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MICROWAVE SYNTHESIS, SPECTRAL ANALYSIS AND BIOLOGICAL SIGNIFICANCE OF SOME TRANSITION METAL COMPLEXES DERIVED FROM 4-BROMOBENZYLIDINE-3-CHLORO-4-FLUOROANILINE LIGAND

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ABSTRACT

Some new Schiff base complexes of Co(II), Ni(II) and Cu(II) derived from 4-bromobenzaldehyde with 3-chloro-4-fluoroaniline (BCA) have been synthesized by conventional as well as microwave methods. These compounds have been characterized by elemental analysis, FT-IR, FAB-mass, molar conductance, electronic spectra, ESR and magnetic susceptibility. The complexes are coloured and stable in air. Analytical data revealed that all the complexes exhibited 1:2 (metal: ligand) ratio with coordination number 4 or 6. FAB-mass data show degradation pattern of the complexes. The Schiff base and metal complexes show a good activity against the Gram-positive bacteria; *Staphylococcus aureus* and Gram-negative bacteria; *Escherichia coli* and fungi *Aspergillus niger* and *Candida albicans*. The antimicrobial results also indicate that the metal complexes are better antimicrobial agents as compared to the Schiff base.

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Key Words

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activities

INTRODUCTION

The present day industrialization has led to immense environmental deterioration. The increasing environmental consciousness throughout the world has put a pressing need to develop an alternate synthetic approach for biologically and synthetically important compounds. This requires a new approach, which will reduce the material and energy intensity of chemical processes and products, minimize or eliminate the dispersion of harmful chemicals in the environment in a way that enhances the industrially benign approach and meets the challenges of green chemistry. Microwave-assisted synthesis is a branch of green chemistry. Microwave irradiated reactions are offering reduced pollution, low cost and offer high yield together with simplicity in processing and handling¹⁻³. Reports on the synthesis of metal complexes by microwave methods have been comparatively less.

Transition metal complexes of Schiff bases have been extensively studied, in past few years due to their unusual magnetic properties, novel structural features and relevance to biological systems. A large number of Schiff bases and their metal complexes have been found to possess important biological and catalytic activity. Due to their great flexibility and diverse structural aspects, a wide range of Schiff bases have been synthesized and their complexation behavior was studied⁴⁻⁸.

In this paper, we have described the synthesis, physicochemical characterization and biological significances of Co(II), Ni(II) and Cu(II) complexes with ligand derived from 4-bromobenzaldehyde with 3-chloro-4-flouroaniline (BCA) (Fig. 1). The reaction was carried out by both conventional and microwave methods.

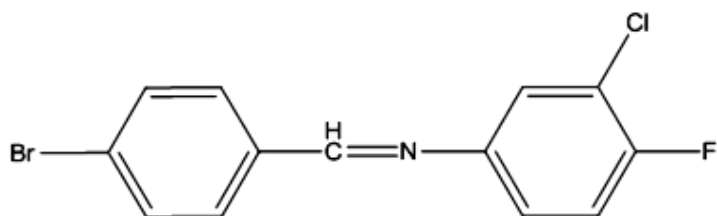


Fig. 1 Structure of 4-bromobenzylidene-3-chloro-4-flouroaniline (BCA)

