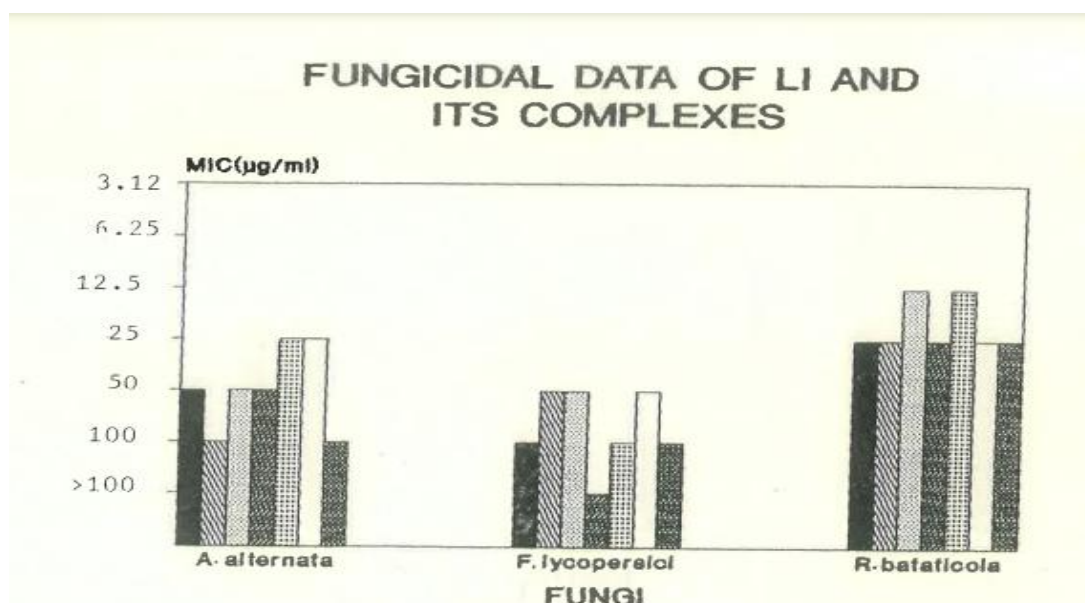
The 2-methyl pyridine and 4-methylpyridine adducts of manganese(II), cobalt(II), nickel(II) and copper(II) complexes showed enhanced activity as compared to parent ligand  $L_I$ . The pyridine adducts of the complexes of oxovanadium(IV) and copper(II) with ligand L, also exhibited improved activity. Antifungal activity of the base adducts of manganese(II) and copper (II) complexes with cyclo(1,2)-dibiguanidiny] bis{2-hydroxy-w- (4-chlorobenzoyl) acetophenone]  $L_{IV}$  was higher than that of the parent ligand.

All the metal complexes of ligands  $L_I$ - $L_{IV}$  and their respective base adducts were active at  $100$  to  $50 \text{ ug ml}^{-1}$  against *Escherichia coli* and at  $100 \text{ ug ml}^{-1}$  against *Xanthomonas compestris* P.v. *compestris* whereas the values for the parent ligands ranged from  $>100$  to  $100 \text{ ug ml}^{-1}$  against both the bacteria.

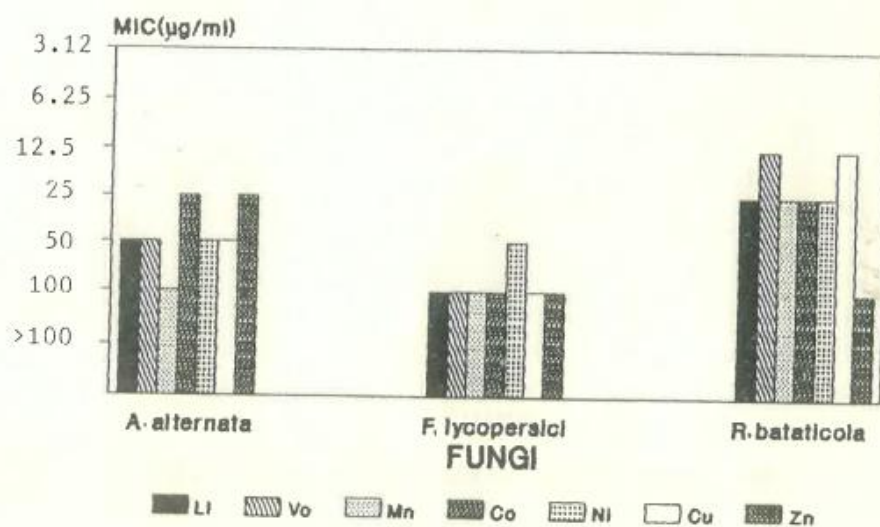
*Escherichia coli* was more affected organism by the coordination compounds and adducts as compared to *Xanthomonas compestris* Py. *compestris*.

