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ANTIFUNGAL SCREENING OF SCHIFF BASE COMPLEXES OF Zn(II), Mn(II), Fe(III), Cu(II), Ni(II) AND Co(III) DERIVED FROM (E)-1-ETHYL-4-HYDROXY-3-(1-(2-PHTHALAZIN-1-YL)HYDRAZINO ETHYL QUINOLINE-2(1H)-ONE AND (E)-4-HYDROXY-1-METHYL-3-(1-(2-(PHTHALAZINE-1-YL)HYDRAZINO)ETHYL QUINOLIN-2(1H)-ONE

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Abstract:
The important pathogens such as Escherichia coli, Salmonella typhi, Staphylococcus aureus, and Bacillus subtilis are wildly caused many diseases. So antifungal activity of Zn (II), Fe(III), Mn (II) Ni (II), Co (III) and Cu (II) Schiff base complexes against four kinds of fungal species was established Methods: In this study, antifungal activity of metal complexes derived from. (E)-1-ethyl-4-hydroxy-3-(1-(2-phthalazin-1-yl)hydrazino ethyl quinoline-2(1H)-one AND (E)-4-hydroxy-1-methyl-3-(1-(2-(phthalazine-1-yl)hydrazino)ethyl quinolin-2(1H)-one. The complexes were characterized by elemental analysis and estimation of metals. Thermal behavior of the complexes was studied by TG-DTA analysis.Structures of the complexes were elucidated by spectroscopic methods like, infrared spectroscopy, UV-visible spectroscopy, mass spectrometry and 1HNMR spectroscopy. The powder X-ray diffraction study suggested crystalline nature of the complexes octahedral geometry. Magnetic moments and electronic spectra reveal octahedral structure of the complexes. Antifungal activity of ligands and their metal complexes were studied in vitro against Aspergillus niger, Aspergillus flavus, Fusarium moniliforme and Penicillium chrysogenumat fixed 1% concentration.
Keywords: Schiff base ligand, metal complex, Aspergillus niger, Aspergillus flavus, Fusarium moniliforme and Penicillium chrysogenum.

Introduction:
The biotic component of the world include vast variety of living organisms. The biotic component which includes all the living organisms belonging to five kingdoms. The fungi represent one of the most important kingdoms of living organisms. Fungi have eukaryotic cellular organization and possess heterotrophic mode of nutrition. They can't synthesis their own organic food through photosynthesis or chemosynthesis and instead obtain it from other sources. The fungi may be unicellular or multi cellular with uni, bi or multinucleate cell. The heterotrophic mode of nutrition in fungi may be saprophytic, parasitic, having definite cell wall but not differentiated into roots, stems and leaves and vascular systems which we find in advance plants. The cell wall composition is not similar in all the fungi. In some fungi cellulose is the chief cell wall constituent. The external factors such as the composition of the medium used for fungal cultivation, pH value and temperature influence the composition of fungal cell walls.[1,2]
Reproduction of fungi take place through the spores which are produced either by asexual or sexual methods. Spores are specialized cells one or more celled, set apart for reproduction. They arises as buds on specialized hyphae (exogeneous) or may be born in special receptacles, The spores fruits (endogeneous) on germination, each spores forms a new haploid mycelium. Fungi also show vegetative method of reproduction. The vegetative multiplication may occur by fragmentation, fission and budding.
The fungi helps in recycling nutrient and play a significant role in some fungi to help in improving the industrial production of various substances like gluconic acid, citric acid, alcohol, other organic acids and enzymes. Fungi also used in agriculture, medicine, food and nutrition. The genus Trichoderma a well known bio-control agent used in present day agriculture for controlling a safe and ecofriendly way of plant disease[3]. Saccharomyces cerevisiae or Baker's yeast, a single-cell fungus, is used to bake bread and other wheat products.[4]
Some mushrooms used as therapeutics in traditional and folk medicines, such as chinese medicine.[5] Penicillium chrysogenum and other fungi produces antibiotics, such as penicillin and cepalosporine[6] etc. Worldwide use of these antibiotics for the treatment of bacterial diseases, such as leprosy, tuberculosis, syphlis and many others. 'White rot fungi' can degrade insecticides, herbicides, coal tars, creosote and heavy fuels and turn them into carbon dioxide, basic element and water.[7]
Some fungi act as pathogens for plants and animals. They can destroy timber, textile. food and leather. In the present study four fungi Aspergillus niger, Penicillium chrysogenum. Fusarium moniliforme and Aspergillus flavus are used.

Aspergillus niger:

Aspergillus niger is a kind of Ascomycetes includes the fungi which are commonly called as black mold or black aspergillis. A. niger is a plant deleterious fungi and air born ascomycetes to which A. niger belong are found on paddy crops. The fungus A. niger is omnivorous in occurrence. The fungi is always associated with food grains, fruits and vegetables during storage and cause spoilage to these stored product.

A. niger is a fungi of great biotechnological importance as it synthesizes useful product of high commercial value. Aspergillus are highly useful in various industrial process such as fermentation, baking, brewing and industrial manufacturing of organic acids, fats, cheese, enzymes, vitamins and antibiotic because of their ability to secrete digestive enzymes. Using A. niger, citric acid and gluconic acid are manufactured commercially on large scale.[8] In Japan, A. oryzae is used in fermentation to manufacture sake, an alcoholic beverages from rice starch and to make various fermentated food products. A. niger is used in the study of many biological process and can detect traces quantities of elements Cu, Fe, Mn and Zn from unknown sample.

The genus is widely distributed in nature. A huge number of spores of these organisms are suspended in air and responsible for varity of allergies and respiratory disorders in human being. A. fumigatus, A. flavus, A. niger and other species cause Aspergillosis disease. The Aspergillosis of the lungs is much more common in birds. It is also common in cattle, sheep, horse and occurs rarely in human being.[9] Several species grow on leather, timber, cloth and reduced their commercial value. They are also common contaminants of cultures in bacteriological and mycological laboratories.

Aspergillus flavus:

A. flavus generaly associated on ceral grains, legumes and tree nuts. A. flavus is a pathogenic and saprophytic.[10] Many strains of Aspergillus produces significant quantity of toxic compounds known as mycotoxins, which, when consumed are toxic to mammals.[11] Aspergillus infections have grown in importance in the last few years. A. flavus is more common in air, A. flavus is the second leading cause of invasive aspergillosis and it is the most common cause of superficial infection. Experimental invasive infection in mice show A. flavus to be 100- fold more virulent than A. fumigatus particularly common clinical syndromes associated with A. flavus include chromic granulomatous sinusitis, keratitis, cutaneous aspergillosis. A. flavus produces aflatoxins, the most toxic and potent hepatocrcinogenic natural compound.

In humans, A. flavus aflatoxin production can lead to acute hepatitis immunosuppression, hepatocellular carcinoma and neutropenia. It is highly possible for A. flavus to invade arteries of lungs or brain and cause infection. A. flavus infection is typically treated with antifungal drug such as amphotericine, itraconazole, oriconanzol, posaconazole and capsofungin.[12]

Fusarium moniliforme:

F. moniliforme is the fungus belonging to phylum Ascomycota also known as Gibberella fujikuroi. It is one of the most prevalent fungi associated with basic human and animal dietary sample such as Corn.

F. moniliforme is a fungal plant pathogen. It causes bakanae disease in rice seedlings, by overloding them with the phytoharmone gibberellin as its metabolic by product. Toxins produced by F. moniliforme are fusaric acid, fusarin, gibberellins, moniliforme and fumonism. There are some opportunistic infectious agents of humans and animals. They also produced trichothecene toxins which cause poisoning of animals if the infected material is eaten.

Penicillium chryogenum :

P. chrygenum fungus belonging to Trichomaceae family. has been used industrially to produce penicillin and xanthocillin. x, to treat pulp mill waste and to produce enzymes polyamine oxidase, phospogluconate dehydrogenase and glucose oxidase.[13-14] It is source of several β-lactum antibiotics, in that most significant is penicillin.

P. chrysogenum usually reproduces by forming dry chains of spores from brush-shaped conidophores. The conida are typically carried by air current to new coloniseation site. P. chrysogenum has number of uses but there are some drawbacks like. It cause penicillium rot blue-eye in plants.[15] The air born asexual spores of p. chrysogenum are important human allergens. Vacuolar and alkaline serine protease have been implicated as he major allergenic protiens.[16]

Fungal Growth

When microorganisms are inoculated in a suitable medium and incubated under appropriate conditions, a tremendous increase in the cell mass or number of cells occurs within a relatively short time. This is called microbial growth. Actually growth may be defined as irreversible increase in mass of the whole or part of living organism by the synthesis of macromolecules.

Factor Affecting on Fungal Growth:

Following factors affect on the fungal growth.

1.Temperature: For any specific organism there will be minimum and maximum temperature which refers to the temperature at which considerable growth occurs. The optimum temperature is the temperature at which the growth rate is high.

2.pH of the medium : Enzyme activity is also known to be conditioned by the composition of medium, although different enzymes have different pH optima for their activity. The general favorable range lies between pH 4 to pH 8.

3.Humidity : A relative humidity between 95 to 100 % generally supports efficient growth of most fungi and that below 80-85 % inhibit their growth.

4.Concentration : A few work have studied the effect of concentration of essential trace elements for their optimum growth. Concentration of essential trace elements higher than the optimum have been found to be inhibitor for the growth of different fungi studied by them. To control the harmful effect of fungi and also to test the biological application of the newly synthesized complexes. It was felt wiser to undertake the antifungal study of the prepared compounds.

To ward off the harmful effect of these friendly fungi and to search control measures for such effects and also to test the biological applications for the newly synthesized complexes it was felt to undertake the study of the present complexes.

Synthesis of ligands

Synthesis of Aryl Hydrazone (B1, B2 Ligands) using 1-Phalazine Hydrazine Hydrochloride:

The heterocyclic compound, 3-acetyl-4-hydroxy-1-ethyl/methyl-2(1H)-quinolone was used for the synthesis of Schiff base hydrazones. A hot 50 mL ethanol was taken in clean and dry round bottomed flask. To this, (9.82 gm 0.05 mol) . 1-phthalazinyl hydrazine hydrochloride was taken. To neutralize the salt of 1- phthalazin hydrazine hydrochloride, strong base triethyl amine was added. The solution was warmed up to dissolution. In this hot solution, (10.85 gm 0.05 mol) of 3-acetyl-1-ethyl/methyl-4-hydroxy-2(1H)-one was added and the solution was warmed with continuous stirring. Yellow solid product formed was filtered off, washed with ethanol and dried in vacuum desiccator.

