

# Synthesis and Antimicrobial Activity of Schiff base metal complexes derived from Ampicillin with Furfural

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## ABSTRACT:

Schiff base ligands are well-known to be good chelating agents as bidentate, tridentate or polydentate ligands, particularly when the group such as –OH/-SH are present close to azomethine group, resulting in the formation of five or six membered ring complexes. However various studies have shown that Schiff base derived from biologically active ingredients present in natural materials in its pure form. In this paper Zn(II), Pb(II), Sr(II), Co(III), and Ba(II) complexes were synthesized from Schiff base derived from ampicillin and Furfural. The ligand and metal complexes have been screened for antimicrobial activity against Bacillus Sp, E-Coli,

K-Pneumonia, Staphylococcus aureus, Pseudomonas aeruginosa and against fungal activities. Result revealed moderate change comparing the ligand.

## **INTRODUCTION:**

Ampicillin has been used extensively to treat bacterial infections since 1961. Derivatization and adulteration of curing agents is a need of time due to rapidly emerging antimicrobial resistance<sup>(1-3)</sup>, Researchers pay their attention in seeking miscellaneous approaches and novel competent molecules that best endure with such crisis and widen the range of drugs<sup>(4-7)</sup>

Ampicillin, an extended spectrum penicillin, is effective against gram positive as well as gram negative microorganisms. Metal -drug complexes compounds are more popular nowadays due to their greater biological activity than uncompleted legands of some drugs<sup>(8)</sup>. In most of cases, it was found that metal into affects the action of drugs and in many cases enhance the efficiency of drugs on coordination<sup>(9)</sup>. Metal ions play an important role in different biological processes and they may act as site specific. In recent years, the requirement of quality control for related substances in chemicals became stricter no matter in structure confirmation or content limitation. Ampicillin was especially degradable in presence of aqueous solution or humid storage environment, which would lead to the formation of a variety of degradation products. These related substances would have a great influence on the quality of the products and clinical medication safety.

Although there has been much research on the related substances of ampicillin, it is not completely explicit so far. To ensure the clinical safety and meet the new requirement of related substances in chemicals, it is still necessary to conduct further studies to develop a rapid and efficient method to describe in more detail the related substances of ampicillin capsule. Biological activity of metal ions depends on their concentration, they may their promoter the health of the organism or cause toxicity<sup>(10)</sup>. In many cases it antimicrobial activity than the un completed legend themselves<sup>(u)</sup>

Antimicrobial resistance is fast becoming a global concern with rapid increases in multidrug resistant bacteria. Some previously treatable pathogens are now becoming untreatable<sup>(12)</sup>. To over some the alarming problem of compounds against new targets is a matter of urgency<sup>(13)</sup>. The present investigation deals with the synthesis of metal complexes of

Zn(II),Pb(II),Co(III),Sr(II) and Ba(II) with the Schiff base derived from Ampicillin and Furfural.. The synthesized metal complexes have been screened for their antimicrobial activities against the selected bacteria and fungi using the well diffusion method.

## **2. EXPERIMENTAL**

### **2.1 Materials and Methods:-**

Ampicillin, Furfural, Sodium hydroxide and other chemicals were used for GR grade quality obtained from Hi-Media chemicals All solvents are purified by standard method Zinc, Lead , Cobalt, Strontium and Barium Nitrate salts used for complex preparation.

### **2.2 Synthesis of Schiff base ligand:**

An equimolar mixture of ampicillin in ethanol and furfural in ethanol was well dissolved .To this homogeneous mixture, NaOH (1ml) was added and refluxed about two hours. Yellow coloration in reaction pot indicated the synthesis of Schiff base ligands. This mixture was poured in ice, the yellow precipitate was filtered washed with water and dried.

### **2.3. Synthesis of Schiff base metal complexes:**

The metal complexes were prepared by adding Zn(II) Pb (II), Co(II), Sr(II) and Ba (II) nitrates to the ligand in ethanol of 1:1 molar ratio and refluxed for about twelve hours in at 70 - 80<sup>0</sup>c, the precipitate was washed with ethanol and dried over anhydrous calcium chloride.

### **2.4. Determination of antimicrobial Activity:**

The synthesized ligand and their metal complexes were screened in – vitro for their antibacterial activity against bacteria: Escherichia coli, pseudomonas aeruginosa, staphylococcus aureus Basillus sp and fungal species like candida albican, Aspergillus niger and aspersillus flavus by Mullar Hitton well diffusion method using nutrient as far as medium.

