

Anti Cytotoxic And Microbial Studies Of Iron Schiff Base Complex With Azide

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Abstract: The aim of this research is to study the role of Iron and the recognition of its complexes as important bioactive compounds in vitro and in vivo arouse an ever-increasing interest in these agents as potential drugs for therapeutic intervention in various diseases. Schiff bases are a critical class of compounds in medical chemistry that have verified significant chemotherapeutic and antibacterial application. Schiff base copper complexes revealed great potential for anti proliferative, anti bacterial, and gastro protective activity. orthophenylenediamine is a wide class of synthetic compound that showed diverse pharmacological activities including anticancer activity. In particular, their antibacterial, antifungal and anticancer activities make the compounds attractive for further derivatization and screening as novel therapeutic agents. Taking these compounds as iron, we have designed and synthesized a new iron complex with ortho phenylene diamine, salicylaldehyde and Acetyl acetone Schiff base ligand.

Keywords: Anti Cancer, Antimicrobial Activity, Schiff Base, Iron, Azide

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I. Introduction:

Transition metal macro cyclic complexes have acknowledged a great attention because of their Biological activities, including antimicrobial, antiviral, and anti carcinogenic properties [1-5]. Such biological activities are basically due to their ability to form tetra dentate chelate with heavy metal ions, bonding through sulfur and nitrogen [6, 7]. The field of coordination chemistry has increased the interest in schiff complex compound identified base, since it has been recognized that many of these organic metal complexes may serve as facsimiles for biologically significant species [8,9]. The design, production and depiction of iron complexes with Schiff base ligands play a relevant role in the coordination chemistry of iron due to their importance as synthetic models for the iron-containing enzymes [10,12], oxidation catalysts [13,14] and stable molecular materials based on temperature, pressure or light induced spin-crossover behavior [15,16]. Schiff base ligands are considered privileged ligands, because they are easily prepared by a simple one-pot condensation of an aldehyde and primary amines in an alcohol solvent [10]. Furthermore it was found that some iron(III) complexes provide a useful structural and electronic model for the similarly coordinated iron(III) sites found in the heme iron enzymes [17]. Mascharaket al. [18, 19] studied the structures and properties of a number of iron (III) metal organic complexes with some amidate ligands because such complexes can be taken as a model for the metal coordination spheres of the anti-tumor drug Bleomycin [20]. From a bioinorganic point of view, the Fe (III) complexes with salicylidene amines ligands provide a useful structural and electronic model for the similarly coordinated iron(III) sites found in the heme iron enzymes [21].

II. Headings

Synthesis of $[(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2] \cdot (SO_4)_2(H_2O)_4 CH_3OH$

A solution of Schiff's base (0.5mmol, 0.156gms) is dissolved in 10ml of hot methanol is added to a solution of Ferrous sulphate (0.5mmol, 0.139gms) is dissolved in 10ml of water, immediately a dark green colored solution is appears. To this, a solution of sodium azide (0.5mmol, 0.032gms) is dissolved in 10ml of water is added, a teak brown colored

precipitate is obtained after one hour on constant stirring at room temperature Anal. exptal. $C_{40}H_{39}N_{10}FeO_2$ (M.Wt.747.65) C, 64.26; H, 5.26; N, 18.73. Found: C, 63.88; H, 4.98; N, 17.39. Important IR absorptions (KBr disk, cm^{-1}): 3728, 3430, 2313, 1728, 1759, 1612, 1276, 1250, 1252, 905. Mass peaks (m/z): 209, 147, 342, 482, 599, 704, 929. Yield: 0.186 gm (56%)

Electronic spectrum of $[(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2] \cdot (SO_4)_2(H_2O)_4 CH_3OH$

Electronic absorption spectra of metal complexes were recorded in DMF in the range 200 – 800 nm. The electronic spectrum of free Schiff base showed three bands around 240, 350 and 450 nm characteristic of $\pi-\pi^*$ and $n-\pi^*$ transitions. In the metal complex, this band is shifted to a longer wave length with increasing intensity. This shift may be attributed to the donation of lone pair of electrons of oxygen of Schiff base to metal ion. The iron complexes exhibits bands around 255-300 nm, 350- 355 nm and 477-498 nm. The broad intense and poorly resolved bands around 350-355 nm may be assigned to LMCT or MLCT. The high intensity band 250 nm is of ligand origin assignable to intra ligand $n-\pi^*$ or $\pi-\pi^*$ transition [22]. The complexes showed shoulder broad bands in the range of 300-325 nm may be assigned to the d-d transition important peaks showed in Fig.1