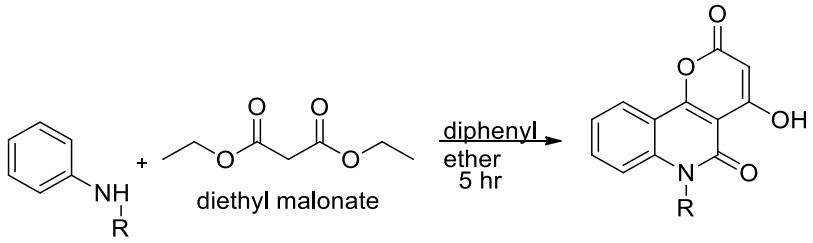
Synthesis of 3-acetyl-1-ethyl/1-methyl-4-hydroxy-2(1H)-quinolone:

The synthesis was carried out in two step:

Thomas Kappe1 et. al. synthesized 3-acetyl-4-hydroxy-2(1H)-quinolones. This was obtained by hydrolytic ring opening and subsequent decarboxylation from the corresponding pyrano [3,2,-c] quinolon-2,5(6H)-diones.

Step I : Synthesis of 4-hydroxy-6-ethyl/methyl-2H-purano[3,2-c]quinoline-2,5(6H)-dione i. e. pyranoquinolone.

A mixture of (12.118 gm 0.1 mole) of N-ethyl-aniline and . (32 gm 0.2 mole) of diethyl malonate was taken. To this, 60 gm of diphenyl ether was added as a solvent. This reaction mixture was refluxed in distillation apparatus equipped with 20-cm Vigureux-column during 3-5 hours. The liberated ethanol about (20 mL) was distilled out until no more ethanol was formed. The mixture was allowed to cool and treated with 50 mL dioxane. It was kept overnight. Brown colored crystalline compound was obtained. This was filtered by suction and washed with dioxane and diethyl ether to remove diphenyl ether. Melting point -218-220 ˚C. Yield - 80 %

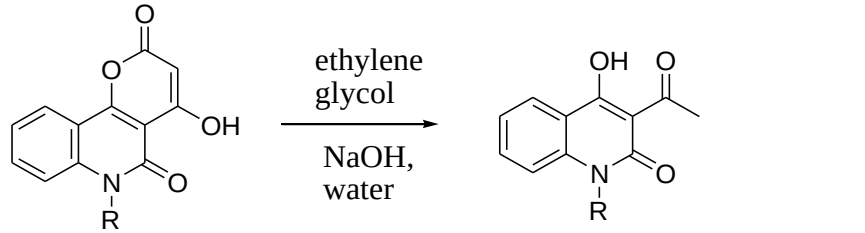


$R=CH_3,C_2H_5$

Step II. Synthesis of 3-acetyl-4-hydroxy-1-ethyl/1-methyl-2(1H)-quinolone:

A suspension of (20 gm. 0078 mole) pyrano quinolone in 250 mL ethylene glycol mono ether was taken and about (16 gm 0.4 mole) of sodium hydroxide dissolved in 30 mL of water was added in it and heated to gentle boiling for one hour and poured on 1000 mL ice cold water. The obtained solution slowly acidified with 50 mL concentrated hydrochloric acid. Strong evolution of carbon dioxide takes places. After complete precipitation and evolution of CO2, the solid obtained was filtered on suction pump and dried at 80˚c and recrystallized from ethanol

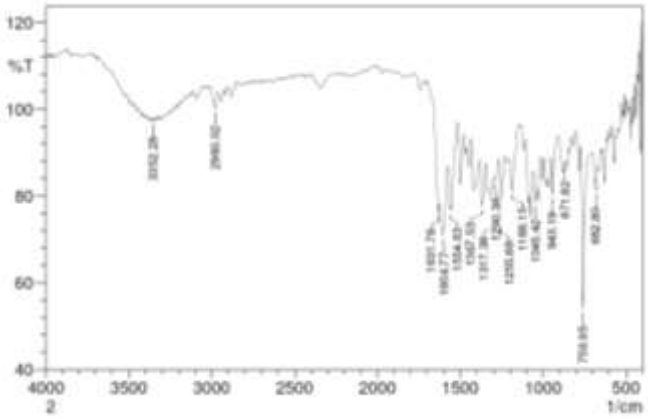
Melting point-113-115 ˚C. Yield -85%.



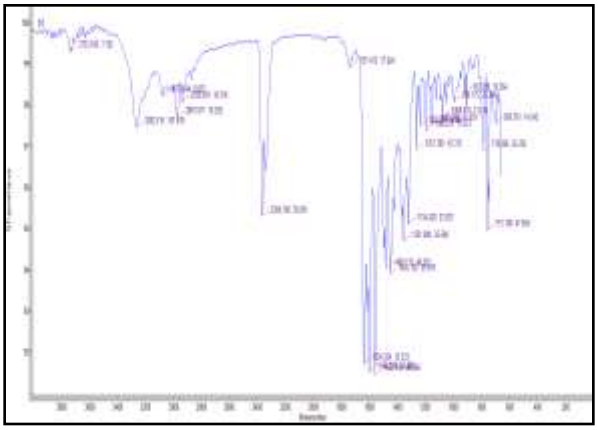
$R=CH_3,C_2H_5$

IR Spectra of 3-acetyl-1-ethyl-4-hydroxy-2(1H)-quinolone shown in

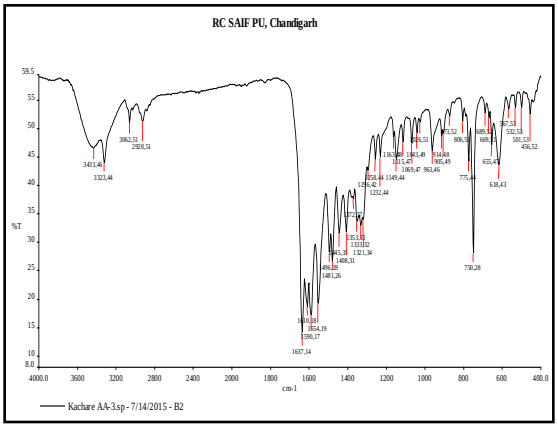
The product was recrystallized from DMF-ethanol mixture (yield 85%)



IR Spectra of 3-acetyl-1-ethyl-4-hydroxy-2(1H)-quinolone

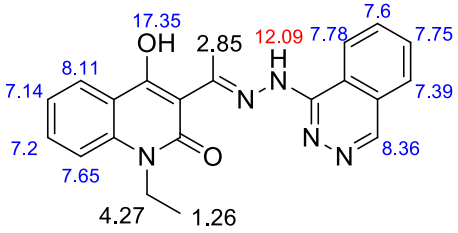


Infrared Spectra of Ligand B1



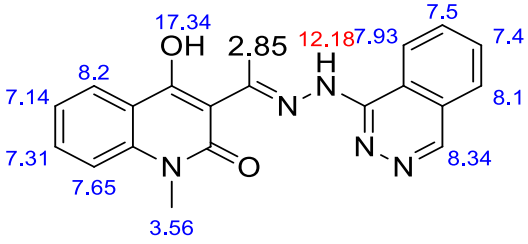
Infrared Spectra of Ligand B2

Ligand B1

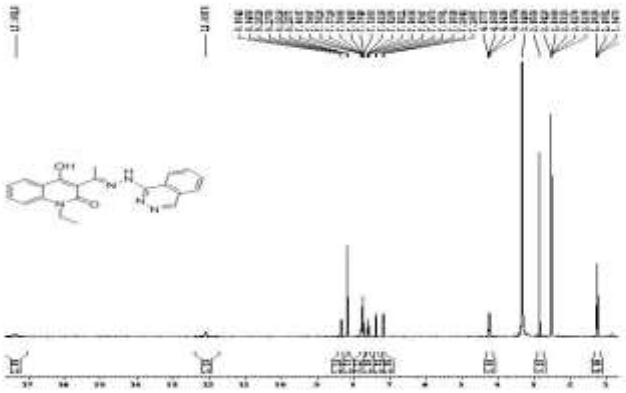


Chemical Formula: $C_{21}H_{19}N_5O_2$

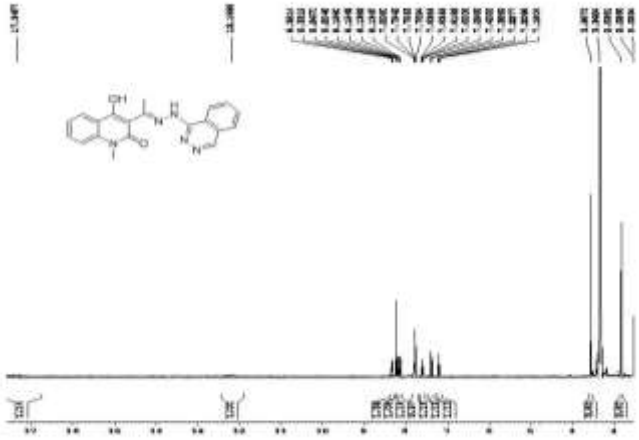
Ligand B2



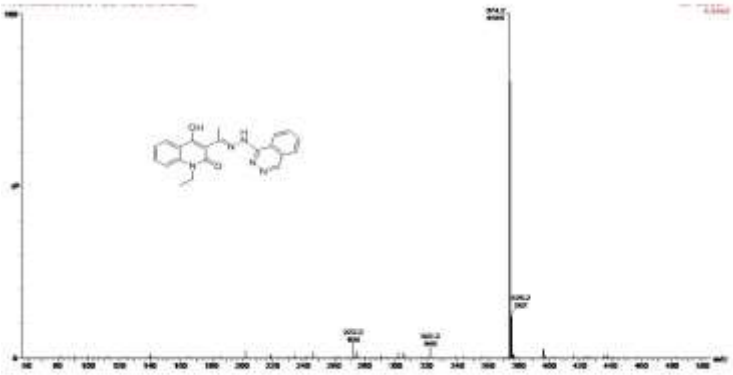
Chemical Formula: $C_{20}H_{17}N_5O_2$



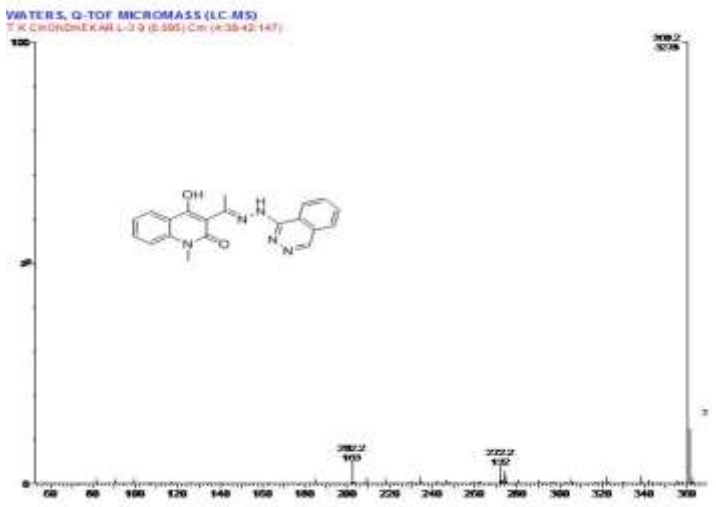
1H Nuclear Magnetic Resonance Spectra of Ligand B1



1H Nuclear Magnetic Resonance Spectra of Ligand B2



Mass spectra of Ligand B1



Mass spectra of Ligand B2

Synthesis of Metal Complexes:

The metal complexes are synthesized by various methods. In the present work, the transition metal complexes of Schiff bases are synthesized by stirring the ethanolic solution of ligand (For B1, B2), methanolic solution of ligand for and metal acetates of Mn(II), Co(II), metal nitrates of (Fe(III), Cu(II), Ni(II) & Zn(II)) in the 2:1 molar ratio. The slightly alkaline condition maintained by adding 10% alcoholic ammonia solution.