All the ligands, metal complexes and their adducts were less effective fungicides and bactericides than Bavistin [2-(methoxy carbamoyl) benzimidazole] (MIC value  $< 1.5 \text{ ug ml}^{-1}$ ) and streptopenicillin (MIC value  $< 1.5 \text{ ug ml}^{-1}$ ) which were used as reference fungicide and bactericide, respectively.

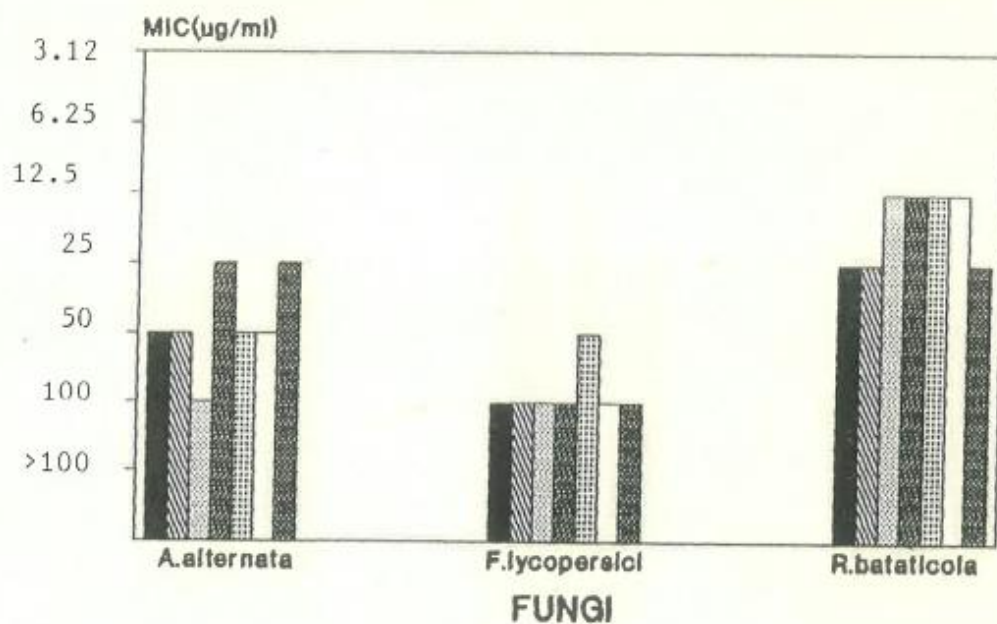
## RESULTS



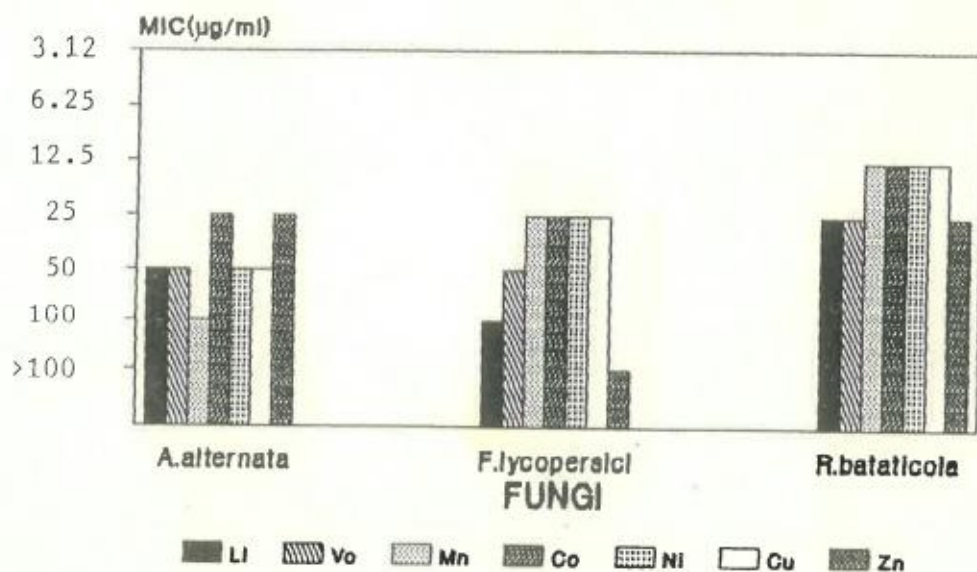
## FUNGICIDAL DATA OF LI AND PYRIDINE ADDUCTS OF COMPLEXES



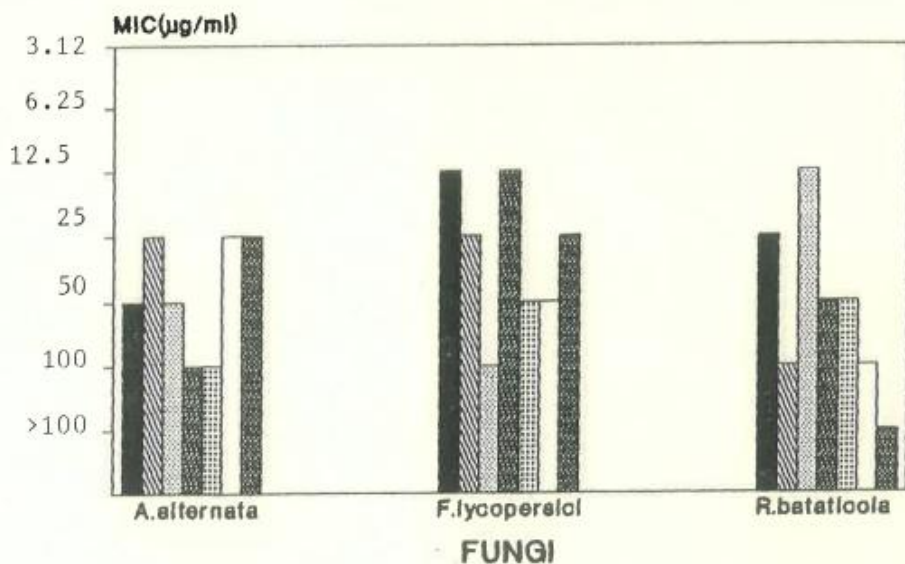
## FUNGICIDAL DATA OF LI AND 2-METHYL PYRIDINE ADDUCTS OF COMPLEXES



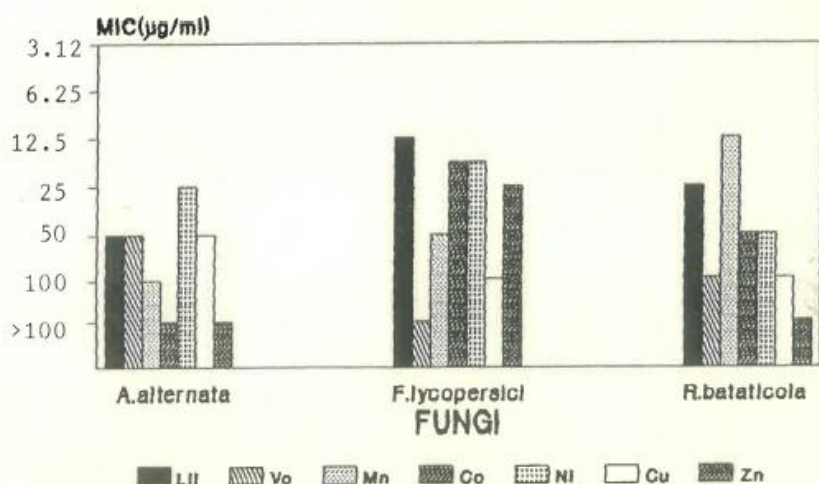
## FUNGICIDAL DATA OF LI AND 4-METHYL PYRIDINE ADDUCTS OF COMPLEXES



## FUNGICIDAL DATA OF LII AND ITS COMPLEXES



## FUNGICIDAL DATA OF LII AND PYRIDINE ADDUCTS OF COMPLEXES



### CONCLUSION

Higher activity exhibited by some of the metal complexes as compared to the free ligands may be due to the effect of metal ions on the normal cell process. The polarity of the metal ion is considerably reduced on chelation because of partial sharing of its positive charge with the donor atoms of the ligand and  $\pi$ -electron delocalization over the whole chelate ring. The chelation increases the lipophilic character of the metal complexes which may lead to the breakdown of permeability barrier of the cell wall resulting in interference with the normal cell process.

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