### **2.5 Larvicidal Activity**

The mosquito larvae were collected from water habitats using wide mouth container. The mosquito samples were brought to the laboratory, morphologically identified using standard

manual and used for larvicidal activity studies. Cleaned sterile beakers were taken and 20 early instar larvae of *Culex* were taken in 100 ml of tap water. To this 100 ppm of synthesized complexes was added. 20 larvae taken in tap water served as control. The beaker were kept for 24h, 48h, 72h and 96h for mortality of the larvae.

### 2.4.2. Experimental Method

The ager well diffusion method was used to serene the antimicrobial activity. Muller Hinton ager medium (20ml) was poured in to each petri plates. The plates were allowed to solidify for 5 minutes and 100  $\mu$ l inoculum suspension was swabbed uniformly and allowed to dry 15 minutes using sterile cork bore of 8 8mm diameter, wells were bored into the seeded after plates and these were located with a 100  $\mu$ l solution of each compound in DMSO and all the plates were incubated at 37°C and the diameter of inhibition zone aloud each dise was measured after 24 hour for bacterial and fungal species .The inhibition zone was developed at which the concentration was noted and the results were recorded from the results, the activity index was calculated using the formulae.

## 3. RESULT AND DISCUSSION

All the metal complexes are color solids, stable towards air and have high melting point. The complexes are soluble in organic solvents.

### 3.1. Antibacterial Activity

The in-vitro biological screening effects of the investigated compounds were tested against various bacterial species like *Bacillus* Sp, *E. Coli*, *K.Pneumonia*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Amikasin is used as positive standard for antibacterial studies.

Sample ID	Zone of inhibition (MM)				
	<i>Bacillus subtilis</i>	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>	<i>Enterobactex aerogenes</i>	<i>E.Coli</i>
Ligand	8	8	8	8	8

Pb	8	13	11	8	7
Co	9	11	9	10	9
Sr	11	10	10	9	8
Ba	7	9	9	11	8
Zn	8	9	12	7	9
Standard Amikacin/Nystatin	20	12	21	19	18

