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Synthesis and antibacterial activity of Schiff base metal complexes

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Abstract

This work was performed to synthesize various Schiff base metal complexes using cobalt, nickel and copper followed by their antibacterial activity. Schiff bases were synthesized by the combination of Ethylene-diam in and salicyldehyde. Metal complexes of these Schiff bases were prepared from nitrate and chloride salts of Ni, Co and Cu in an alcoholic medium. The chemical structures of Schiff base metal complexes were established by infrared spectroscopy. The antimicrobial activities of these complexes were checked against *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumonia, Bacillus cereus, Salmonella typhi*and *Staphylococcus aureus*. Disc diffusion method was used to assess their inhibiting potential. The copper based Schiff complex displayed 9.5, 9.0 and 8.0mm zone of inhibitions against *E. coli, S. typhi* and *S. aureus*at the concentration level of 16.6µg/ 100µL. The results of antibacterial activity of the copper complexes at the concentration of 33.2µg/100µL showed 18.5, 10.5 and 10mm zone of inhibitions against *E. coli, S. typhi* and *S. aureus*. The nickel base complex showed no activity against the tested organisms at both concentrations. The cobalt based Schiff complex showed 17,19,22.5 and 26.5 zones of inhibition against *E. coli, B. cereus, K. pneumonia* and *S. aureus,* respectively at16.6µg/100µL. While at 33.2µg/ 100µL this complex displayed 23.5, 30.5, 26.5 and 28.5mm zones of inhibition against *E. coli, B. cereus, K. pneumonia* and *S. aureus*. These new derivatives may provide a wide choices and flexibility for the development of new, safe and highly active antibiotics.

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Introduction

The compounds having azomethine group (-CH=N-) are known as Schiff bases. They are usually prepared by the condensation of primary amines with carbonyl compounds (Bell *et al.,* 1963). In chemistry, Schiff bases find wide applications. Some of these are the basic units of certain dyes, while, some are employed as liquid crystals. Schiff base reactions are frequently used in organic synthesis for making carbon-nitrogen bonds (Brand., 1943). Metal complexes of Schiff bases have taken a dominant place in the progress of coordination chemistry, especially after the basic work of Jorgensen and Wiener (Basolo and Johnson., 1965). A series of complexes based on Schiff bases of salicyldehyde and their products are reported now (Altun and Köseoğlu., 2006). There are a large number of metal complexes. Some metals such as Copper exist in the form of Cu (I), Cu (II) and Cu (III) states in its complexes. Cu (III), being very easily reduced, generally regarded as uncommon but it has now importance because of its involvement in a number of biological processes (Hamilton and Ribner., 1978; Sillen and Martell., 1971). A large number of Cu (I) and Cu (II) complexes with both active and inactive ligands were prepared and studied for their biological activities (Sorenson and Hangarter., 1977). Other well-known antibiotics like bacitracin, penicillin, tetracycline, streptomycin, etc. are chelating agents; whose activities can be improved by the presence of trivial quantities of metal ions (Kirchner *et al.,* 1966; Johson *et al.,* 1952). Chelates compounds got from Schiff bases reactions are used both for studying changes in structure as well as related biological activities (Johnson *et al.,* 1952; Jensen *et al.*, 1934). The chelating characteristics of antibiotics may be employed in metal transportation across the membrane or to adhere the antibiotics to particular position from where it can interact with the growth of bacteria (Huheey., 1983).

Development of new chemotherapeutic Schiff basses currently enticing the attention of phytochemists (Schiff., 1864). Many studies have revealed a large number of biological activities of various Schiff bases, like anticancer (Basolo and Johnson., 1965; Schiff., 1869; Altun and Köseoğlu., 2006), antimicrobial (Hamilton and Ribner., 1078; Sillen and Martell., 1971), antifungal and herbicidal etc. (Carrico and Densth., 1973). Numerous studies have been conducted to check the effects of various metals on the pharmacological actions of Schiff bases (McMurray *et al.,* 1975; Sorenson and Hangarter., 1977; Das., 1990; Kirchner *et al.,* 1966; Johnson *et al.,* 1952).