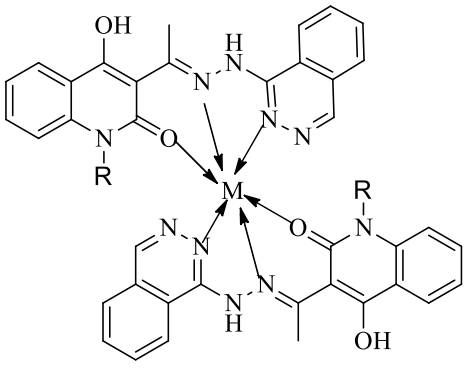
Procedure:

0.02 mole of ligand was taken in round bottomed flask containing 30 mL. of anhydrous ethanol (For B1, B2), methanolic solution of ligand was used and boiled for few minutes. A hot solution of 0.01 mole of metal salt in 20 mL of ethanol was added drop wise to the solution of the ligand. To this reaction mixture, 10% alcoholic ammonia was added up to slightly alkaline pH. The complexes of different metals were precipitated at different pH range. This pH range was definite for a given complex and found to be characteristic of that complex. The contents were stirred on magnetic stirrer for 5 hr. The solid metal complex separated out and washed with ethanol/methanol three to four times. Dried in vacuum desiccators over anhydrous granular calcium chloride.

The metal salts used for the synthesis of metal complexes were Mn(II) acetate, Co(II) acetate, and Nitrates of Fe(III), Ni(II), Cu(II) and Zn(II).

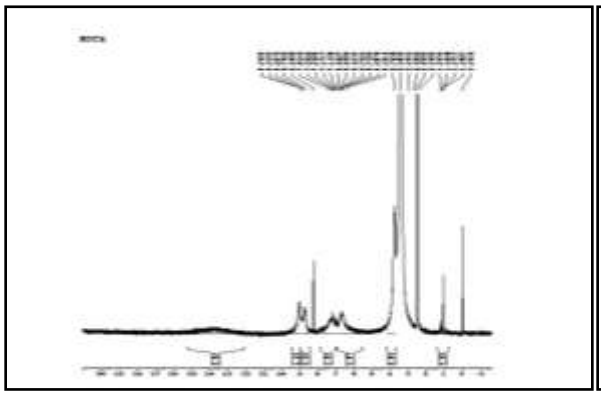
In case of cobalt complexes interesting structural features are reported. The most common oxidation states for cobalt are +2 and +3, where the +2 and +3 ions result in the formation of paramagnetic and diamagnetic complexes respectively. For the synthesis of present cobalt complexes, cobalt(II) acetate was used as metal salt13 but we get the Co(III) complexes due to air oxidation.[17-19] The melting point/decomposition temperature of the complexes were determined by Thiele's melting apparatus. The pH range, observed melting points and colors of metal complexes are tabulated in

Structure for B_1 and B_2 ligand metal complexes

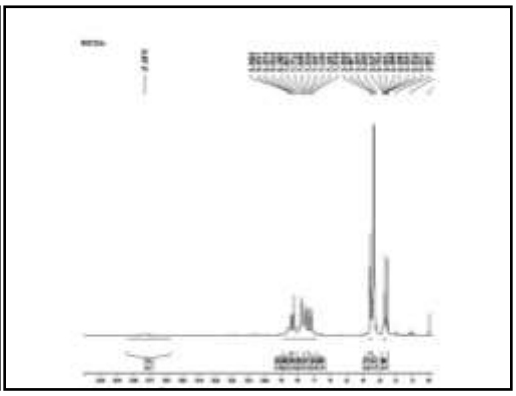


R=CH_2-CH_3, CH_3

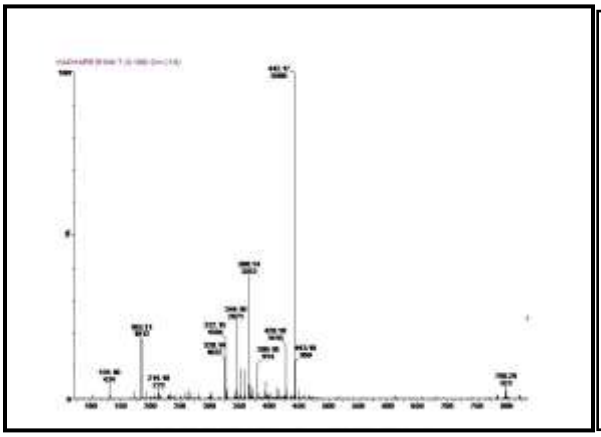
Sr. No.	B1 Complexes	pH range of precipitation	Color	Melting point / Decomposition Temp. 0C
1	Zinc (II)	7.5 -8.5	Yellow	>300
2	Mn(II)	7.5 -8.5	Brown	>300
3	Fe(III)	7.5 -8.5	Reddish brown	>300
4	Cu(II)	7.0 - 7.5	Reddish brown	>270
5	Ni(II)	7.0 - 7.5	Brown	>260
6	Co(III)	7.5 -8.5	Reddish brown	>300
Sr. No.	B2 Complexes	pH range of precipitation	Color	Melting point / Decomposition Temp. 0C
7	Zinc (II)	7.5 -8.5	Yellow	>300
8	Mn(II)	7.5 -8.5	Coffee brown	>300
9	Fe(III)	7.5 -8.5	Coffee	>300
10	Cu(II)	7.0 - 7.5	Reddish brown	>270
11	Ni(II)	7.0 - 7.5	Brown	>270
12	Co(III)	7.5 -8.5	Dark brown	>300



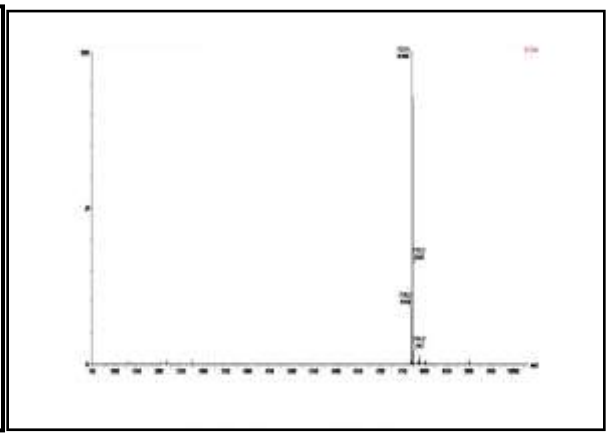
^{1}H Spectra of B2Cu Complex



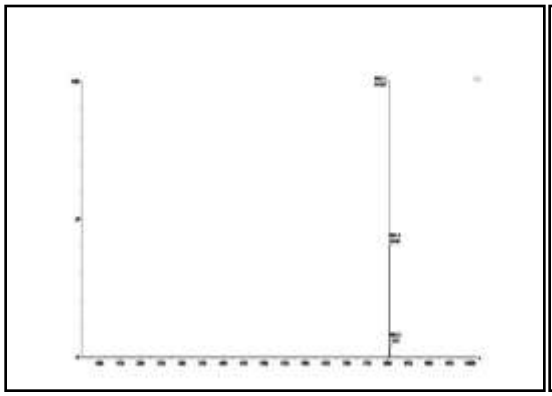
^{1}H Spectra of B_2Zn Complex



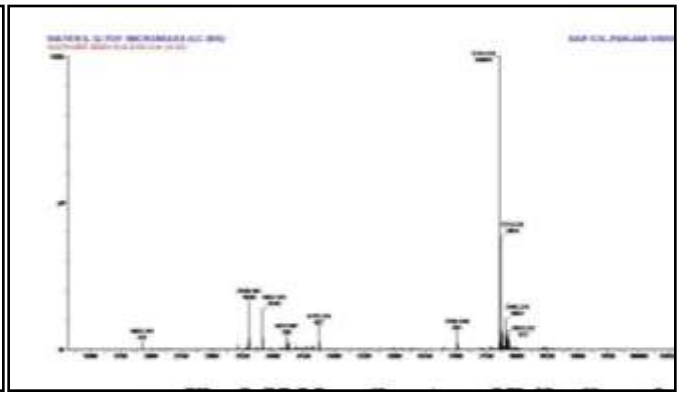
Mass Spectra Of B1Mn Complex



Mass Spectra Of B1Fe Complex



Mass Spectra Of B1Co Complex



Mass Spectra Of B2ZnComplex

Experimental: Antifungal Activity

The Schiff base binuclear metal complexes are screened in vitro for antifungal activity. The fungal toxicity of Schiff base ligands and their metal complexes were studied in vitro against Aspergillus niger, Aspergillus flavus, Fusarium moniliforme and Penicillium chrysogenumat fixed 1% concentration. The method used followed R. J. Cruickshank, P. Dugnid, R. R. Swain. The species were collected from department of Microbiology N.S.B. college Nanded.

Experimental Procedure for Antifungal Activity:

Antifungal activity was performed by Poison Plate Method. The medium used was Potato Dextrose Agar (Himedia). The medium was prepared and sterilized at 10 Psi in autoclave for 15 minutes. Then the compound to be tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. A plate with DMSO was prepared as blank (negativecontrol) similarly a plate with 1% Gresiofulvin was prepared as standard reference plate (positivecontrol).

Aspergillus niger, Penicilliumchrysogenum, Fusarium moniliforme and Aspergillusflavus were selected as test fungal cultures. They were allowed to grow on slant for 48 hr. so as to get profuse sporulation. 5mL of 1:100 aqueous solution of Tween 80 was added to the slant and spores were scraped with the help of nicrome wire loop to form suspension. The fungal suspension was spot inoculated on the plates prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hr. After incubation, plates were observed for the growth of inoculated fungi. Results were recorded as growth of fungi (no antifungal activity), reduced growth of fungi (moderate antifungal activity), and no growth of inoculated fungi.

Test Compounds	Antifungal growth			
	Aspergillus niger	***Aspergillus flavus***	***Fusarium moniliforme***	***Penicillium chrysogenum***
	1%	**1%**	**1%**	**1%**
B_1	+ve	+ve	+ve	+ve
B_1-Mn	+ve	RG	RG	RG
B_1-Fe	+ve	+ve	+ve	+ve
B_1-Co	RG	RG	-ve	RG
B_1-Ni	RG	+ve	RG	RG
B_1-Cu	+ve	+ve	+ve	+ve
B_1-Zn	+ve	+ve	+ve	+ve
B_2	+ve	+ve	+ve	+ve
B_2-Mn	RG	+ve	RG	RG
B_2-Fe	+ve	+ve	+ve	+ve
B_2-Co	RG	+ve	RG	RG
B_2-Ni	+ve	+ve	+ve	+ve
B_2-Cu	+ve	+ve	+ve	+ve
B_2-Zn	+ve	RG	-ve	RG
+ve control (DMSO)	+ve	+ve	+ve	+ve
-ve control (Griseofulvin)	-ve	-ve	-ve	-ve

Legends: +ve growth = (Antifungal activity absent)
-ve growth = (Antifungal activity present)
RG = Reduced growth (More than 50% reduction in growth observed)

Results and Discussion:

Antifungal activity of ligand and complexes were tested in vitro against fungi that is Aspergillus niger, Penicillum chrysoganum, Fusarium moniliforme and Aspergillus flavus by poison plate method using potato dextrose agar medium at fixed 1% concentrationin DMSO.

