

Antimicrobial activity of Schiff Base of 2-Amino 5-Nitrothiazole and its Copper complex

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ABSTRACT

In an attempt to find out a new class of antimicrobial agents new schiff base ligand of 2-amino 5-nitro thiazole and its copper complex were prepared. The Microwave assisted synthesis was carried out by condensation of 2-amino 5-nitro thiazole and substituted salicyldehyde. The newly synthesized schiff base ligand and its copper complex were tested against representatives of gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*) and gram-negative bacteria (*E. coli*, *Pseudomonas putida*) and fungi (*Candida albicans*, *Aspergillus niger*) by disc diffusion method.

Keywords: Schiff base, Antimicrobial activity, Disc diffusion, Microwave assisted, Biological activity

INTRODUCTION

Microwave heating technology is green chemical process, the application of microwave-assisted is useful technology in drug synthesis because it is simple, sensitive, reducing the hazard, often possible to reduce reaction times to a few minutes under solvent free or lower solvent and increase the yields and easier work up as compared to conventional methods (Ahmed Hassen et al.,2016). Those compounds which containing imine group ($-HC=N-$) are known as Schiff bases, which were first reported by Hugo Schiff in 1864 and formed by condensation of a primary amine with an active carbonyl compound, and generally take place under acid, base catalysis or with heat (Gadada Naganagowda.,2014). Heterocyclic ring -containing Schiff bases can show naturally increased biological activities.

The literature survey reveals that the thiazole ring is present in various natural compounds which show useful biological activities. It occurs for example, in thiamine, a coenzyme is required for the oxidative decarboxylation of α -keto acids. A tetra hydrothiazole also appears in the skeleton of penicillin, which is one of the first and still most important broad-spectrum antibiotics.

Thiazole, thiazol amines are valuable medicines (Dash B,1981; Metzger J V.,1979; Troutman H D.,

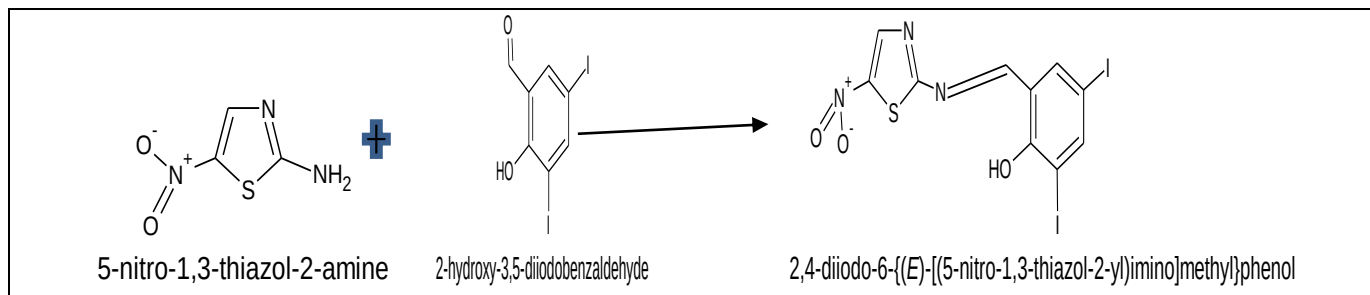
1948;). It is obvious that compounds with the thiazole ring have a potential biological activity. The thiazole derivatives gained more importance and interest due to their anticancer (Ahmed R. Ali.,2014; Funda Tay., 2017; Sobhi M. Gomha,2017;), anticonvulsant (Faiz Arshad,2014; Nour E. A. Abdel-Sattar,2017), antitumor (S. Muralikrishna,2013; Wen-Xi Cai, 2016;) antiviral (Nuray Ulusoy Guzeldemirci, 2017;)and fungicidal activities (Khalid Mohammed Khan, 2012;). They are also used as, anti-inflammatory (Firas A. Hassan,2012;) and anthelmintic agents (Amit S. Lunkad.,2013; Balaji P. N.,2014;) agents. Metal ions play a vital role in a vast number of different biological processes through co-enzymatic systems. The interaction of these ions with biologically active ligands, for instance in drugs, is a subject of great interest. Some biologically energetic compounds act via chelation, but for most of them little is known about how metal coordination influences their activity.

We report here the Microwave assisted synthesis and antimicrobial evaluation of schiff base ligand 2,4-diiodo-6- $\{ (E)-[(5\text{-nitro-1,3-thiazol-2-yl}) \text{ imino}] \text{ methyl} \}$ phenol and its copper complex incorporating both thiazole moiety and substituted salicyldehyde through imine linkages at 2-position of thiazole.

MATERIAL AND METHODS**Microwave assisted Synthesis of schiff base ligand**

2-amino 5-nitro thiazole (0.01 mol) and 3,5-diiodosalicylaldehyde (0.01 mol), and were mixed thoroughly in ethanol and small amount of glacial acetic acid was added and were taken in Erlen Meyer flask capped with a funnel placed in a microwave

oven and irradiated an interval of 1 min at 450W for about 5-8 min. After completion the reaction, the reaction mixture was allowed to attain room temperature and solid separated was filtered. The resulting product was then recrystallized with ethanol, finally dried under reduced pressure over anhydrous CaCl_2 in a desiccator. Yield: 70-90%.