In view of the above cited literature it has been observed that Schiff bases possess strong biological activities and there is a greater need of synthesis of new Schiff base metal complexes to cope with some incurable diseases. In the ongoing research work Schiff base metal complexes of Cobalt, Copper and Nickle were synthesized and tested for their biological potency.

Materials and methods

Synthesis of Schiff base metal complexes

Synthesis of Schiff base

Ethylene-di-amine (3.005g) and salicyldehyde (6.11g) were mixed with each other. The mixture was refluxed in ethyl acetate at 150°C. The yellow crystalline precipitates of desirable Schiff base were obtained from the bottom of the quick fit round bottom flask.

Synthesis of complexes

The ligands obtained were taken (2.8g) in ethyl acetate and mixed with 3.4g of $CuCl_2$. The reaction mixture was then refluxed for 5 hours with constant stirring. The mixture was centrifuged and filtered to remove the impurities. The filtrate was then heated on hot plate at 75°C to evaporate the solvent. The obtained complexes were in both liquid and solid forms. The mixture was then freeze for 23h to get Schiff base $CuCl_2$ complexes. The same procedure was repeated to form the complexes of Schiff base with $NiNO_3$ (11.89gm) and $CoCl_2$ (5.89g). All the complexes were diluted to obtain 16.6 and 33.2µg/100µl in DMSO.

Compound identification

The unknown compounds were identified by comparing its IR spectrum with the available data in the literature (Table 1 and 2).

Table 1. Infrared peaks of synthesize complexes.

Compounds	υ (Aro-CH)	υ (-NH2)	υ (OH)	M←N	M—O
Ni-complex	3000cm^{-1}	--	--	902.59 cm^{-1}	750 cm^{-1}
Co-complex	3000 cm^{-1}	3360 cm^{-1}	--	1033.85 cm^{-1}	758.10 cm^{-1}
Cu-complex	3020.53 cm^{-1}	3118.90 cm^{-1}	2604.50 cm^{-1}	1085.92 cm^{-1}	550 cm^{-1}

Table 2. Characteristics of synthesize complexes.

S.No	Molecular formula	Formula weight	Elemental analysis				
			% of C	% of H	% of O	% of N	% of M
1	$C_{10}H_{18}O_4NNi$	274	43.80	6.56	23.35	5.10	21.16
2	$C_{10}H_{16}O_3NCo$	256.93	46.70	6.22	18.68	5.44	22.93
3	$C_{10}H_6O_3NCu$	261.54	45.88	6.11	18.35	5.35	24.29

Disc diffusion method

The disc diffusion method was used for antimicrobial assay. Nutrient agar medium was used for the growth of bacterial strains including, *Pseudomonas aeruginosa, Salmonella typhi, Staphylococcus aureus, E. coli, Bacillus cereus* and *K. pneumonia.* Nutrient agar medium was prepared by mixing ingredients given in (Table 3).

The mixture was then sterilized by placing it in the autoclave at 121°C, 15psi for 15 minutes and stored in the refrigerator for further use. The inoculums were prepared in tryptic soy broths by selecting three to five well-isolated colonies of the same morphological type from an agar plate culture. The tubes were incubated at 35°C until it attains or surpass the turbidity of the 0.5 Mc Farl and standards (typically 2 to 6 hours) by using photometric device.

The inoculums were transferred with sterile cotton swab to nutrient agar plates carefully. The plates were kept for 3 to 5 minutes to absorb excess surface moisture before applying the drug impregnated disks (5mm, diameter) carefully.

The preset battery of antimicrobial discs was placed with sterile forceps on the surface of the inoculated agar plates properly, so that they were at a distance of 24mm from center to center. The plates were inverted and placed in an incubator, set at 37°C within 15 minutes. Each plate was checked after 18 to 24 hours of incubation. The zones of inhibition were measured to the nearest whole millimeter, using sliding calipers or a ruler. The assessment of antimicrobial activity was based on measurement of the diameter.