IR Spectrum of $[(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2] \cdot (SO_4)_2(H_2O)_4 CH_3OH$

In the IR spectrum of the Schiff bases ligand a sharp band observed at 1612 cm^{-1} is assigned to the $\nu(C=N)$ mode of the azomethine group. This shifts to lower wave numbers, $1604-1609\text{ cm}^{-1}$ in the complex suggesting the non co-ordinated azomethine nitrogen to the metal centre.[23]. The characteristic phenolic $\nu(O-H)$ mode due to presence of a hydroxyl group at ortho position in the ligand is observed around $3200-3500\text{ cm}^{-1}$. The appearance of a new band around $500-543\text{ cm}^{-1}$ in the complex due to $\nu(M-O)$ bond formation [24]. A sharp band observed at 1720 cm^{-1} is assigned to $\nu(C=O)$ of acetyl acetone in ligands the intensity of this band has not only reduced but has shifted to lower wave numbers in the corresponding metal complexes confirming the involvement of the carbonyl group in complexation with metal ion [25]. The weak band at 1317 cm^{-1} suggests presence of free sulphate ions in the outer sphere. band at 2830 cm^{-1} indicates the presence of un coordinate methanol in the outer sphere. The presence of co-ordinated Iron in the complex is confirmed by the presence of bands around $875-923\text{ cm}^{-1}$ [26].

The weak broad bands in the region $3746-3423\text{ cm}^{-1}$ due to hydrogen bonded OH group. This indicates that the phenolic oxygen atoms present in the Schiff bases are coordinated to the metal centers. The strong $\nu(C=N)$ bands occurring in the range of $1617-1611\text{ cm}^{-1}$ are shifted slightly toward lower frequency 1607 cm^{-1} compared to the free Schiff bases indicating the non Co-ordinated azomethine nitrogen atom to the metal center. The $\nu(CN)$ absorption at 2115 cm^{-1} as a single peak suggests the presence of N-coordinated terminal azide group. (NNN) appears at 2115 cm^{-1} as a single peak indicating the presence of terminal azide ion coordination to the metal center. important peaks presented in Fig.2

LC-MS Spectrum OF $[(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2] \cdot (SO_4)_2(H_2O)_4 CH_3OH$

The peak at $929(m/z)$ refers to the complex bound to one iron, two salicylaldehyde, two OPD, two acetyl acetone, two azides, two sulphate, one methanol and four water molecules represented as $[(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2(CH_3OH)(SO_4)_2(H_2O)_4]$. the peak at $704(m/z)$ is complex of two salicylaldehyde, two OPD, two acetyl acetone, one methanol, one sulphate, two water fragments embodied as $[(SAL)_2(OPD)_2(AA)_2(OCH_3)(SO_4)(H_2O)_2]$. peak at $599(m/z)$ states complex destined to two salicylaldehyde, two OPD, one acetyl acetone, one sulphate, one methanol and one water molecules

$[(\text{SAL})_2(\text{OPD})_2(\text{AA})(\text{SO}_4)(\text{CH}_3\text{OH})(\text{H}_2\text{O})]$. The peak at 482(m/z) refers to the complex bound to two salicylaldehyde, one OPD, one acetyl acetone, one sulphate and one methanol that is $[(\text{SAL})_2(\text{OPD})(\text{AA})(\text{SO}_4)(\text{CH}_3\text{OH})]$ The peak at 342(m/z) is endorses one salicylaldehyde, one OPD, one acetyl acetone and one sulphate molecules embodied as $[(\text{SAL})(\text{OPD})(\text{AA})(\text{SO}_4)]$. The base peak 209(m/z) is characterizes $[(\text{SAL})(\text{OPD})]$ and finally peak at 147(m/z) is indicates $[(\text{OPD})(\text{N}_3)]$. Fragmentation showed in Fig.3

$^1\text{H-NMR}$ Spectrum of $[(\text{Fe})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{N}_3)_2].(\text{SO}_4)_2(\text{H}_2\text{O})_4 \text{CH}_3\text{OH}$

The $^1\text{H-NMR}$ spectra of Schiff bases are recorded in dimethyl sulfoxide (DMSO) solution, using tetra methyl silane (TMS) as internal standard. The NMR spectra of the Schiff bases, the spectra of the complexes are examined in comparison with those of the parent Schiff bases. Upon examination it was found that the N-CH signal that appeared in the spectrum of the ligand at 8.85-8.96ppm, is appeared in the spectrum of its iron complex, indicating that the Presence of azomethine group in the complex. moreover, signals observed at 2.5ppm indicating the free methyl groups of acetyl acetone. New signal is observed at 3-3.5 ppm assigned to presence of methanol in the complex. Spectrum presented in Fig.4