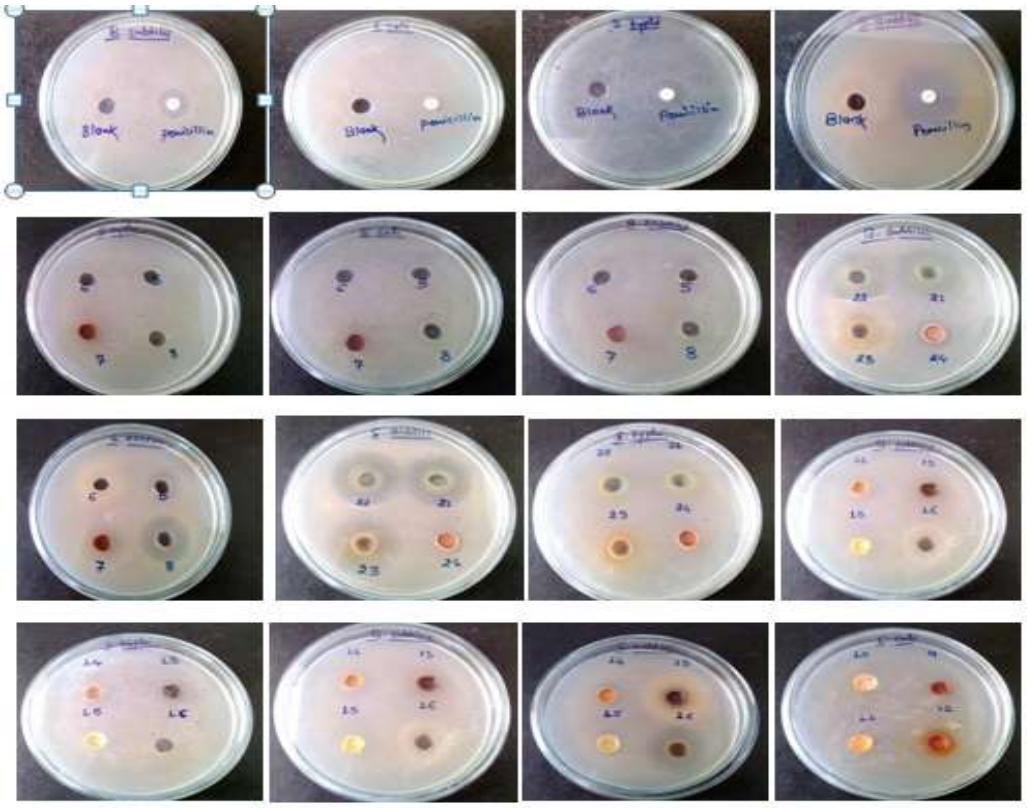
Gresiofulvin was prepared as standard reference plate. The ligand show moderate activity against F. moniliforme but antifungal activity not observed against other three fungi. Ligand do not show antifungal activity but their complexes shows appreciable activity. Antifungal activity of complexes increased several times on being coordinated with metal ions. Co(III) complex show more than 90% reduction of fungal growth for all fungi. Mn(II) complexes also show more than 90% fungal growth reduction for F. moniliforme. All other complexes shows more than 50% reduction in fungal growth for all fungi.

The fungicidal activity of the metal complexes may be due to the change in structure because of coordination or chelation which tend to make complexes more powerful fungicidal agents, thus inhibiting the growth of fungi.[21] Fungicidal activity in complexes is higher because of the increased lipid solubility of the metal complexes as compared to ligand towards fungal cell membrane.[22-23] This increased lipophilicity enhance the penetration of the complexes in to lipid membrane.

The results indicate that the complexes show more activity and the ligands have comparatively less activity against some organisms under identical experimental conditions. This would suggest that the chelation facilitate the ability of a complexes to cross a cell membrane and can be explained on the basis of Tweedy's chelation theory and overtone's concept. Overtone concept states that, antimicrobial activity in complexes is higher because of the increased lipid solubility of the metal complexes as compared to ligand towards the cell membrane.

Antifungal activity is absent in ligands but the complexes show more than 90% activity. In some complexes more than 50% reduction in fungal growth is observed.

Antifungal Activities of Representative Ligands and Their Metal Complexes



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FE (III) TRANSITION METAL COMPLEX OF HYDRAZONE SCHIFF BASE LIGAND DERIVED FROM 1-ETHYL-4-HYDROXY-QUINOLINE-2(*1H*)-ONE AND 1-ETHYL-2-HYDRAZINO BENZOTHIAZOLE ITS SYNTHESIS OF CHARACTERIZATION AND ANTIMICROBIAL STUDIES.

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Abstract:
Coordination compound of Fe (III) ions with newly synthesized Schiff base ligand (E)-3-(1-(2-(benzo[d]thiazol-2yl)hydrazono)ethyl)-1-ethyl-4-hydroxyquinolin-2(1*H*)-one. The obtained compounds and its complexes are characterized on the basis of elemental analysis, magnetic susceptibility, UV visible spectra, FTIR ,^{1}H NMR spectra, mass spectra, and TG-DTA Form the analytical data the stoichiometry of metal complex has been found to be the 2:1 ligand to metal ratio. Therefore the complex may be formulated as [Fe (L_2). All the analysis data shows that complex are monomeric hexa coordinated octahedral structure. The ligand and complex have been screened for their antibacterial activity using the Agar cup method at fixed concentration of 1% against microbial strains, *Eschershia coli, Salmonalla typhi, Staphylococcus aureus, Bacillus substilis*. The antibacterial activity of ligand and its complex illustrates that the ligand and complex seems to be inert towards the E *.coli , S. typhi* the its complex show higher activity than ligand against *Staphylococcus aureus* and *Bacillus substill*. Antifungal activity of ligand and complex were tested against in vitro against fungi that is *Aspergillus niger, Penicilum chrysoganum, Fusarium moniliforme, Aspergillus flavus* by poison plate method using potato dextrose agar medium at fixed (1%) concentration. Ligand does not show fungal activity but it's complex show better activity in Fe(III) complex, which suggest that the incorporation of metal in the ligand results in increasing the antimicrobial activity.

Introduction:

Transition metal complexes containing Schiff base hydrazone ligands have been specific interest for many years (1). Transition metal complexes of hydrazone compounds have been screened for their medicinal properties (2). The metal complexes of Schiff base derived from heterocyclic compounds have been a center of attraction of many workers in recent years (3). But the chelating abilities of Schiff bases derived from nitrogen heterocyclic is 2-quinolone. Quinolones are famous categories of compounds known by their intensive biological activity and their vital importance in medicines and pharmaceuticals this prompted us to carry out intensive research work on these class of compounds(4,5).

In the present communication, we describe the synthesis and characterization of Fe(III) transition metal complex containing a tridentate (NNO) Schiff base ligand. In addition to physicochemical studies, the complex have been tested in vitro to assess their antibacterial activities against some common reference bacteria and fungi and results were compared with standard.

Experimental

Material and Methods:

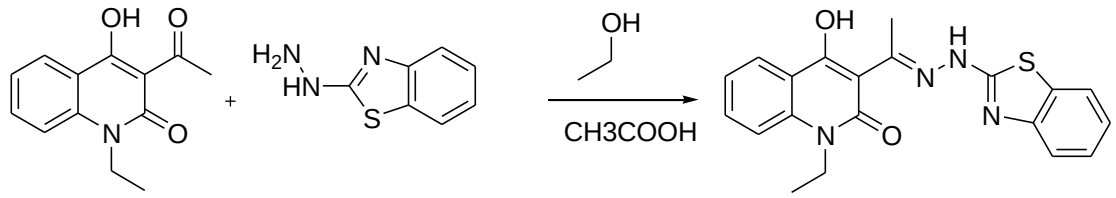
All chemicals were of AR grade purchased from Sigma Aldrich and used for synthesis of ligand. AR grade metal nitrate of Fe (III) from S. D. Fine chemicals were used for complex preparation. Spectral grade solvents were used for spectral measurements. The carbon, hydrogen, nitrogen contents were determined on Perkin Elmer (2400) CHNS analyzer. IR spectra were recorded on a FTIR Brucker spectrophotometer in 400-4000cm-^{1} range. The UV/ Vis spectra were recorded on Shimadzu UV 160 spectrophotometer for complex in DMSO. ^{1}H-NMR spectra of ligand measured in DMSO using TMS as an internal standard. The LC- MS spectra were recorded on a Waters, Q-TOF Micro mass

(LC-MS). Magnetic moments were measured by Guoy's method and were corrected for diamagnetism of the components using Pascal's constants. Conductance were measured on Elico Cm-180 Conductometer using 10^{-3} M solution in DMSO. Powder XRD studies were carried out with a Bruker AXS D8 Advance X-ray diffractometer.

Synthesis of ligand:

3-Acetyl-1-ethyl-4-hydroxy-2(*1H*)-quinolone (5.47 gm 0.025 mol) was taken in clean and dry round bottomed flask and 50 mL ethanol was added in it. The solution was warmed. To this, 5-10 mL of glacial acetic acid was added as a catalyst and (4.13 gm, 0.025 mol) of 2-hydrazino benzothiazole was added in it. This reaction mixture was refluxed and stirred for 1/2 hr. on rotaheatingmantel. Yellow solid product formed was filtered off, washed with ethanol and dried in vacuum desiccators (6).

The product was recrystallized from DMF-ethanol mixture (yield 85%)



Synthesis reaction of ligand

Synthesis of metal complex:

To the hot solution of ligand in ethanol (0.02 mol in 25mL), hot ethanolic solution of Iron nitrate metal salt (0.01 mol in 25 mL) was added drop wise. To this reaction mixture, 10% ethanolic ammonia was added to adjust the pH of solution to 7.5 to 8.5. The reaction mixture stirred for 3-5 hours in warm condition on magnetic stirrer to get complex in solid form. The solid complex was filtered off, washed several times with ethanol and dried in vacuum over $CaCl_2$.

Results and Discussion

Complex is colored solids, stable for air and heat. Insoluble in water, ethanol, methanol, DCM but easily soluble in polar solvents DMF /DMSO.

The analytical data like color, melting point, % of elements, magnetic moments and conductance are presented in Table 1. The elemental analysis and mass spectra of the complex show 1:2 (metal: ligand) stoichiometry.