Table (1 ) Antibacties of ligand and their metal complexes

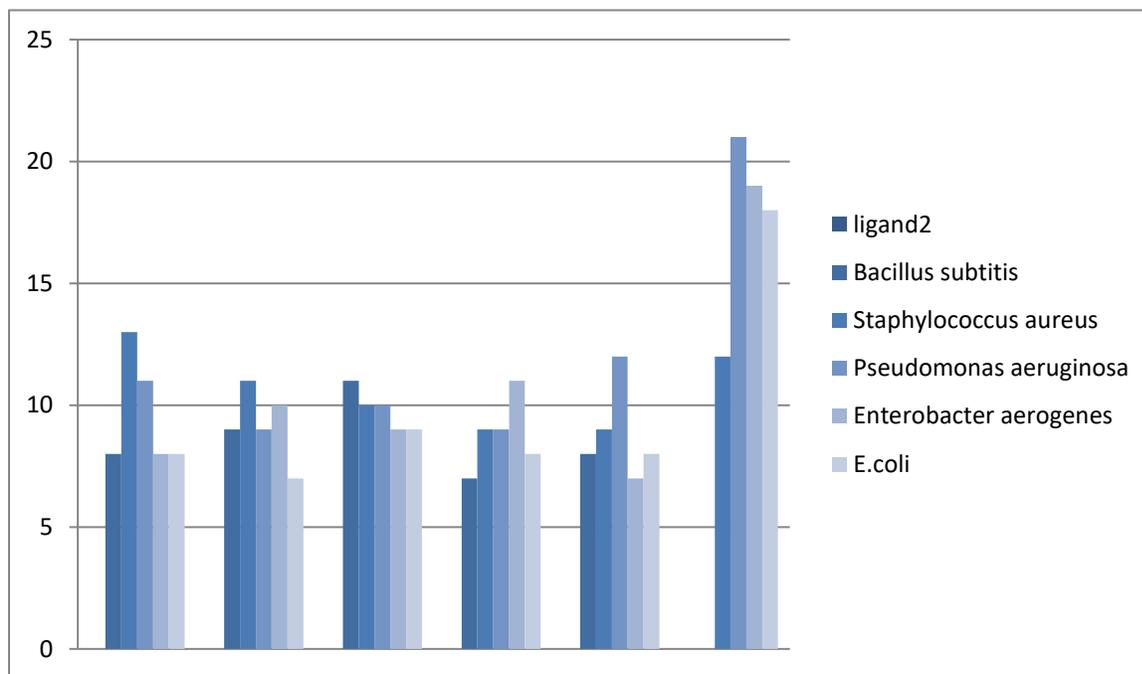


Fig (1) Antibacterial activities of ligand and their metal complex

Sample ID	Zone of inhibition (MM)	
	Penicillium notatum	Aspesillus niser
Lisand	9	9

Pb	9	8
Co	10	9
Sr	8	11
Ba	8	9
Zn	9	9
Standand	16	15

Table(2) Antifungal activation of ligand and their metal complex.

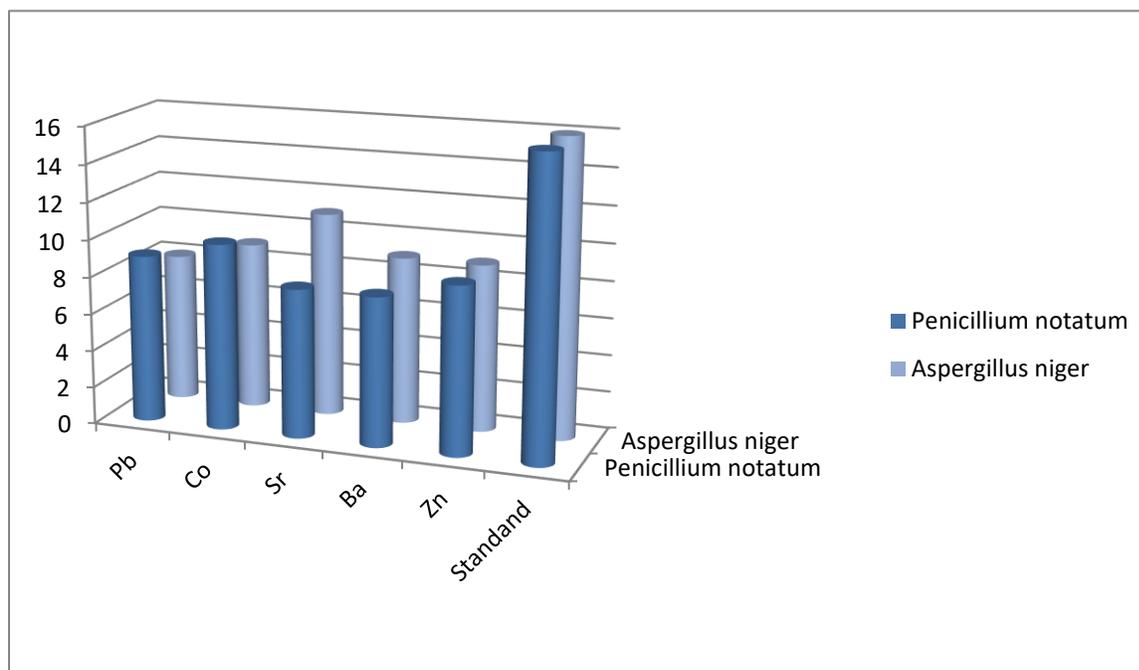
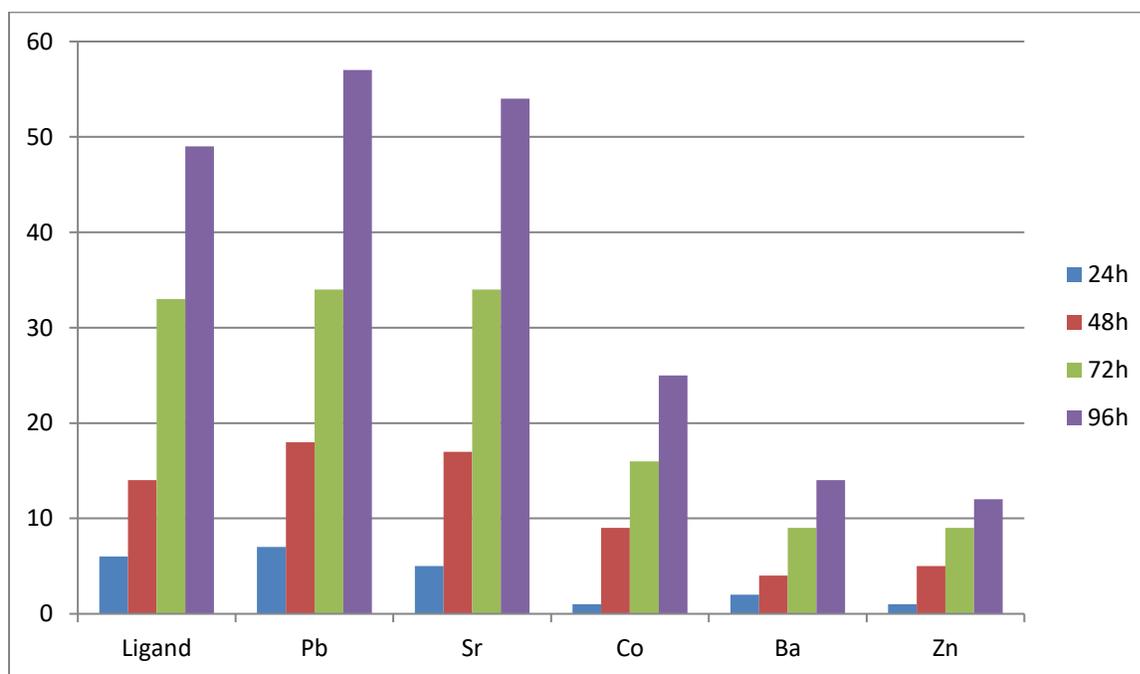