Thermal Gravimetric Analysis of $[(\text{Fe})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{N}_3)_2].(\text{SO}_4)_2(\text{H}_2\text{O})_4 \text{CH}_3\text{OH}$

The complex, $[(\text{Fe})_2(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{N}_3)_2(\text{OCH}_3)(\text{H}_2\text{O})_4].\text{SO}_4$ presented in Fig.5 is well defined, consisting of three stages. In the first step, dehydration of the complex occurs in the temperature interval of 40 – 170°C corresponding to elimination of coordinated water molecules (Remaining Wt. %, Obs. /Calcd., 5.32/5.41). After this temperature, a loss in weight is observed in general up to 400°C corresponding to the loss of partially decomposed ligand part from the complex (Remaining Wt. %, Obs./Calcd., 12.3/12.9). Above this temperature, a weight loss has been occurred upto 500°C. This corresponds to metal oxide as an ultimate pyrolysis product (Remaining Wt. %, Obs./Calcd., 13.93/13.72). The thermal analysis evaluates the thermal stability of the metal complexes, this study also helped to characterize the metal complexes.

Powder diffractogram of $[(\text{Fe})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{N}_3)_2].(\text{SO}_4)_2(\text{H}_2\text{O})_4 \text{CH}_3\text{OH}$

Crystallite size is obtained using Scherer's equation, $D = K\lambda/(\beta \cos\theta)$, where D is the particle size in nm of the crystal grain has been calculated using maximum intensity peak; K is the Scherer's constant; λ is the wavelength of target used; β is the full width at half maximum reflection height in terms of radian and θ is the Bragg diffraction angle at peak position in degree. Crystallite size showed in Table.1

Anti-microbial Screening of $[(\text{Fe})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{N}_3)_2].(\text{SO}_4)_2(\text{H}_2\text{O})_4 \text{CH}_3\text{OH}$

The complex is screened invitro for antibacterial activity against E.coli, B.subtilis and antifungal activity against A.niger by Agar-well diffusion method[27-30] The antibacterial and antifungal activities of complex are listed in table .2

Cytotoxic studies of $[(\text{Fe})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{N}_3)_2].(\text{SO}_4)_2(\text{H}_2\text{O})_4 \text{CH}_3\text{OH}$

The synthesized complex is screened for their cytotoxicity (MCF-7, cell lines).[31-62] from the data, it is observed that the complex displayed their cytotoxic activities as IC_{50} ($\mu\text{g}/\text{mL}$) against breast cancer MCF-7, The IC_{50} values of the complex are showed in Fig.9

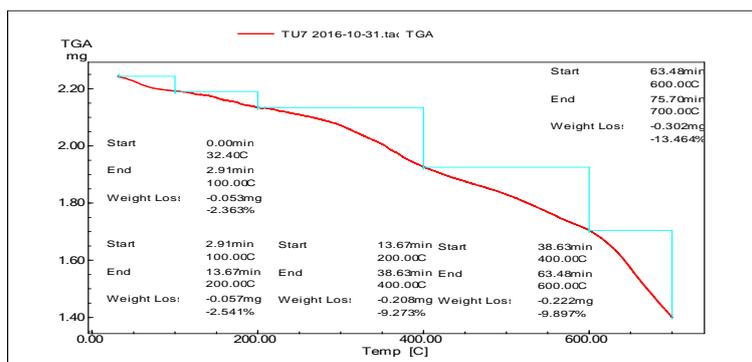


Fig.5. Thermal Gravimetric Analysis of $[(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2] \cdot (SO_4)_2(H_2O)_4 CH_3OH$

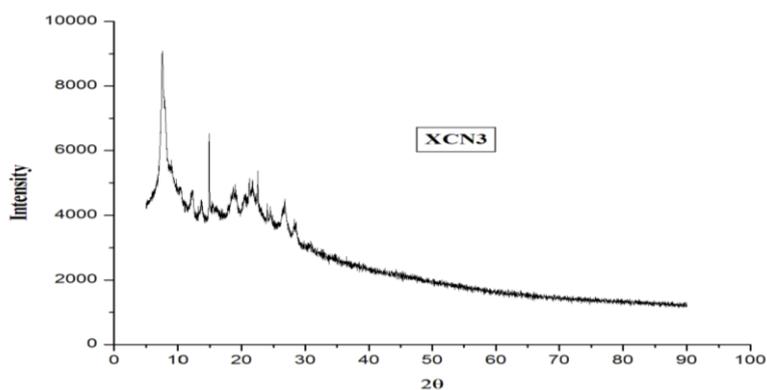


Fig.6. Powder diffractogram of $[(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2] \cdot (SO_4)_2(H_2O)_4 CH_3OH$