Molar conductance and Magnetic susceptibility measurements:

Molar conductance measurements were performed in DMSO (10^{-3}M) solutions at room temperature. The molar conductance data indicate that both complex is non electrolytic in nature. Magnetic susceptibility of the powdered complex was carried out by using Guoy's balance method at room temperature with $Hg[Co(SCN)_4]$ as a calibrant.

The complex shows magnetic moment 6.02 BM indicative of five unpaired electrons in agreement with reported value for high spin octahedral Fe(III) complex(6).

Table 1 : Physical, Analytical Data of Ligand and its Metal Complexes:

Compound	**Mol. formula**	**Colour**	**M.P .˚C**	**Mol. Wt.**	**C%**	**H %**	**N%**	**O%**	**S%**	**Metal %**	**$\mu_{(eff)}$ B.M.**	**Molar conductance Ohm^{-1} cm^2 mol^{-1}**
HL	$[C_{20}H_{18}N_4O_2S]$	Yellow	241	378	63.10 (63.48)	4.34 (4.79)	15.18 (14.80)	8.91 (8.46)	8.47 (8.47)			---

(FeL_2)	[$C_{40}H_{36}N_8O_4S_2Fe$]	Coffee	>300	812	56.89 (56.16)	14.47 (14.28)	13.37 (13.78)	7.92 (7.87)	8.16 (7.89)	7.10 (6.87)	6.02	20

Electronic absorption spectra:

The electronic absorption spectra of ligand and complex was recorded in DMSO over the range 200-800 nm. The electronic spectrum of ligand exhibit two absorption transitions at 27248 cm^{-1} (367.5nm) and 30581 cm^{-1} (327nm) assigned to the n-π* and π-π* transitions of azomethine and 2-quinolone. Electronic spectra of Fe(III) complex show transitions at 25316 cm^{-1} (395nm) due to $^6A_{1g} \rightarrow {}^4T_{2g}$ and charge transfer band at 34542 cm^{-1} (289nm) (7,8,9,).

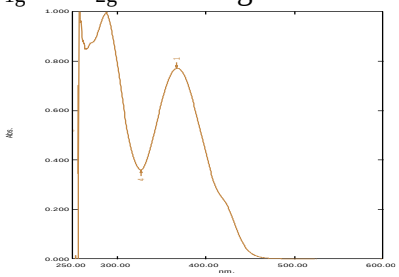


Fig. 1 UV spectra of ligand

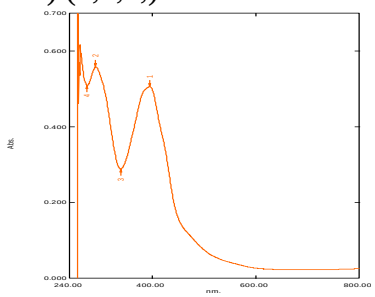


Fig. 2 UV Spectra of Fe (III) complex

FTIR spectra:

The FTIR spectrum of metal complex was compared with that of free ligand in order to investigate the mode of chelation of metal ions with ligand. In FTIR spectrum of free ligand, some characteristic bands at 3398, 3109, 1654, 1594, 1556, 742 cm^{-1} assigned to enolic -OH, NH, C=O(quinolone), >C=N(azomethine), >C=N (ring), N-H out of plane stretching respectively. In complex the ligand behaves as a ONN tridentate via the >C=O (quinolone), >C=N (azomethine) and >C=N (in benzothiazole ring) groups (10,11). This fact is supported by the following evidences. In complex there is presence of a band in the region 3385 cm^{-1} due to OH indicating 4-hydroxy group of quinolone does not take part in coordination. The IR stretching frequency of >C=O (quinolone) in the complex observed in the region 1609 $cm^{-1.}$ This Shift to lower frequency of carbonyl group of quinolone by 43 cm^{-1}. The shift of azomethine >C=N group to lower frequency region by 5 cm^{-1} with respect to free ligand, indicates that the nitrogen of the azomethine group coordinate to the metal ion. The >C=N (ring nitrogen) groups shift to lower frequency range by 58-36 cm^{-1} which indicates that they form coordinate bond with metal atom. The IR stretching frequency of >C=O (quinolone), >C=N(azomethine), >C=N (ring) groups shift to higher frequency range which indicates that they form coordinate bond with metal atom. Which is further supported by observation of (M-N) and υ (M-O) stretching frequency 450cm^{-1} and 500 cm^{-1} in complex (12,13).

Table 2 : Salient Features of IR Spectral Data of Ligands.

(Assignment of band frequencies to bond vibration modes)

Ligands	**υ(OH) Enolic**	**υ (NH) Hydrazone**	**υ (C=O) Quinolone**	**υ (C=N) Azomethine**	**υ (C=N) Ring nitrogen**	**υ (C=C)**	**υ (-NH) out of plane**	**υ (M-N)**	**υ (M-O)**
Ligand	3398 (m)	3109 (m)	1654 (s)	1594 (b)	1556	1467 (s)	742 (s)	-	-
FeL2 Complex	-	3057 (s)	1609 (s)	1589 (s)	1590 (s)	1365 (s)	745 (s)	450	500

The IR Spectra of ligand and Fe(III) complex are presented in Fig. 3 to Fig. 4 and their group absorption frequencies are given in Table 2.

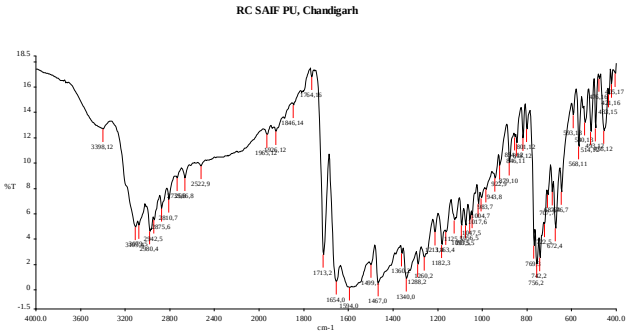


Fig. 3 IR Spectra of ligand

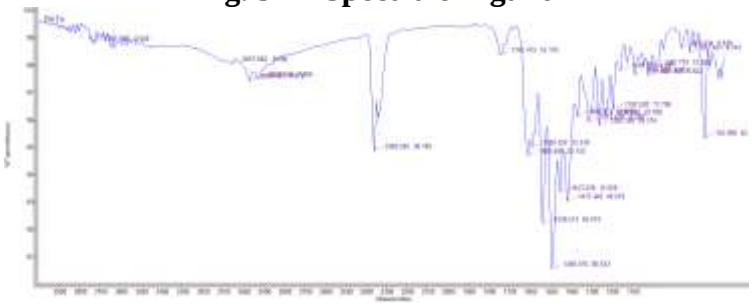


Fig. 4 IR Spectra of Fe (III) complex

^{1}H-NMR Spectra of Ligand.

^{1}H- NMR Spectra of ligand was recorded in DMSO. It shows signals at 1.34 (t, 3H, N-CH_{2}-- CH_{3}^{*}) (14), 2.76 ppm. (s,3H, N=C-CH_{3})(15), 4.44 ppm.(s,2H,N-CH_{2}), 7.18-8.21 ppm. (m, 8H, H_{arom}), 11.98 ppm. (s,1H, N-H), 16.81 δ (s,1H,OH_{enolic}) (16).

Fig. 5 ^{1}H-NMR Spectra of Ligand.

Mass spectra of ligand and Fe (III) complex:

Mass spectrum of the ligand supports its proposed formulation. It reveals the molecular ion peak m/z at 378.1 a.m.u, consistent with the molecular weight of the ligand. Also there is presence of [M+2], [M+1], at m/z 380.19, 379.20. Due to loss of enolic OH proton by forming stable ion. The mass spectra of the complex of Fe (III), support their proposed structure (17). Fe (III) complex show [M^{+}] molecular ion peak at m/z 810.91 which exactly match with their calculated mass. Observed mass of ligand and Fe (III) complex exactly match with their calculated mass(18).

Table 3

Sr. No.	Name of Ligand/Complex	Calculated Mass of ligand / Complex	Found Mass of ligand/Complex	Fragmentation Peaks.
1	Ligand	378.1 (378.45)	378.1 379 380.19	379(M+1) 380.19(M+2)
2	FeL_{2}	812.58	810.91	808, 807

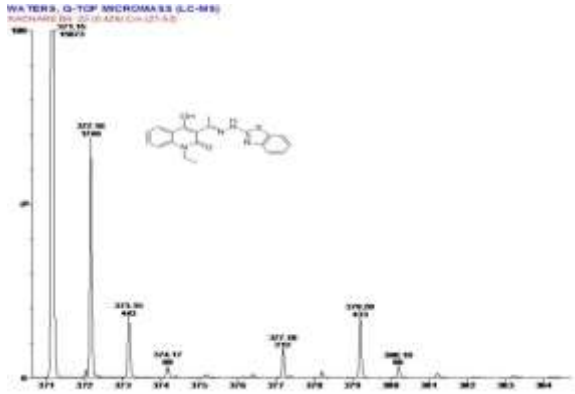


Fig. 6 Mass spectra of ligand

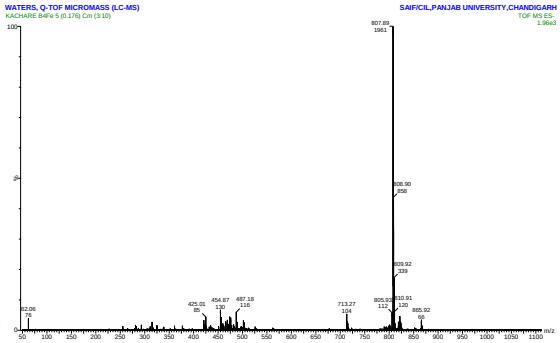


Fig. 7 Mass spectra of Fe (III) complex

Thermogravimetric Studies:

The simultaneous TG/DT analysis of Fe (III) complex was studied. The TG-DTA curve of Fe (III) complex of shows first weight loss at 57.62˚C indicating presence of lattice water. The anhydrous compound undergoes two step decomposition. The first step shows decomposition within temperature range 276-14˚C with 54% (calc. wt. loss 54.31%). This may be due to oxidative decomposition of non-coordinated part of ligand. Which is authenticated by broad endothermic peak in DTA at 276.78˚C. The second step of decomposition with weight loss 38% within temperature range 477.48˚C, which is supported by broad endothermic peak in DTA curve at 643.06˚C, corresponds to the decomposition of coordinated part of the complex. Above 750˚C, TG curve attain a constant level corresponding to metal oxide.

The thermal kinetic parameters ΔS, Ea and Z for non- isothermal decomposition of complexes have been calculated by Horowitz-Metzger (19) and Coats-Redfern (20) method from TG-DTA curves (Fig. 8) and are presented in Table 2.

Generally, with decreasing value of ΔE, the value of Z increases, and higher value of activation energy suggest higher stability (21). In the present complexes, the value of E_a decrease with the increasing value of (Z) i.e. frequency factor indicating that the activated complexes have more ordered or more rigid structure than the reactants or intermediate and that the reactions are slower than normal (22).