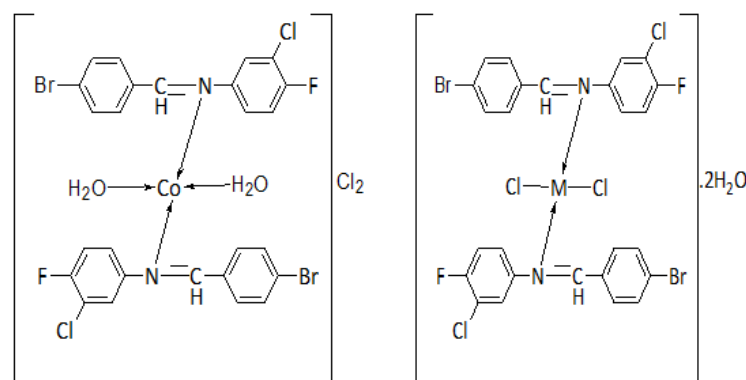


Fig. 2 Proposed structure of metal complexes of BCA

EXPERIMENTAL

Melting points were taken in open glass capillaries and are uncorrected. Progress of reaction was monitored by silica gel-G coated TLC plates using MeOH:CHCl₃ system (1:9). The spot was visualized by exposing dry plate at iodine vapours chamber. All the used chemicals and solvents were of Anal R grade. All the reagents used for the preparation of the Schiff bases were obtained from Sigma Aldrich. Metal salts were purchased from Loba Chemie. Elemental analyses were performed on an Elemental Vario EL III Carlo Erba 1108 analyzer. FAB-mass spectra were recorded on a JEOL SX 102/DA 6000 Mass Spectrometer using argon/xenon (6 kV, 10 mA) as the FAB gas. The accelerating voltage was 10 kV and the spectra were recorded at room temperature. Electronic spectra (in DMSO) were recorded on Perkin Elmer Lambda-2B-spectrophotometer. Molar conductance measurements were conducted using 10⁻³ M solutions of the complexes in DMSO on Elico-CM 82 Conductivity Bridge at room temperature. Magnetic susceptibility measurements were carried out on a Gouy balance at room temperature using CuSO₄.5H₂O as the calibrant. FT-IR spectra were recorded in KBr medium on a Perkin Elmer RX1 spectrophotometer in wave number region 4000-400 cm⁻¹. X-band EPR spectra were recorded on a Varian E-112 spectrometer at room temperature operating at the X-band region with 100 kHz modulation frequency, 5 mw microwave power and 1 G modulation amplitude using TCNE as the internal standard. Microwave assisted synthesis were carried out in open glass vessel on a modified microwave oven model 2001 ETB with rotating tray and a power source 230 V, microwave energy output 800W and microwave frequency 2450 MHz. A thermocouple device was used

to monitor the temperature inside the vessel of the microwave. The microwave reactions were performed using on/off cycling to control the temperature.

Biological Activity

The *in-vitro* biological activity of the investigated Schiff base and its metal complexes was tested against the bacteria *Escherichia coli* and *Staphylococcus aureus* by disc diffusion method using nutrient agar as medium and streptomycin as control. The antifungal activities of the compounds were also tested by the Well diffusion method against the fungi *Aspergillus niger* and *Candida albicans*, on potato dextrose agar as the medium and grasiofulvin as control. The stock solution was prepared by dissolving the compounds in DMSO. In a typical procedure, a well was made on agar medium inoculated with microorganism. The well was filled with the test solution using a micropipette and the plate was incubated 24 h for bacteria at 37 °C and 72 h for fungi at 30 °C. After inoculation, the diameter of the clear zone of inhibition surrounding the sample is taken as a measure of the inhibitory power of the sample against the particular test organism.

Conventional Synthesis of Schiff base

The Schiff base BCA has been synthesized by adding the methanolic solution of 3-chloro-4-fluoroaniline with methanolic solution of 4-bromobenzaldehyde in equimolar ratio. The reaction mixture was then refluxed on water bath for about 5 hour. The condensation product was filtered, thoroughly washed with ethanol and ether, recrystallized and dried in vacuo. The Purity of the synthesized compound was monitored by TLC using silica gel G (Yield: 78 %).

Microwave method for the Synthesis of Schiff base

The equimolar (1:1) ratio of 4-bromobenzaldehyde and 3-chloro-4-fluoroaniline (BCA) were mixed thoroughly in a grinder. The reaction mixture was then irradiated by the microwave oven by taking 3-4 ml solvent. The reaction was completed in a short time (4.5 min) with higher yields. The resulting product was then recrystallized with ethanol and finally dried under reduced pressure over anhydrous CaCl₂ in a desiccator. The progress of the reaction and purity of the product was monitored by TLC using silica gel G (yield: 89%).

Conventional Synthesis of metal complexes

The metal complexes have been prepared by the mixing of (50 ml) methanolic solution of CoCl₂.6H₂O/NiCl₂.6H₂O/CuCl₂.2H₂O with the (50 ml) methanolic solution of Schiff base (BCA) in 1:2 (metal:ligand) ratio. The resulting mixture was refluxed on water bath for 8-10 h. A coloured product appeared on standing and cooling the above solution. The precipitated complex was, filtered washed with ether and recrystallized with ethanol several times and dried under the reduced pressure over anhydrous CaCl₂ in a desiccator. It was further dried in electric oven at 50-70 °C (yield: 64-70%).

Microwave method for the Synthesis of metal complexes

The ligand and the metal salts were mixed in 1:2 (metal:ligand) ratio in a grinder. The reaction mixture was then irradiated by the microwave oven by taking 3-5 ml solvent. The reaction was completed in a short time (7-9 min) with higher yields. The resulting product was then recrystallized with ethanol and ether and finally dried under reduced pressure over anhydrous CaCl₂ in a desiccator. The progress of the reaction and purity of the product was monitored by TLC using silica gel G (yield: 78-84%).