Scheme-1, Microwave assisted synthesis of schiff base

EXPERIMENTAL**ANTIMICROBIAL ACTIVITY**

The newly synthesized schiff base ligand 2,4-diiodo-6-((E)-[(5-nitro-1,3-thiazol-2-yl) imino] methyl} phenol and its copper complex were evaluated for in vitro bacterial activity against as example of Gram-positive bacteria (*staphylococcus aureus* and *Bacillus Subtilis*) and gram negative bacteria (*E. coli*, *Pseudomonas putida*) by disc diffusion method was for the determination of the preliminary antibacterial activity.

The bacterial cultures were incubated at $30 \pm 0.1^\circ\text{C}$ for 24 hours by inoculation into nutrient agar. The compounds were dissolved in test solution (DMSO) and the disc of Whatman filter paper No. 41 having the diameter 4mm were prepared and soaked in it. These soaked discs were placed on nutrient agar plates inoculated with bacteria. These plates were incubated for 36 hrs at 30°C . The inhibition zone was observed after 36 hr.

Anti-fungal screening: The fungal strains were directly mixed with the PDA medium (potato dextrose agar) and dispersed into the petri plates. Filter paper discs of 4 mm diameter were prepared prior to the experiment. These discs were soaked in DMSO in which the schiff base and its copper complex were dissolved and DMSO was used as a control. The filter paper discs were placed on

nutrient medium mixed with fungal strains. These Petri dishes were incubated at 35°C for 48 hrs. The growth of the fungus was measured by recording the diameter of fungal mycelia.

The result was recorded for schiff base and its copper complex as the average diameter of inhibition zones (IZ) of bacterial growth around the discs in mm. The antibacterial activity of schiff base and their copper complex in DMSO against of Gram-positive bacteria (*staphylococcus aureus* and *Bacillus subtilis*) and gram negative bacteria (*E. coli*, *Pseudomonas putida*) is shown in Table-1 and fungal activity results shown in Table-2.

RESULTS AND DISCUSSION

Antibacterial activity results, Table 1 showed that free Schiff base ligand showed no activity against bacterial strains. The schiff base Cu(II) complex exhibited moderate activity against *S. aureus*, and *E. coli* and had a higher effect against *Bacillus subtilis* but no activity against *Pseudomonas putida* microorganism. The results of antifungal activities of synthesized complex are summarized in table 2. The in vitro antifungal activity of metal complex showed very good inhibition than the schiff's base ligand against fungal strains under investigation.

Antibacterial and antifungal activities of the schiff base ligand and its copper complex were compared

with those of the standard drugs ampicillin and fluconazole. The discrepancy in the activity of copper complex against different microorganisms depends on the permeability of the cell or differences in the ribosomes in the microbial cells. (S. K. Sengupta, 1998;) The lipid membrane surrounding the cell of microorganism favours the passage of any lipid soluble materials and it is known that liposolubility is an important factor controlling antimicrobial activity (J. Parekh, 2005; Y. Vaghasia, 2004;). It was evident from the data that in vitro significantly increased on

coordination. Moreover, coordination reduces the polarity (B.C.J. Bayer, 1962; R. Pal, 2014;) of the metal ion mainly because of the partial sharing of its positive charge with the donor groups (A.B.P. Lever, 1984) within the chelate ring system formed. This process, in turn, leads to increase in the lipophilic character of metal chelate so as to make it more permeable through the lipid layer of microorganism (Chohan ZH, U.M. Hassan, 2002;) thus destroying them more aggressively.

Table -1: Antibacterial Activity of the Schiff's base Ligand and its complex

S.No	Compound code	Zone of Inhibition (diameter in mm)			
		<i>E.coli</i>	<i>S. Aureus</i>	<i>Pseudomonas putida</i>	<i>B. Subtilis</i>
1	ATDI-S	-	-	-	-
2	ATDI-C	-	15	-	26.5
3	Positive Control	40	24	34	46

Table-2: Antifungal activity of schiff base ligand and its copper complex

S.NO	Compound Code	Zone of Inhibition (diameter in mm)	
		<i>Candida albicans</i>	<i>Aspergillus niger</i>
1	ATDI-S	11	-
2	ATDI-C	20	19
3	Positive Control	24	25

