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ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF MACROCYCLIC SCHIFF'S BASES AND THEIR METAL CHELATES WITH COBALT (II)

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ABSTRACT

The synthesized macrocyclic Schiff's bases and their metal chelates with cobalt (II) were screened for antibacterial and antifungal activity. The biological activities of metal chelates revealed enhanced activity as compared to corresponding ligands.

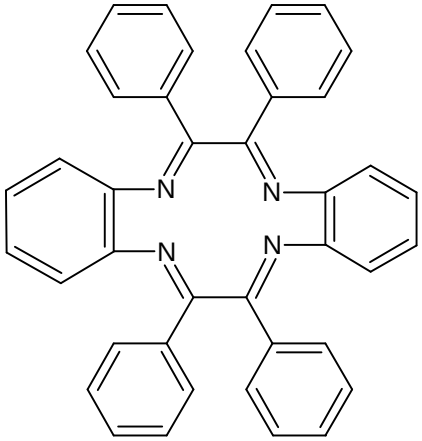
KEYWORDS: Macrocyclic Schiff's bases, metal chelates, antibacterial, antifungal activity.

INTRODUCTION

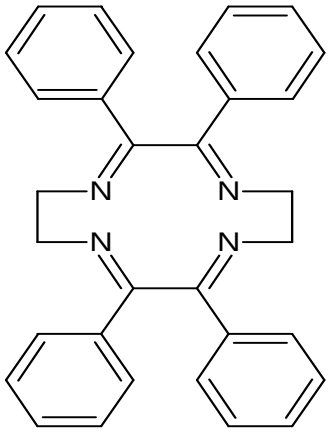
The design and synthesis of well-arranged metal-containing macrocycles is an interesting field of macrocyclic synthetic chemistry.[1,2] In addition to their particular structural features, supramolecular species formed by self-assembly of transition metals introduce many special functional and biological properties. The macrocyclic Schiff base ligands have received vital attention not only because of their pharmacological properties like antifungal, anticancer, antiviral, antibacterial character[3,4] and their mixed soft-hard donor character, versatile coordination behavior[5,6], but also for their capacity for chemical recognition of anions and metals of biochemical, medical and environmental importance.[7,8] In case of N and C based functionalized macrocyclic ligands, the mode of metal incorporation is very much similar to that of metalloproteins in which the requisite metal is bound in a macrocyclic cavity or cleft produced by the conformational arrangement of the protein. The attachment of metal ions to proteins such as monoclonal antibodies can create new tools for use in biology and medicine.[9]

In light of above facts the present paper has been devoted to the studies of biological activities of metal chelates of cobalt (II) with macrocyclic Schiff's bases and compare them with the biological activities of pure ligands. Macrocyclic Schiff's bases chosen for this purpose are as follows.

a. Macrocyclic Schiff's base derived from benzil and o-phenylenediamine



b. Macrocyclic Schiff's base derived from benzil and ethylenediamine



MATERIAL AND METHODS

Culture and Maintenance of microorganisms

Pure cultures of all experimental bacteria and fungi were obtained from the Microbial Type Culture Collection and Gene Bank (MTCC), Institute of Microbial Technology (IMTECH), Chandigarh. The pure bacterial cultures were maintained on nutrient agar medium and fungal culture on potato dextrose agar (PDA) medium. Each bacterial and fungal culture was further maintained by subculturing regularly on the same medium and stored at $4^{o}C$ before use in experiments.

For the present study following pure bacterial and fungal cultures were taken.

Bacterial culture

S.No.	Name	Type	MTCC No.
1	Pseudomonas aeruginosa	Gram negative	424
2	Klebsiella pneumonia	Gram negative	39
3	Escherichia coli	Gram negative	40

Fungal culture

S.No.	Name	MTCC No.
1	Aspergillus flavus	3306
2	Aspergillus tubingensis	2208

Microbiological screening

Antimicrobial activities of synthesized Schiff's bases and their metal complexes were evaluated by the agar well diffusion method (Murray *et al*.)[10] modified by (Olurinola).[11]

Agar-well diffusion method: 5 ml aliquot of nutrient broth was inoculated with the test organism and incubated at 37^0C for 24 hours. Sterile nutrient agar plates were also prepared and holes of 5 mm diameter were cut using a sterile cork borer ensuring proper distribution. The test organisms after 24 hours of incubation were spread onto separate agar plates. The chemical compounds were dissolved in DMSO at a particular concentration and poured into appropriately labeled holes using a pipette in aseptic conditions. A hole containing DMSO served as a control. The plates were left at room temperature for two hours to allow the diffusion of the sample followed by incubation at 37^0C for 24 hours in inverted position. The antimicrobial activity was determined by measuring the diameter of the zone (mm) showing complete inhibition with respect to control (DMSO).

RESULTS

In the present investigation, the inhibitory effect of synthesized Schiff's bases and their metal chelates with cobalt (II) were evaluated against both fungicidal and bacterial strains. The antimicrobial activity was determined using agar well diffusion method and summarized in Table I-IV. The activity was quantitatively assessed on the basis of zone of inhibition.

Table-I: Effect of macrocyclic Schiff's bases on bacterial growth.

Compd.	Zone of inhibition (mm)								
	100 µg/ml			500 µg/ml			1000 µg/ml		
	P.aeruginosa (424)	K.pneumoniae (39)	E.coli (40)	P.aeruginosa (424)	K.pneumoniae (39)	E.coli (40)	P.aeruginosa (424)	K.pneumoniae (39)	E.coli (40)
a	20	35	11	17	22	14	-	18	12
b	19	33	12	23	24	-	21	21	13
DMSO	-	-	-	-	-	-	-	-	-

Table-II: Effect of metal chelates on bacterial growth.

SB + Cobalt (II)	Zone of inhibition (mm)								
	100 µg/ml			500 µg/ml			1000 µg/ml		
	P.aeruginosa (424)	K.pneumoniae (39)	E.coli (40)	P.aeruginosa (424)	K.pneumoniae (39)	E.coli (40)	P.aeruginosa (424)	K.pneumoniae (39)	E.coli (40)
1	23	39	14	18	25	16	12	20	14
2	21	36	16	28	26	15	23	27	19
DMSO	-	-	-	-	-	-	-	-	-

Antifungal activity: The antifungal activity was performed by cup plate method at concentration 100 µg / ml, 500 µg / ml and 1000 µg / ml.

Table-III: Antifungal activity of macrocyclic Schiff's bases.

Compd.	Zone of inhibition (mm)					
	100 µg / ml.		500 µg / ml.		1000 µg / ml.	
	A.tubingensis (2208)	A.flavus (3306)	A.tubingensis (2208)	A.flavus (3306)	A.tubingensis (2208)	A.flavus (3306)
a	-	-	52	50	81	78
b	-	-	50	48	84	85
DMSO	-	-	-	-	-	--

Table-IV: Antifungal activity of metal chelates.

SB + Copper (II)	Zone of inhibition (mm)					
	100 µg / ml.		500 µg / ml.		1000 µg / ml.	
	A.tubingensis (2208)	A.flavus (3306)	A.tubingensis (2208)	A.flavus (3306)	A.tubingensis (2208)	A.flavus (3306)
1	17	13	57	57	83	80
2	13	11	52	52	88	89
DMSO	-	-	-	-	-	--

(-) Indicates No activity

CONCLUSION

On comparing the results of biological activity, it may be concluded that metal chelates have greater inhibiting power than the free ligands against all the microbes. Although it is difficult to make out an exact structure activity relationship between the biological activity and the structure of these complexes. These results also indicate a combination of metal and ligand environment plays a vital role in increasing a degree of inhibition.

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