COMPLEX	2θ	Crystallite size
$(Fe)(SAL)_2(OPD)_2(AA)_2(N_3)_2(SO_4)_2(H_2O)_4(CH_3OH)$	7.3528	24.74nm

Table.1.crystallite size of Schiff's Base complex

Bacteria	Inhibition zone (mm)
E.coli	16
B.subtilis	12
Fungi	Inhibition zone (mm)
A.Niger	Nil

Table.2.Antimicrobial activities of Schiff's base complex

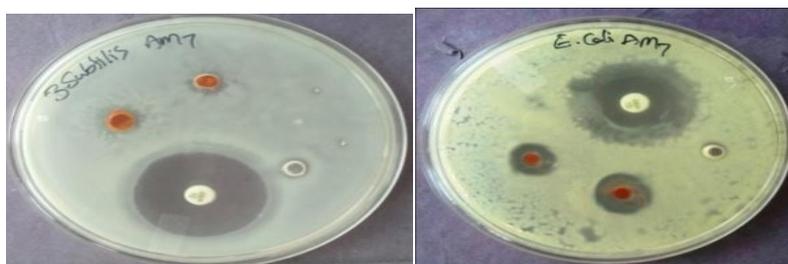
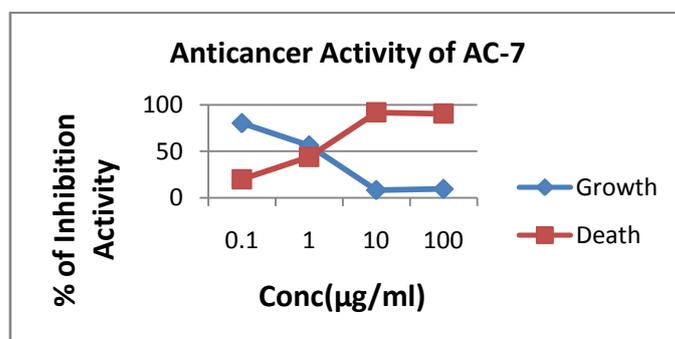


Fig.7. Inhibition zones for Schiff's base complex against. B.subtilis E.coli



Fig.8. Inhibition zones for Schiff's base complex against A.niger



IC50

2.14µg/mL

Fig.9. Effect of complex on MCF7 Cell viability for 24h Incubation time

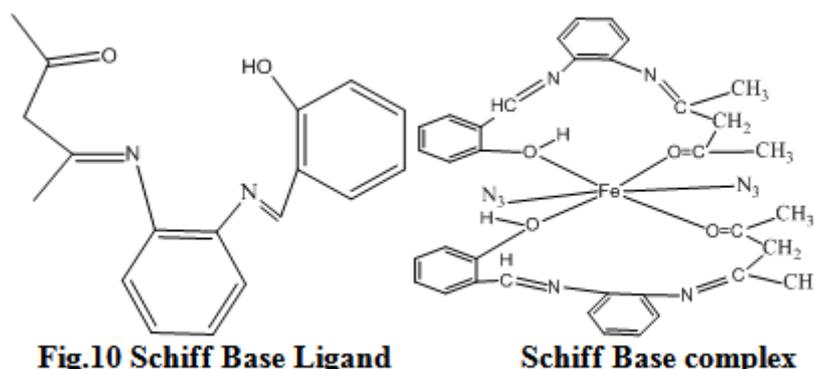


Fig.10 Schiff Base Ligand

Schiff Base complex

IV. Conclusion

In this paper we have reported the synthesis of Iron Schiff base, Pseudo halide ligand complex has been synthesized by using the self-assembly method. The ligand and complex is characterized by spectroscopic studies. The antimicrobial studies are carried out with the complex confirm that they are good anti-microbial agents with their MIC values being 12 and 16 for bacterial organisms and no activity for fungal organisms. The cytotoxic studies are carried out with the complex confirm that they are good anti-cancer activity against MCF-7 (Breast cancer). by the means of ic_{50} value.

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