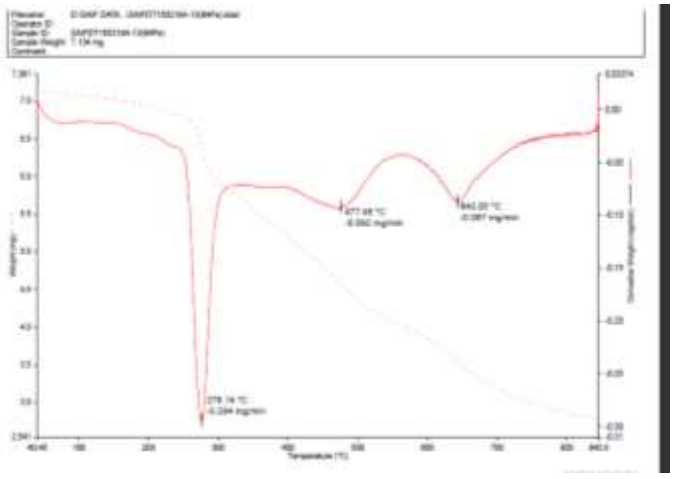


Fig. 8 TG/ DTA of Fe(III) Complex

Table 4 : Thermodynamic and Kinetic Parameters

Metal complex	Method	Step	Decomp. Temp.	Order of Reaction	Ea(KJ mol^{-1})	ΔS(KJ mol^{-1})	ΔG(KJ mol^{-1})	Z (S^{-1})	Correlation Coefficient (r)
FeL_2	H-M C-R	I	276.14	0.55	44.59 33.93	-185 -	58.46 50.53	121736.63 1080757546	0.976 0.989

						221.64			
	H-M **C-R**	II	750	0.55	32.26 26.75	- 259.41 -245.7	57.10 54.22	132386 1211966	0.999 0.998

Biological activity of the compounds:

***In vitro* antibacterial activity of the compounds**

The antimicrobial activity of the ligand and the complex were tested against the standard microbial strains, *Escherishia coli*, *Salmonella typhi*, *staphylococcus aurus*, *Bacillus substilis* by agar cup method at fixed concentration of 1% in DMSO. The test was performed on nutrient agar Cup of 10 mm diameter were borered in the agar plate with stirile cork borer. All solutions were prepared in DMSO(1%) was add on cup, One cup for DMSO as blank and other for standard reference penicillium was also placed on the seeded nutrient agar. Then the plates were shifted to incubator at 37˚c and incubated for 24 hours. Activity measured in diameter (mm). The results obtained are presented in (Table 5)

Inspection of the data revealed that complex and ligand lack the activity towards the Gram-negative bacteria *E. coli* and *S. typhi*. On the other hand, ligand and complex shows activity against Gram-positive bacteria *S. aureus* and *B. substilius*. Activity of Fe(III) complex shows highest antibacterial activity(23,24).

Table 5: Report for antibacterial testing.

Medium - Nutrient Agar Method- Agar cup method

Dose of compound - 1% cup size - 10 mm

Compound	*Escherishia coli*	*Salmonella typhi*	*Stapylococcus aureus*	*Bacillus subtilis*
Ligand(L)	--	--	13	-ve
(FeL_2)	--	--	24	15
Penicillin	28	36	14	20

Legends: -ve = No Antibacterial Activity

Zone of inhibition = --- mm

***In vitro* antifungal activity of the compounds**

Compound were screened in vitro against *Aspergillus niger* , *Penicilium chrysogenum* , *fusarium moneliforme* , *Aspergillus flavus*, by poison plate method with potato dextrose agar media. the compound were tested at the 1% concentration in DMSO and compared with control.

Gresiofulvin was prepared as standard reference plate. The fungal suspension was spot inoculated on the plates prepared using compound with nicrome wire loop. The plates were incubated at room temperature for 48 hours. The result obtained are presented in Table 6. The ligand does not show antifungal activity. Antifungal activity of complex increased several times on being coordinated with metal ions (25). Fe (III) complex shows more than 90% reduction of fungal growth for all fungi(26).

Table 6 : Report for Antifungal testing

Ligands	Antifungal growth			
	Aspergillus niger	*Aspergillus flavus*	*Fusarium moniliforme*	*Penicillium chrysogenum*
	1%	**1%**	**1%**	**1%**
L	-ve	-ve	-ve	-ve
(FeL_2)	RG	-ve	-ve	-ve
+ve control	+ve	+ve	+ve	+ve

(DMSO)				
-ve control (Griseofulvin)	-ve	-ve	-ve	-ve

Legends: +ve growth = (Antifungal activity absent)
-ve growth = (Antifungal activity present)
RG = Reduced growth (More than 50% reduction in growth observed)

Conclusion:

In the light of above discussion we have proposed octahedral geometry for iron complex. On the basis of physicochemical and spectral data discussed above, one can assume that the ligand behaves as, ONN tridentate, coordinating via quinolone carbonyl, azomethine nitrogen and nitrogen of benzothiazole ring in complex. The mass spectra of ligand and its metal complex are in great accordance with calculated and observed. Thermogravimeric studies revealed that complex is rigid and stable. The Fe (III) complex is biologically active and are having greater activity compared to free ligand.

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ANTIFUNGAL SCREENING OF HOMO AND HETERODINUCLEAR SCHIFF BASE COMPLEXES OF Zn(II), Mn(II), Fe(II), Cu(II), Ni(II)) AND Co(II) DERIVED FROM 2-AMINO 3-HYDROXY PYRIDINE AND 2- HYDROXYL 1-NAPTHALDEHYDE

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Abstract:
The important pathogens such as Escherichia coli, Salmonella typhi, Staphylococcus aureus, and Bacillus subtilis are wildly caused many diseases. So antifungal activity of Zn (II), Fe(II), Mn (II) Ni (II), Co (II) and Cu (II) Homo and hetero binuclear Schiff base complexes against four kinds of fungal species was established Methods: In this study, antifungal activity of metal complexes derived from. 2-amino 3-hydroxy pyridine and 3-ethoxy salysialaldehyde by inter-complex reaction. The complexes were characterized by elemental analysis and estimation of metals. Thermal behavior of the complexes was studied by TG-DTA analysis. Structures of the complexes were elucidated by spectroscopic methods like, infrared spectroscopy, UV-visible spectroscopy, mass spectrometry and 1HNMR spectroscopy. The powder X-ray diffraction study suggested crystalline nature of the complexes with tetragonal geometry. Magnetic moments and electronic spectra reveal tetrahedral structure of the complexes. Antifungal activity of ligands and their binuclear complexes were studied in vitro against Aspergillus niger, Aspergillus flavus, Fusarium moniliforme and Penicillium chrysogenumat fixed 1% concentration.
Keywords: Schiff base, inter-complex reaction, binuclear complex, Aspergillus niger, Aspergillus flavus, Fusarium moniliforme and Penicillium chrysogenum.

Introduction:
The biotic component of the world include vast variety of living organisms. The biotic component which includes all the living organisms belonging to five kingdoms. The fungi represent one of the most important kingdoms of living organisms. Fungi have eukaryotic cellular organization and possess heterotrophic mode of nutrition. They can't synthesis their own organic food through photosynthesis or chemosynthesis and instead obtain it from other sources. The fungi may be unicellular or multi cellular with -uni, -bi or multinucleate cell. The heterotrophic mode of nutrition in fungi may be saprophytic, parasitic, having definite cell wall but not differentiated into roots, stems and leaves and vascular systems which we find in advance plants. The cell wall composition is not similar in all the fungi. In some fungi cellulose is the chief cell wall constituent. The external factors such as the composition of the medium used for fungal cultivation, pH value and temperature influence the composition of fungal cell walls.[1]Reproduction of fungi take place through the spores which are produced either by asexual or sexual methods. Spores are specialized cells one or more celled, set apart for reproduction. They arises as buds on specialized hyphae (exogeneous) or may be born in special receptacles, The spores fruits (endogeneous) on germination, each spores forms a new haploid mycelium. Fungi also show vegetative method of reproduction. The vegetative multiplication may occur by fragmentation, fission and budding.The fungi helps in recycling nutrient and play a significant role in some fungi to help in improving the industrial production of various substances like gluconic acid, citric acid, alcohol, other organic acids and enzymes. Fungi also used in agriculture, medicine, food and nutrition. The genus Trichoderma a well known bio-control agent used in present day agriculture for controlling a safe and ecofriendly way of plant disease[2]. Saccharomyces cerevisiae or Baker's yeast, a single-cell fungus, is used to bake bread and other wheat products.[3-4]. Some mushrooms used as therapeutics in traditional and folk medicines, such as chinesemedicine.[5] Penicilliumchrysogenum and other fungi produces antibiotics, such as penicillin and cepalosporine etc. Worldwide use of these antibiotics for the treatment of bacterial diseases, such as leprosy, tuberculosis, syphlis and many others. 'White rot fungi' can degrade insecticides, herbicides, coal tars, creosote and heavy fuels and turn them into carbon dioxide, basic element and water.[6] Some fungi act as pathogens for plants and animals. They can destroy timber, textile. food and leather. In the present study four fungi Aspergillus niger, Penicilliumchrysogenum. Fusarium moniliforme and Aspergillus flavus are used.

Aspergillus niger:

Aspergillus niger is a kind of Ascomycetes includes the fungi which are commonly called as black mold or black aspergillis. A. niger is a plant deleterious fungi and air born as comycetes to which A. niger belong are found on paddy crops.

The fungus A. niger is omnivorous in occurrence. The fungi is always associated with food grains, fruits and vegetables during

storage and cause spoilage to these stored product.

A. niger is a fungi of great biotechnological importance as it synthesizes useful product of high commercial value. Aspergillus are highly useful in various industrial process such as fermentation, baking, brewing and industrial manufacturing of organic acids, fats, cheese, enzymes, vitamins and antibiotic because of their ability to secrete digestive enzymes. Using A. niger, citric acid and gluconic acid are manufactured commercially on large scale.[7] In Japan, A. oryzae is used in fermentation to manufacture sake, an alcoholic beverages from rice starch and to make various fermentated food products. A. niger is used in the study of many biological process and can detect traces quantities of elements Cu, Fe, Mn and Zn from unknown sample.

The genus is widely distributed in nature. A huge number of spores of these organisms are suspended in air and responsible for varity of allergies and respiratory disorders in human being. A. fumigatus, A. flavus, A. niger and other species cause Aspergillosis disease. The Aspergillosis of the lungs is much more common in birds. It is also common in cattle, sheep, horse and occurs rarely in human being. [8] Several species grow on leather, timber, cloth and reduced their commercial value. They are also common contaminants of cultures in bacteriological and mycological laboratories.

Penicillium chryogenum :

P. chrygenum fungus belonging to Trichomaceae family.has been used industrially to produce penicillin and xanthocillin. x, to treat pulp mill waste and to produce enzymes polyamine oxidase, phospogluconate dehydrogenase and glucose oxidase.[9] It is source of several β-lactum antibiotics, in that most significant is penicillin.