Table 3. Composition of Nutrient agar.

Serial No.	Components	Amounts
1	Yeast extract	2g/l
2	Beef extract	1g/l
3	Peptones	5g/l
4	Glucose-monohydrates	5g/l
5	Agar	15g/l
6	Sodium chloride	5g/l

Results and discussion

In the current research work Schiff bases metal complexes of different metal such as Cobalt, Copper and Nickle were synthesized and tested for their biological potency. The structures of the synthesized Schiff base metal complexes of Ni, Co and Cu are given in (Fig 1 to 3) and the antibacterial activity results are illustrated in (Tables 4 and 5). The metal complexes and standard antibiotics produced different inhibition zones against the selected bacterial strains. The antibacterial activity of the cobalt Schiff base complex against *E. coli* is 17.0 and 23.5mm inhibitory zonesfor 16.6 and 33.2µg/ 100µL, respectively. Copper complex of Schiff base shows 9.5 and 18.5mm inhibitory zones for 16.6 and 33.2µg/ 100µL, respectively.

The complex can be used for the treatment of intra-uterine infections such as chorimniontis, neonatal bacterial infections in babies, as the causative agent of these diseases is *E. coli* (Ross and Peutherer, 1987). While complex of Nickel with Schiff base didnot show any inhibitory activity against this bacterial strain, as indicated in (Table 4, 5) and (Fig 4, 5). The antibacterial activity of Schiff base metal cobalt complex against *B. cereus* were 19 and 13.5mm zones of inhibitions at concentration levels of 16.6 and

33.2µg/ 100µL, respectively, while other two complexes did not show any inhibitory effects against this strain, as shown in (Table4, 5) and (Fig 4, 5). The antibacterial activity against gram-negative bacterium *S. aureus* shows that the complex of copper have inhibitory zones of 8 and 10mm at concentrations of 16.6 and 33.2µg/ 100µL, respectively. Nickel complex showed no activity for both concentrations, while cobalt complex showed 26.5 and 28.5mm inhibitory zones at 16.6 and 33.2µg/ 100µL, respectively. The complexes of Cu and Co with Schiff base inhibit the proliferation phase of a bacterium during which a segmental twisting and untwisting of the chromosome takes place. It can be used against osteomyelitis, endocarditis, and urinary infection, necrosis of tissue and hospital cross-infection because the causative agent of these diseases are *S. aureus*. The complexes of cobalt with Schiff base inhibit the growth of *K. pneumonia*by exhibiting inhibitory zones of 22.5 and 26.5mm at 16.6 and 33.2µg/ 100µL, respectively. The complex can be used against urinary tract infection (UTI) and sepsis. While the remaining two complexes of Schiff base with Ni and Cu did not show any inhibitory activity as shown in (Table 4, 5) and (Fig 4, 5). The Schiff base metal complexes fail to inhibit the growth of gram-negative bacterium *P. aeruginosa* (Table 4, 5) and (Fig 4, 5) at both tested concentrations. The complex of Cu with Schiff base shows the inhibitory zones 9.0 and 10.5mm against gram-negative bacterium *S. typhi* at 16.6 and 33.2µg/ 100µL, respectively, as shown in (Table 4, 5) and (Fig 4, 5). From the results obtained it is clear that Schiff bases metal complexes can play a vital role against various diseases and synthesis of new and novel Schiff bases can be used as alternative medicines to fight against various pathogenic diseases.

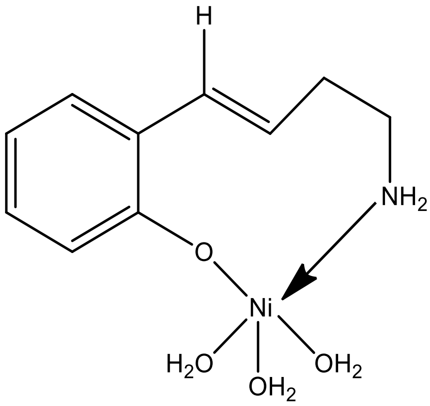

Fig 1. Structure of Schiff base Ni complex.