RESULTS AND DISCUSSION

As a result of microwave assisted synthesis, it was observed that the reaction was completed in a short time with higher yields compared to the conventional method. In the microwave method homogeneity of reaction mixture was increased by the rotating of reaction platform tray. The confirming of the results was also checked by the repeating of the synthesis process. All the metal complexes are colored, solid and stable towards air and moisture at room temperature. They decompose at high temperature on heating. The comparative results of conventional and microwave methods and analytical data of the compounds, together with their physical properties are consistent with proposed molecular formula and magnetic moment values are given in Table 1. The metal complexes exhibit 1: 2 (metal:ligand) stoichiometry.

Table 1. The comparative results of conventional and microwave methods, analytical, physical data of the compounds

Molecular Formula/ Mol. Wt./ (Colour)	Reaction period		Yield (%)		Elemental Analysis, Found (Calcd.) %				* Λ_m
	CM (h.)	MM (min.)	CM	MM	C	H	N	Metal	
C ₁₃ H ₈ NCIFBr (BCA) 312 (Yellow)	5.0	4.5	78	89	49.24 (50.10)	2.20 (2.56)	4.18 (4.48)	-	-
[Co(BCA) ₂ (H ₂ O) ₂]Cl ₂ 791 (Green)	9.8	8.2	64	78	38.82 (39.48)	2.29 (2.55)	3.10 (3.54)	7.12 (7.45)	120.5
[Ni(BCA) ₂ Cl ₂].2H ₂ O 791 (Yellowish green)	8.1	7.6	68	84	39.10 (39.49)	2.21 (2.55)	3.32 (3.54)	6.98 (7.42)	36.8
[Cu(BCA) ₂ Cl ₂].2H ₂ O 795 (Black)	7.8	7.8	70	82	39.32 (39.34)	3.58 (3.77)	3.30 (3.52)	8.21 (7.99)	42.3

$$*\Lambda_m = (\Omega^{-1} \text{cm}^2 \text{mol}^{-1})$$

FAB-mass spectra

The FAB mass spectra of the ligand (BCA) and its copper complex [Cu(BCA)₂Cl₂].2H₂O were recorded and they are used to compare their stoichiometry composition. The Schiff base shows a molecular ion peak at m/z 315. The [Cu(BCA)₂Cl₂].2H₂O complex showed a molecular ion peak at m/z 796 confirm the stoichiometry of metal complexes as ML₂ type. It is good agreement with the microanalytical data^{9,10}.

IR spectra

The IR spectra of the complexes were compared with those of the free ligand in order to determine the involvement of coordination sites in chelation. Characteristic peaks in the spectra of the ligand and complexes were considered and compared.

The BCA ligand band at 1627 cm⁻¹ due to $\nu(\text{C}=\text{N})$ azomethine group in chelation shifts down to 1602-1610 cm⁻¹, suggesting participation of azomethine group in complexation, indicating the bonding of nitrogen of the azomethine group to the metal ion and this can be explained by the donation of electrons from nitrogen to the empty d-orbital of the metal atom. The appearance of broad band around 3345-3362 cm⁻¹ in the spectra of complexes may be due to ν_{stre} of water molecule. A medium intensity band at 796 cm⁻¹ suggests the presence of coordinated water in Co(II) complex. The new band of weak intensity at 484-490 cm⁻¹ in the complexes has tentatively been assigned to $\nu(\text{M}-\text{N})$ mode¹¹⁻¹⁵.

Electronic spectra and magnetic moment

The nature of the ligand field around the metal ion has been deduced from the electronic spectra.

Co(II)-BCA complex shows two bands of appreciable intensity at 12245 cm⁻¹ and 20072 cm⁻¹. These transitions have tentatively been assigned to ${}^4A_2 \rightarrow {}^4T_1(\nu_2)$ and ${}^4A_2 \rightarrow {}^4T_1(P)(\nu_3)$ cm⁻¹ respectively. The magnetic moment is 4.40 B.M. Thus, the tetrahedral geometry has been suggested for this complex. The electronic spectrum of Ni(II)-BCA complex exhibited two bands at 12324 cm⁻¹ and 23355 cm⁻¹, which are assignable to ${}^1A_{1g}(F) \rightarrow {}^2E_g(\nu_1)$ and ${}^1A_{1g} \rightarrow {}^1B_{2g}(\nu_2)$ transitions, respectively. It is a diamagnetic complex. Therefore, square planar geometry has been suggested for this complex. The absorption spectrum of Cu(II)-BCA complex shows two bands at 13288 and 18512 cm⁻¹ which have been assigned to ${}^2B_{1g} \rightarrow {}^2A_{1g}$ and ${}^2B_{1g} \rightarrow {}^2E_g$ transition respectively. The magnetic moment of the complex is 1.94 B.M and transitions suggest the geometry to be square planar¹⁶⁻¹⁹.