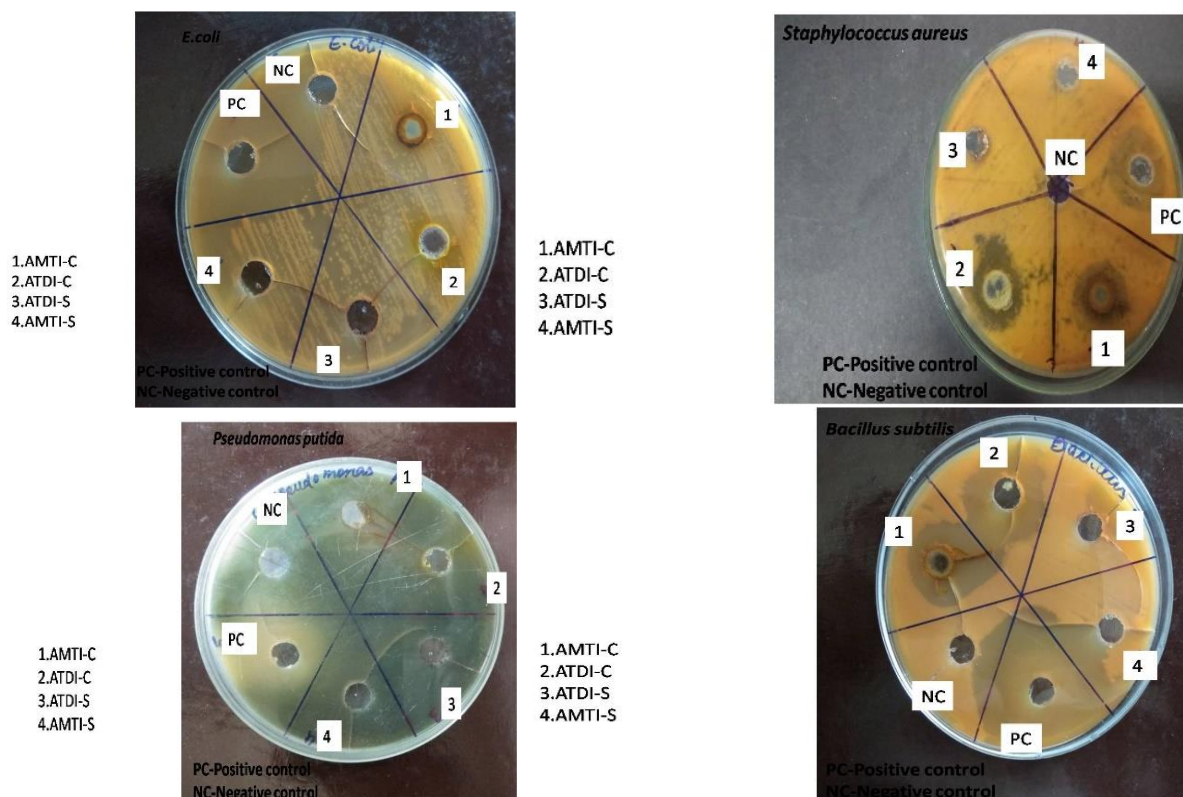


Fig-1 Antibacterial activity of schiff base and its copper complex.

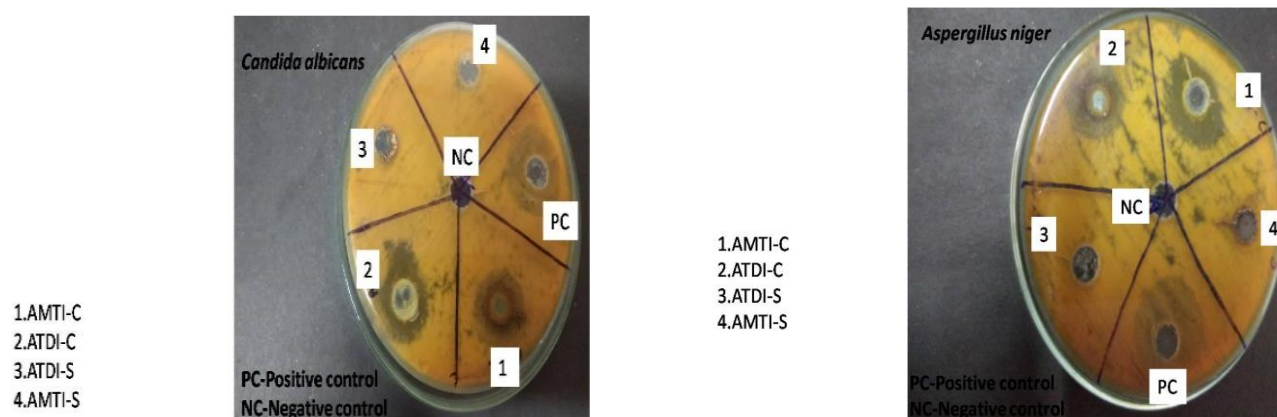


Fig-2 Antifungal activity of schiff base ligand and copper complex

CONCLUSION

In present study we reported a nonconventional microwave assisted synthesis of schiff base ligand 2,4-diiodo-6- $\{(E)-[(5\text{-nitro-1,3-thiazol-2-yl})\text{ imino}] \text{ methyl}\}$ and their copper complex. In vitro antimicrobial activity of copper complex and ligand were studied and it has been observed that copper complex of schiff base were found to display higher antibacterial activity than free schiff base ligand under identical experimental condition. Some structural modification in free schiff base ligand (2,4-diiodo-6- $\{(E)-[(5\text{-nitro-1,3-thiazol-2-yl})\text{ imino}] \text{ methyl}\}$) can tune the antimicrobial activity and may serve as a model compound for the development of some efficient antimicrobial activity.

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Conflict of Interest: None

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