Fig (2) Antifungal activities of ligand and their metal complex

Sample	Larvicidal activity(%)			
	24h	48h	72h	96h
Ligand	6	14	33	49

Pb	7	18	34	57
Sr	5	17	34	54
Co	1	9	16	25
Ba	2	4	9	14
Zn	1	5	9	12

**Table 3: Larvicidal activity of metal complexes**



**Fig (17) Larvicidal activity of metal complexes**

The metal complexes showed enhanced larvicidal activity than the Schiff base. The increased mortality rate observed for lead complex can be attributed to the increase in lipophilicity on complexation. Chelation increase the lipophilicity nature of the central metal

atom, which in turn, favours the molecules in crossing the cell membrane of the microorganism and enhancing the larvicidal activity of complex.

The antimicrobial activities of ligand and its metal complexes are shown in table-1. Antimicrobial results showed that all synthesized compounds possess biological activity. The increased activity of metal complexes may be considered due to chelation of metal ions with Schiff base which enhanced lipophilicity due to delocalization of electrons over the whole chelate ring. These increased lipophilicity enhances the penetration of complexes into the lipid membranes and blocks the metal binding sites in enzymes of microorganisms.

This data deals that the activity of the ligand enhanced on complexation but less than the standard used. Comparative study of ligand and its metal complexes showed moderate activity. The Sr complex showed 11mm zone of inhibition against *Bacillus subtilis*. This value is lower than the standard. Pb complex showed more activity against *Staphylococcus aureus* comparatively higher than standard one. Zn complex showed better activity, against *Pseudomonas aeruginosa* than other complexes.

In Pb complex less activity against *E. coli* and *Bacillus subtilis* but more with *Staphylococcus aureus* and *Pseudomonas aeruginosa*. It is found that the reactivity is higher than ligand. In Zn complex the reactivity against *Pseudomonas aeruginosa* is more comparatively with ligand. Such increased activity of the metal complexes can be explained on the basis of Overman's concept and chelating theory.

In antifungal activity the result shows the reactivity of the complex is not much comparing the ligand.

## CONCLUSION

In this study, Schiff base ligand of with Ampicillin and Furfural was synthesized. With the ligand stable metal complexes of metal ions such as Pb(II), Zn(II), Sr(II), Co(III) and Ba (II) were prepared. Both ligand and metal complexes were stable at room temperature and are soluble in organic solvents specifically ethanol. The compounds were examined biologically for anti microbial, antifungal and larvicidal activity, showed moderate activities than ligand which

may due to its higher lipid solubility, and can be used as gags after in vivo and can be used as drugs after in vivo studies and otter studies like XRD, SEM etc.

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