P. chrysogenum usually reproduces by forming dry chains of spores from brush-shaped conidophores. The conida are typically carried by air current to new coloniseation site. P.chrysogenum has number of uses but there are some drawbacks like. It cause penicillium rot blue-eye in plants.[10] The air born asexual spores of p. chrysogenum are important human allergens. Vacuolar and alkaline serine protease have been implicated as he major allergenic protiens. [11]

Fusarium moniliforme:

F. moniliforme is the fungus belonging to phylum Ascomycota also known as Gibberellafujikuroi. It is one of the most prevalent fungi associated with basic human and animal dietary sample such as Corn.

F. moniliforme is a fungal plant pathogen. It causes bakanae disease in rice seedlings, by overloding them with the phytoharmone gibberellin as its metabolic by product. Toxins produced by F. moniliforme are fusaric acid, fusarin, gibberellins, moniliforme and fumonism. There are some opportunistic infectious agents of humans and animals. They also produced trichothecene toxins which cause poisoning of animals if the infected material is eaten.

Aspergillus flavus:

A. flavus generally associated on ceral grains, legumes and tree nuts. A. flavus is a pathogenic and saprophytic.[12] Many strains of Aspergillus produces significant quantity of toxic compounds known as mycotoxins, which, when consumed are toxic to mammals.[13] Aspergillus infections have grown in importance in the last few years. A. flavus is more common in air, A. flavus is the second leading cause of invasive aspergillosis and it is the most common cause of superficial infection. Experimental invasive infection in mice show A. flavus to be 100- fold more virulent than A. fumigatus particularly common clinical syndromes associated with A.flavusinclude chromic granulomatous sinusitis, keratitis, cutaneous aspergillosis. A. flavus produces aflatoxins, the most toxic and potent hepatocrcinogenic natural compound.

In humans, A. flavus aflatoxin production can lead to acute hepatitis immunosuppression, hepatocellular carcinoma and neutropenia. It is highly possible for A. flavus to invade arteries of lungs or brain and cause infection. A. flavus infection is typically treated with antifungal drug such as amphotericine, itraconazole, oriconanzol, posaconazole and capsofungin.[14]

Fungal Growth

When microorganisms are inoculated in a suitable medium and incubated under appropriate conditions, a tremendous increase in the cell mass or number of cells occurs within a relatively short time. This is called microbial growth. Actually growth may be defined as irreversible increase in mass of the whole or part of living organism by the synthesis of macromolecules.

Factor Affecting Fungal Growth:

Following factors affect the fungal growth.

1. Temperature: For any specific organism there will be minimum and maximum temperature which refers to the temperature at which considerable growth occurs. The optimum temperature is the temperature at which the growth rate is high.
2. pH of the medium : Enzyme activity is also known to be conditioned by the composition of medium, although different enzymes have different pH optima for their activity. The general favorable range lies between pH 4 to pH 8.
3. Humidity: A relative humidity between 95 to 100 % generally supports efficient growth of most fungi and that below 80-85 % inhibit their growth.
4. Concentration : A few work have studied the effect of concentration of essential trace elements for their optimum growth. Concentration of essential trace elements higher than the optimum have been found to be inhibitor for the growth of different fungi studied by them. To control the harmful effect of fungi and also to test the biological application of the newly synthesized complexes. It was felt wiser to undertake the antifungal study of the prepared compounds.

To ward off the harmful effect of these friendly fungi and to search control measures for such effects and also to test the biological applications for the newly synthesized complexes it was felt to undertake the study of the present complexes.

Synthesis of Metal Complexes:

The method used in the synthesis of metal complexes consists of following three steps. In the first step, 2-amino-3-hydroxy pyridine (2A-3OH-PYR), (0.404gm) in absolute alcohol (~20mL) was prepared and a solution of iron, manganese, zinc, copper, nickel and cobalt acetates (0.439g/0.347g/0.490g/0.998g/0.0.497g/0.498g) in rectified spirit (20mL),were mixed, stirred for an hour to obtain a four coordinated complex, M(2A-3OH-PYR)2 in solution as shown in equation-1,

$$M+2(2A\text{-}3OH\text{-}PYR) \rightarrow M(2A\text{-}3OH\text{-}PYR)_2 \quad 1$$

In the second step,3-ethoxy salicylaldehyde(3E-SAL),(0.665 g) in absolute alcohol (~20ml) was prepared and a solution of iron, manganese, zinc, copper, nickel and cobalt acetates (0.439g/0.347g/0.490g/0.998g/0.0.497g/0.498g) in rectified spirit(~20ml), were mixed and stirred for an hour to obtain a four coordinated complex, M'(3E-SAL)2 in solution. The reaction is shown in equation 2.

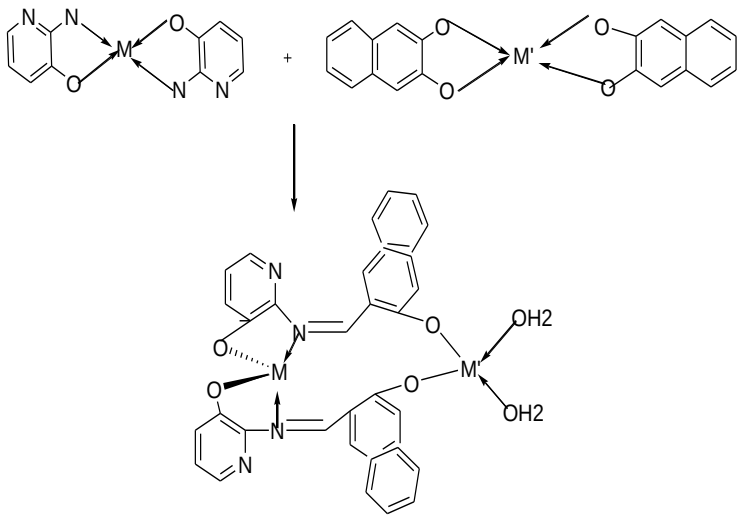
$$M'+ (3E\text{-}SAL)_2 \rightarrow \quad M' (3E\text{-}SAL)_2 \quad 2$$

In third step, a solution of M (2A-3OH-PYR) 2 was added to the refluxing solution of M' (3E-SAL) 2.The reaction mixture was refluxed for 6-hours in a water bath to obtain the product under slightly alkaline condition created by sodium hydroxide. The precipitate was then filtered, washed with ethanol and dried over fused CaCl2. The third step of the reaction is depicted in equation 3.

$$M (2A\text{-}3OH\text{-}PYR)_2 + M' (3E\text{-}SAL)_2 \rightarrow MM'(SB)_2(H_2O)_2 \quad 3$$

All complexes were prepared by the above discussed method .The heterodinuclear complex, whereas homobinuclear complexes were obtained when M & M'=Zn (II),Mn (II),Fe(II) ,Cu(II),Ni(II)and Co(II) respectively in heterodinuclear complexes and M & M'=Fe,(II) Zn (II),Mn (II), Cu(II),Ni(II) and Co(II) in mononuclear complex. The melting points of all the complexes were found to be higher than 300^0C.

Fig :1 Reaction Scheme



Experimental : Antifungal Activity

The Schiff base binuclear metal complexes are screened in vitro for antifungal activity. The fungal toxicity of Schiff base ligands and their metal complexes were studied in vitro against Aspergillus niger, Aspergillus flavus, Fusarium moniliforme and Penicillium chrysogenumat fixed 1% concentration. The method used followed R. J. Cruickshank, P. Dugnid, R. R. Swain. The species were collected from department of Microbiology N.S.B. college Nanded.

Experimental Procedure for Antifungal Activity:

Antifungal activity was performed by Poison Plate Method. The medium used was Potato Dextrose Agar (Himedia). The medium was prepared and sterilized at 10 Psi in autoclave for 15 minutes. Then the compound to be tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. A plate with DMSO was prepared as blank (negativecontrol) similarly a plate with 1% Gresiofulvin was prepared as standard reference plate (positivecontrol).

Aspergillus niger, Penicilliumchrysogenum, Fusarium moniliforme and Aspergillusflavus were selected as test fungal cultures. They were allowed to grow on slant for 48 hr. so as to get profuse sporulation. 5mL of 1:100 aqueous solution of Tween 80 was added to the slant and spores were scraped with the help of nicrome wire loop to form suspension.

The fungal suspension was spot inoculated on the plates prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hr. After incubation, plates were observed for the growth of inoculated fungi. Results

were recorded as growth of fungi (no antifungal activity), reduced growth of fungi (moderate antifungal activity), and no growth of inoculated fungi.

Results and discussion

Antifungal activity of ligands and their complexes were tested in-vitro against fungi. ie. Aspergillus niger, Penicillium chrysogenum Fusarium moneliforme and Aspergillus flavus by poision plate method using potato dextrose agar medium at fixed 1 % concentration in DMSO. Griseofulvin was prepared as standard reference plate. The results of antifungal activity screeing of the metal complexes are presented in Table6.1-3.

All the metal organic ligands show variable activity. ligands L2 show good antifugal activity against all the fungal species studied. 50% Activity is shown by ligands L4, against second species and remain inactive against remaining all other fungal species. 50% activity is shown by ligand L1 against IInd and iv th species and remain inactive against Ist and IIIrd fungal species studied. ligand L3 show good antifungal activity against second species and 50% activity is shown by remaining fungal species studied. Antifungal activity of dinuclear complexes is shown in Table 2 and 3. In general, most of these complexes are found to be inactive against all fungal species.

Few complexes like, Mn2 and Fe2 show more than 50% activity against all fungal species. Over all, Zn Zinc is a moderately toxic element and the toxicity of the element is throught to be due to the poisoning of enzymes by way of complexing reactive sites such as amino, imino and sulphydryal groups present on enzymes.[14]

Nickel is essential in trace amounts but toxic at higher concentrations.[15] The release of Ni+2 from the complexes in excess amounts would interrupt the biological processes, the toxic effect of the metal thus being exerted.

Copper in biological systems is known to be present in several different forms such as Cu+, Cu^2+, blue Cu+, coupled $(Cu^2+)_2$ etc. and because of this, it is difficult to understand the mode of its antimicrobidal action.[16] Most probably, the Cu+2 would be exerting its toxicity through redox processes shultling between Cu+2 and Cu+. Damage of membrane is also possible in case of copper if its concentration is more.

The fungicidal activity of the metal complexes may be due to the change in structure because of coordination or chelation which tend to make complexes more powerful fungicidal agents.[17] thus inhibiting the growth of fungi.

Fungicidal activity in complexes is higher because of the increased lipid solubility of the metal complexes as compared to ligand towards fungal cell membrane. [18-19] This increased lipophilicity enhance the penetration of the complexes in to lipid membrane.

The result indicates that the metal organic ligands as well as the bimetallic complexes show variable activity against same organisms under identical experimental conditions.