ESR Spectra

The spectra of Cu(II) complex have been recorded on X-band at frequency 9.5 GHz under the magnetic field strength 3400 Gauss. The values of ESR parameters of Cu(II)-BCA complex viz. g^{11} , g^\perp , g_{av} and G are as 2.2482, 2.1291, 2.1688 and 1.9225 respectively.

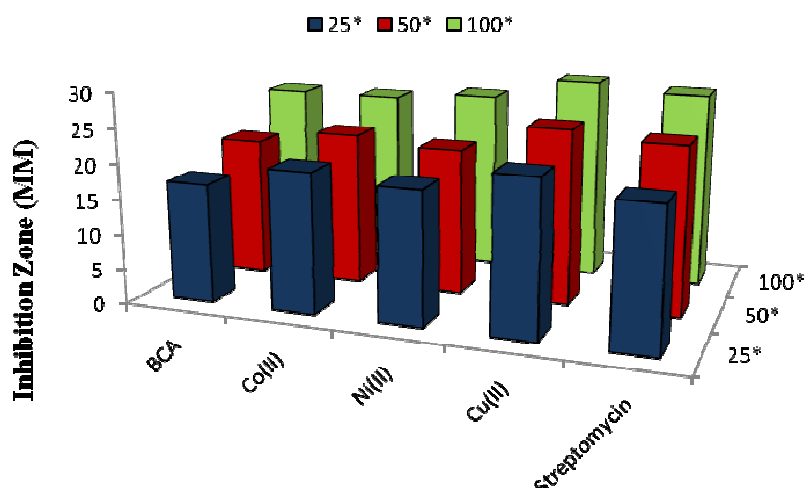
The parameter g_{av} was obtained by equation [$g_{\text{av}} = 1/3(2g^\perp + g^{11})$]. The g-tensor values of Cu(II) complex can be used to derive the ground state. The value of $g^{11} > g^\perp$

in the complex, suggest that the unpaired electron is localized in $d_{x^2-y^2}$ orbital. The value of g^{11} for the Cu(II) complex indicates the prevalence of covalent character in the metal-ligand bond. The g values are related to the axial symmetry parameter G by the Hathaway expression $G = (g^{11}-2) / (g^{\perp}-2)$. According to Hathaway if the value of G is greater than four ($G > 4.0$), the exchange interaction is negligible. Whereas when the value of G is less than four ($G < 4.0$) a considerable exchange interaction is indicated in the complex^{20, 21}.

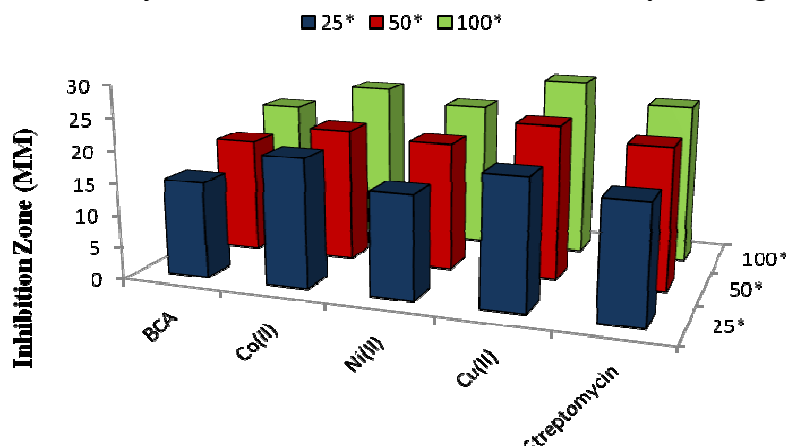
Antimicrobial activities

The *in vitro* Antimicrobial activity of the synthesized Schiff base ligands and their corresponding metal complexes (Fig. 3) on selected bacteria *E. coli* and *S. aureus* and two fungi *A. niger* and *C. albicans* was carried out. All of the tested compounds showed good biological activity against microorganism. On comparing the biological activity of the Schiff base and its metal