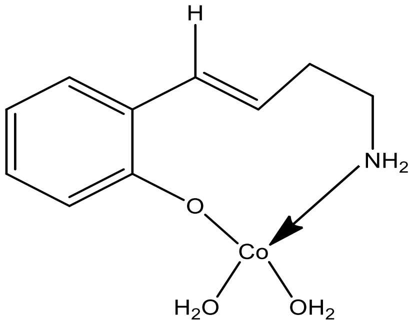

Fig. 2. Structure of Schiff base Co complex.

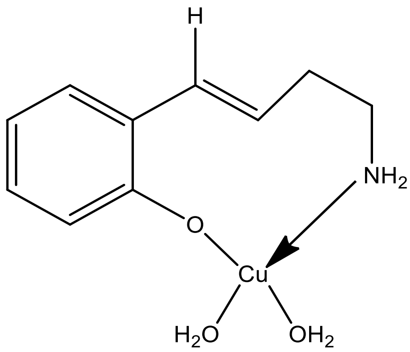

Fig. 3. Structure of Schiff base Cu complex.

Table 4. Bacterial growth inhibition shown by applying 16.6µg/ 100µL of SB-I metal complexes.

Samples	*E. coli*	*B. cereus*	*S. typhi*	*K. pneumonia*	*P. aeruginosa*	*S. aureus*
SBI-Ni	nd	nd	nd	nd	nd	nd
SBI-Cu	9.5	nd	9.0	nd	nd	8.0
SBI-Co	17	19	nd	22.5	nd	26.5
Positive control (Ciprofloxacin)	31	30	29	18	26.5	-
Positive control (erythromycin)	-	-	-	-	-	26.5
Negative control (DMSO)	nd	nd	nd	nd	nd	nd

High inhibition is shown by SB-I Co against *S. aureus*
- = not checked, nd = not detected

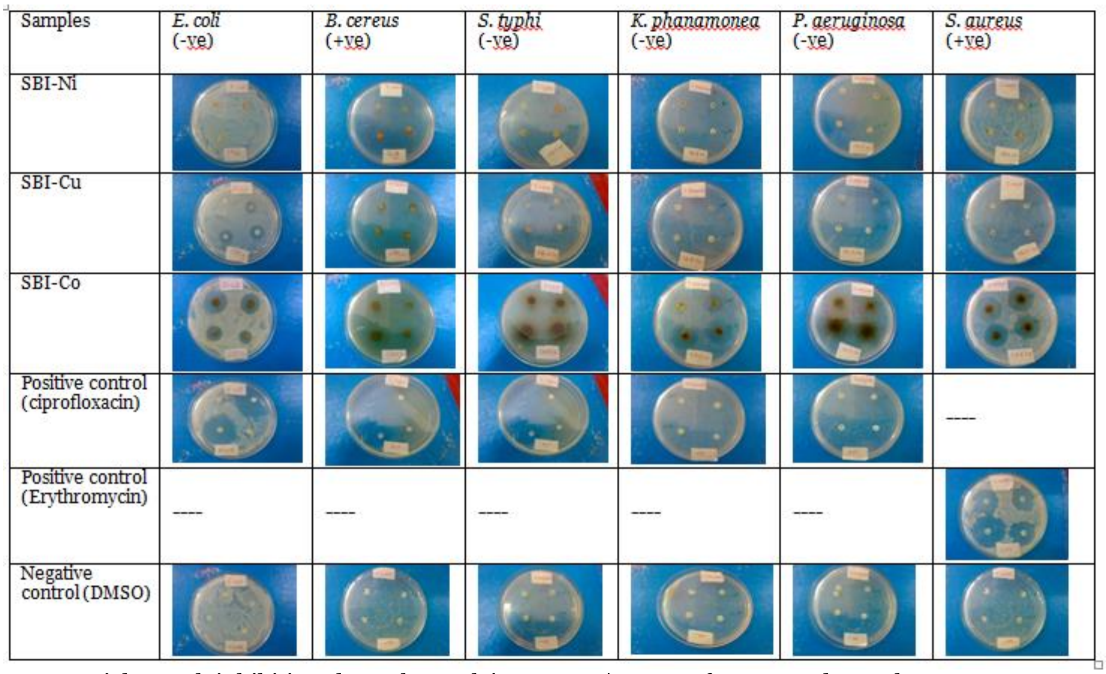

Fig. 4. Bacterial growth inhibition shown by applying 16.6µg/ 100µL of SB-I metal complexes.

