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ANTIMICROBIAL STUDIES OF THE SCHIFF BASE DERIVED FROM ACETOACETANILIDE AND ANTHRANILIC ACID AND ITS COMPLEXES

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ABSTRACT

The *in vitro* antimicrobial activity of the Schiff base ligand, derived from acetoacetanilide and anthranilic acid, and its Cu (II), Ni (II), Co (II) and Zn (II) metal complexes against the microorganisms *Salmonella typhi*, *Bacillus subtilis*, *Escherchia coli*, *Pseudomonas aeruginosa*, *Rhizopus stolinifer* and *Penicillium chrysogenum* has been carried out. The zone of inhibition of the synthesized compound is compared with the standards. Most of the complexes have higher antimicrobial activity than the free ligand.

Key words : Antimicrobial effect, Schiff base, Acetoacetanilide, Anthranilic acid.

INTRODUCTION

It is well known that various organic ligands possess strong antibacterial, herbicidal, insecticidal and fungicidal properties[1]. It has also been reported that the activity of biometals is very often altered through the formation of chelates with different bioligands[2–5]. It is suggested that the compounds having antimicrobial activity may act either by killing the microbe or by inhibiting multiplicity of the microbe or blocking their active site [6–8]. In addition to this, the antimicrobial activity of the compounds also depends upon the nature of the microorganisms. The literature survey reveals that Schiff base ligand is an excellent coordinating ligand. During the past three decades, considerable attention has been paid to the chemistry of the complexes of the Schiff base containing nitrogen and other donors. This may be attributed to their stability, biological activity and potential applications in many fields such as oxidation, catalysis[9–12], electrochemistry, etc. The coordination chemistry of amino acid– Schiff base ligands is of considerable interest due to their biological importance[13–17]. Recently, Raman *et al.*[18] synthesized this new Schiff base and its metal complexes by condensing anthranilic acid with acetoacetanilide. They elucidated the structures of both; the Schiff base and its metal complexes. The literature survey reveals that no work has been done on the antimicrobial effect of this Schiff base and its complexes. Hence, in the present work, it has been attempted to know

whether the outimicrobial activity of the Schiff base ligand is enhanced by the presence of metal ion upon coordination.

EXPERIMENTAL

Synthesis of Schiff base

An ethanolic/methanolic solution (50.0 mL) of anthranilic acid (1.02 g, 5 mmol) and acetoacetanilide (2.03 g, 10 mmol) was boiled under reflux for *ca.* 5 h. The solution was reduced to one–third on a water bath and the hot solution was poured into hot water to remove any unreacted anthranilic acid. The pasty mass obtained after decantation was crystallized from ethanol (Yield: 85% m.p.: 180°C).

Metal complexes syntheses

The Schiff base (2.97 g, 10 mmol) dissolved in hot ethanol/methanol (50.0 mL) was added to a hot ethanolic/methanolic solution (25.0 mL) of the metal salts (5 mmol). The pH of the reaction mixture was adjusted to 6–7 by the addition of aqueous ammonia. The solid complexes separated were filtered, washed with ethanol and dried *in vacuo*. Yield: 52%.

Antimicrobial activity

The *in vitro* biological screening effects of the investigated compounds were tested against the bacteria *Salmonella typhi*, *Bacillus subtilis*, *Escherchia coli* and *Pseudomonas aeruginosa* by the well diffusion method, using agar nutrient as the medium and ampicillin as control. The antifungal activities of the compounds were evaluated by the well diffusion method against the fungi, namely *Rhizopus stolinifer* and *Penicillium chrysogenum* cultured on potato dextrose agar as medium and the drug amphotericin as control. The blank discs were moistened with solvent. The test solutions were prepared by dissolving the compounds in DMSO. In a typical procedure[19], a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using a micropipette and the plate was incubated at 35°C for 24 h for bacteria and 72 h for fungi. During this period, the test solution was diffused and the growth of the inoculated microorganisms was affected. The inhibition zone developed on the plate was measured.

RESULTS AND DISCUSSION

The Schiff base, formed by the condensation of anthranilic acid and acetoacetanilide, and its metal complexes have been synthesized and characterized following the procedure adopted by Raman *et al*[18]. The analytical and the spectral data correspond well with the data reported by them. Antimicrobial activity of the compounds was tested *in vitro* (100 µg/10 µL per test) against the above mentioned bacteria and fungi. The zone of inhibition against the growth of the microorganisms for all the synthesized compounds and the control (ampicillin) is given in Table

1 and for the fungi and its standard (amphotericin) is given in Table–2. From the tables, it is clear that the zone of inhibition area for the copper and cobalt complexes is much larger than the free ligand and standards, ampicillin and amphotericin but the zinc and nickel complexes have no activity, may be due to the their acidic nature. Such increased activity of the metal chelates can be explained on the basis of chelation theory[20]. On chelation, the polarity of the metal ion is reduced to a greater extent due to the overlap of the ligand orbital. Further, it reduces the delocalisation of π–electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity leads to break–down of the permeability of barrier of the cell and thus, retards the normal cell processes.

Table 1. Antibacterial activity of the synthesized compounds (zone of inhibition in mm)

Compound	*E. coli*	S. typhi	*B. subtilis*	*P. aerugenosa*
Ampicillin	15	18	10	8
Schiff base (L)*	9	11	7	–
CuL	25	21	19	12
NiL	–	–	–	–
CoL	20	18	21	6
ZnL	–	–	–	–

***L=Schiff base formed by the condensation of anthranilic acid and acetoacetanilide**

Table 2. Antifungal activity of the synthesized compounds (zone of inhibition in mm)

Compound	*R. stolinifer*	*P. chrysogenum*
Amphotericin	5	9
Schiff base (L)*	8	6
CuL	10	11
NiL	–	–
CoL	7	9
ZnL	–	–

***L=Schiff base formed by the condensation of anthranilic acid and acetoacetanilide**

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