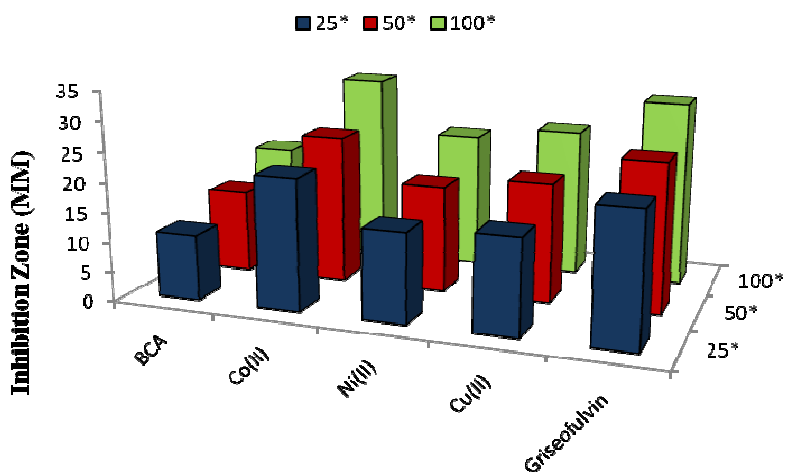
complexes with the standard bactericide and fungicide, it is show that the some metal complexes have good activity as compared to the standard but all the complexes are more active than their respective ligands. The higher inhibition zone of metal complexes than those of the ligands can be explained on the basis of Overtone's concept and Chelation theory. On chelation, the polarity of the metal ion will be reduced to greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelating ring and enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. There are other factors which also increase the activity are solubility, conductivity and bond length between the metal and ligand²²⁻²⁵.



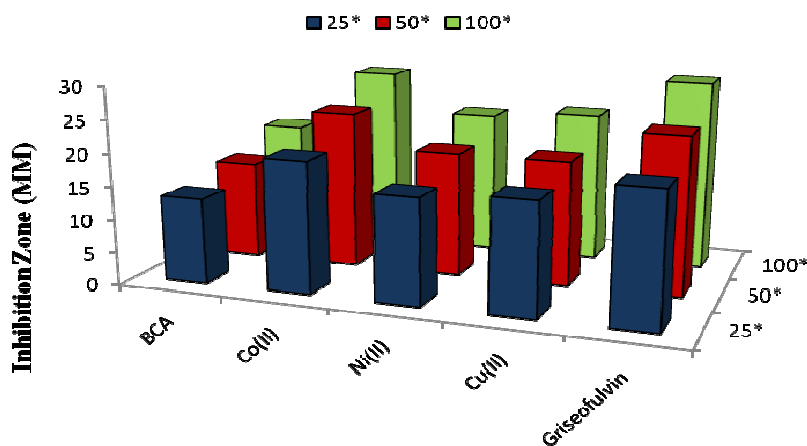
Antibacterial activity of BCA Schiff base and its metal complexes against *E. coli*



Antibacterial activity of BCA Schiff base and its metal complexes against *S. aureus*



Antifungal activity of BCA Schiff base and its metal complexes against *A. niger*



Antifungal activity of BCA Schiff base and its metal complexes against *C. albicans*

Fig. 3 Biological activity of Schiff bases and their metal complexes

The antibacterial and antifungal data are listed in Table 2. The investigation of antibacterial data revealed that

the Co(II) and Cu(II) complex of displayed highly activity against bactericide and fungicide.

Table 2. *In-vitro* antibacterial activity of compounds and their inhibition zone (%)

Compound	Diameter of inhibition zone (mm), Concentration in ppm											
	Antibacterial screening data						Antifungal screening data					
	<i>E. coli</i>			<i>S. aureus</i>			<i>A. niger</i>			<i>C. albicans</i>		
	25	50	100	25	50	100	25	50	100	25	50	100
BCA	17	20	25	15	18	21	11	14	18	13	15	18
Co(II)- BCA	20	22	25	20	21	25	22	25	32	20	24	28

Ni(II)- BCA	19	21	26	16	20	23	15	18	23	16	19	22
Cu(II)- BCA	22	25	29	20	24	28	16	20	25	17	19	23
Streptomycin	20	24	28	18	22	25	-	-	-	-	-	-
Griseofulvin	-	-	-	-	-	-	22	25	31	20	24	29

CONCLUSION

In the present research studies, our efforts are synthesized of some newly compounds from the conventional as well as microwave methods. These synthesized compounds characterized by various physicochemical and spectral analyses. In the result of microwave assisted synthesis, it has been observed that the reaction time decreased from hours to minutes and availability of the product within better yields compared to the conventional methods. FAB-mass shows degradation pattern of the complexes. The antimicrobial data show that the metal complexes to be more biological active compared to those parent Schiff base ligand against all pathogenic species. The compounds also inhibit the growth of fungi and bacteria to a greater extent as the concentration is increased.

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