Table 5. Bacterial growth inhibition shown by applying 32.2µg/ 100µL of SB-I metal complexes.

Samples	*E. coli*	*B. cereus*	*S. typhi*	*K. pneumonia*	*P. aeruginosa*	*S. aureus*
SBI-Ni	nd	nd	nd	nd	nd	nd
SBI-Cu	18.5	nd	10.5	nd	nd	10
SBI-Co	23.5	30.5	nd	26.5	nd	28.5
Positive control (Ciprofloxacin)	30	30	35	19.5	35	-
Positive control (Erythromycin)	-	-	-	-	-	31
Negative control(DMSO)	nd	nd	nd	nd	nd	nd

High inhibition is shown by SB-I Co against *B.cereus*.
- = not checked, nd = not detected

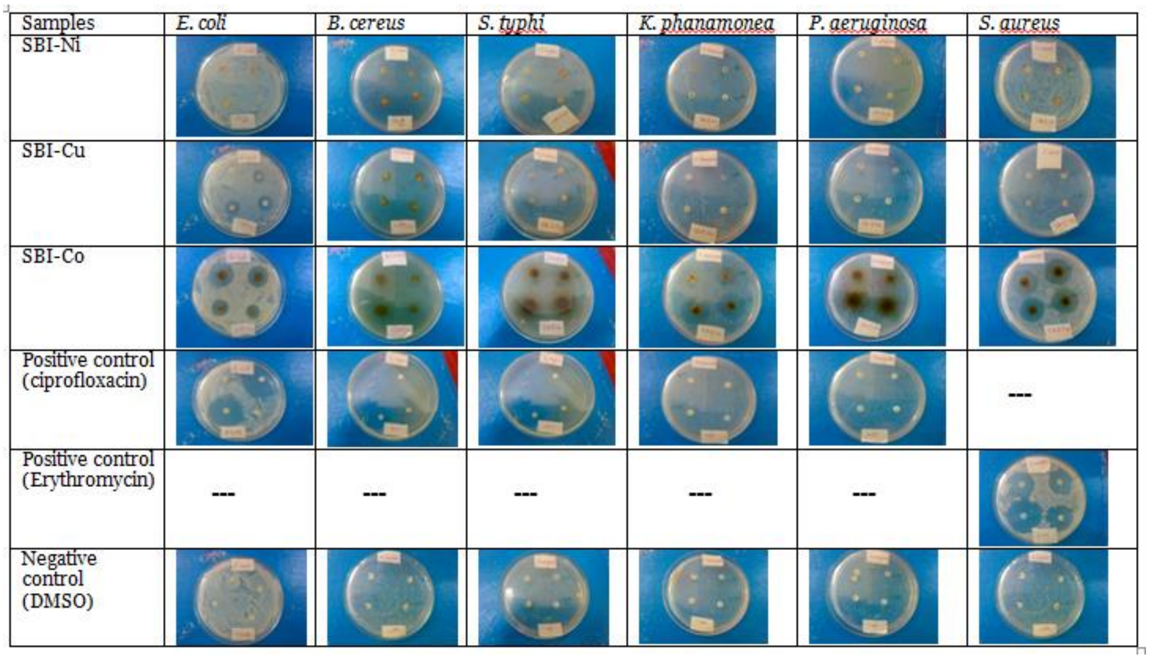

Fig. 5. Bacterial growth inhibition shown by applying 33.2µg/100µLof SB-I metal complexes.

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Conflicts of interest

Authors have none to declare.

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