Table 1: Antifungal Activity of Ligands

Test compound	Inhibit			
	Aspergillus niger	Penicillium chrysogenum	Fusarium moneliforme	Aspergillus flavus
	1%	**1%**	**1%**	**1%**
Griseofrin	-ve	-ve	-ve	-ve
DMSO	+ve	+ve	+ve	+ve
L_5	RG	RG	-ve	RG
L_6	+ve	RG	+ve	+ve
L_7	-ve	-ve	-ve	-ve
L_8	+ve	RG	+ve	+ve

Legends: +ve growth = (Antifungal activity absent)
-ve growth = (Antifungal activity present)
RG = Reduced growth (More than 50% reduction in growth observed)

Antifungal Activity of Dinuclear Complexes of 3-Ethoxy Salicylaldehyde and 2-Amino 3-Hydroxy Pyridine with Zn(II),Mn(II) and Fe(II).

Table 2 : Report for Antifungal Testing

Test compound	Inhibit			
	Aspergillus niger	Penicillium chrysogenum	Fusarium moneliforme	Aspergillus flavus
	1%	**1%**	**1%**	**1%**
Griseofrin	-ve	-ve	-ve	-ve
$Zn_2(SB)_2(H_2O)_2$	+ve	+ve	+ve	RG
$ZnFe(SB)_2(H_2O)_2$	+ve	+ve	RG	RG
$ZnMn(SB)_2(H_2O)_2$	+ve	+ve	RG	RG

$Mn_2(SB)_2(H_2O)_2$	RG	RG	RG	RG
$MnFe(SB)_2(H_2O)_2$	+ve	RG	RG	RG
$MnZn(SB)_2(H_2O)_2$	RG	RG	RG	+ve
$Fe_2(SB)_2(H_2O)_2$	RG	RG	RG	RG
$FeZn(SB)_2(H_2O)_2$	+ve	+ve	+ve	+ve
$FeMn(SB)_2(H_2O)_2$	RG	RG	RG	+ve
DMSO	+ve	+ve	+ve	+ve

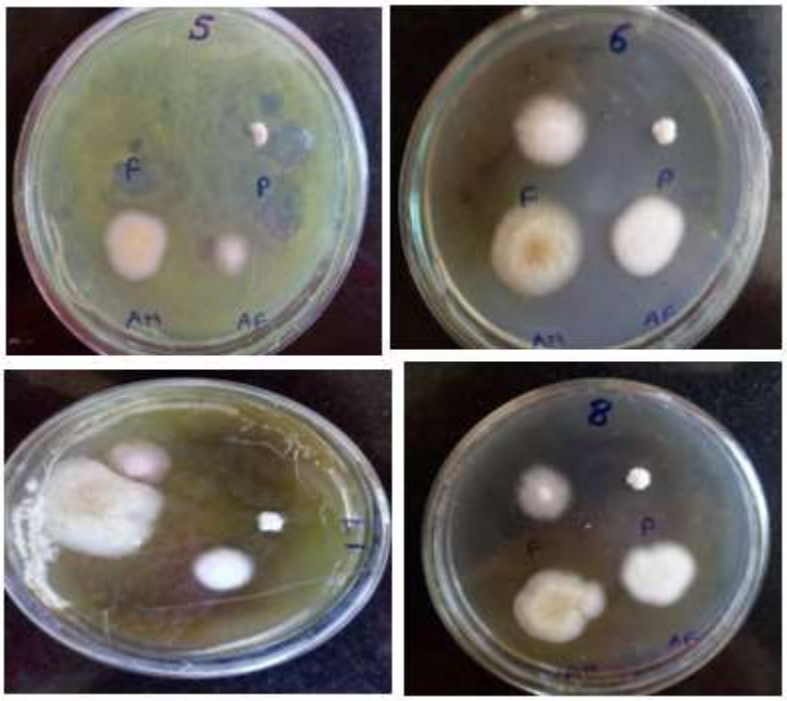
Complex: +ve growth = Antifungal activity absent
-ve growth = Antifungal activity present
RG = reduced growth (more than 50% reduction in growth observed)

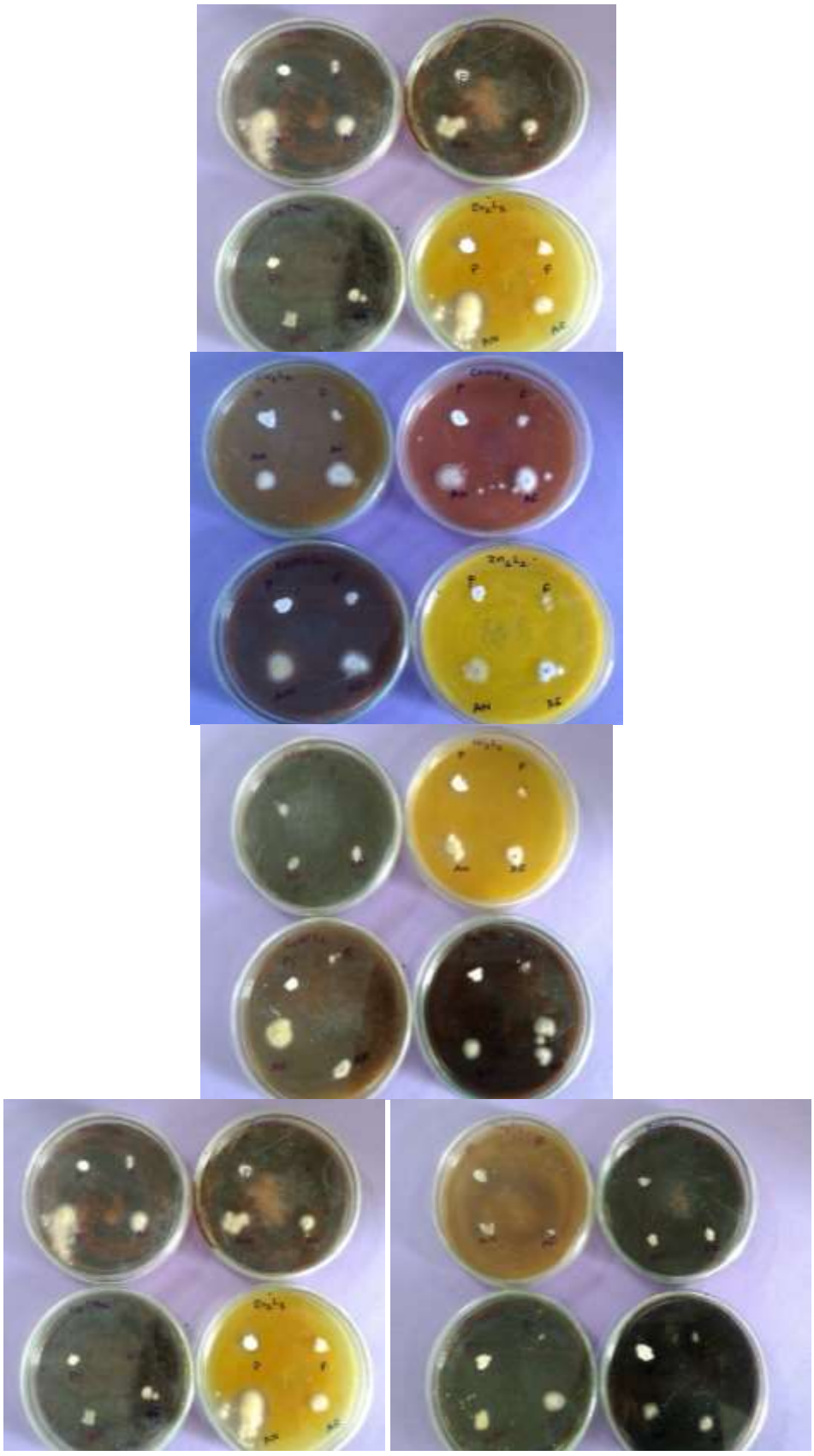
Antifungal Activity of Dinuclear Complexes of 3-Ethoxy Salicylaldehyde and 2-Amino 3-Hydroxy Pyridine with Co(II),Ni(II) and Cu(II).

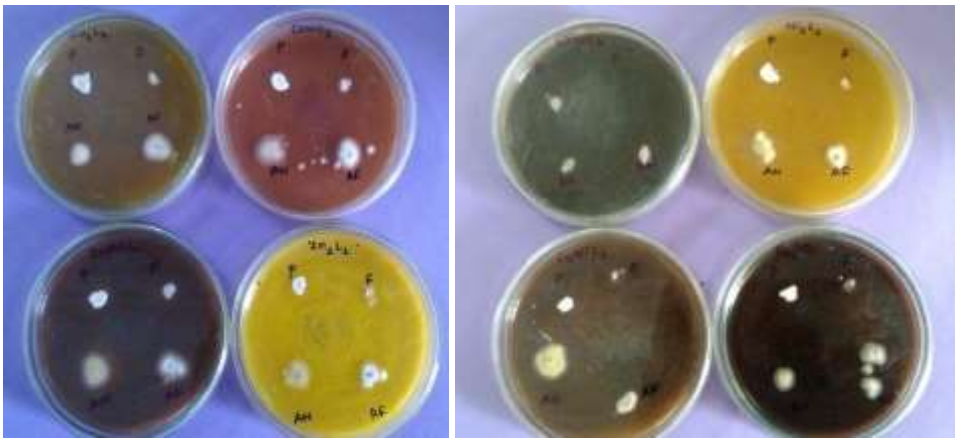
Table 3: Report for Antifungal Testing

Test compound	Inhibit			
	Aspergillus niger	Penicillium chrysogenum	Fusarium moneliforme	Aspergillus flavus
	1%	**1%**	**1%**	**1%**
Griseofrin	-ve	-ve	-ve	-ve
$Co_2(SB)_2(H_2O)_2$	RG	RG	+ve	RG
$CoNi(SB)_2(H_2O)_2$	RG	RG	-ve	RG
$CoCu(SB)_2(H_2O)_2$	RG	RG	-ve	RG
$Ni_2(SB)_2(H_2O)_2$	+ve	+ve	-ve	RG
$NiCu(SB)_2(H_2O)_2$	RG	RG	-ve	RG
$NiCo(SB)_2(H_2O)_2$	RG	RG	-ve	RG
$Cu_2(SB)_2(H_2O)_2$	-ve	+ve	-ve	-ve
$CuCo(SB)_2(H_2O)_2$	RG	RG	-ve	RG
$CuNi(SB)_2(H_2O)_2$	RG	-ve	-ve	RG
DMSO	+ve	+ve	+ve	+ve

Complex: +ve growth = Antifungal activity absent
-ve growth = Antifungal activity present
RG = reduced growth (more than 50% reduction in growth observed







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Synthesis, Characterization And Biological Study Of 3-Acetyl-4-Hydroxy-1-Methyl-2*(1H)*-Quinolone Hydrazone Based Cu(II) Metal Complex

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ABSTRACT : The present study emphasizes hydrazone Schiff base of 3-acetyl-4-hydroxy-1- methyl-2(1H)-quinolone and its Cu(II) metal complex. The metal complex was synthesized using Schiff base hydrazone synthesized from 4-hydroxybenzhydrazide and 3-acetyl-4-hydroxy-1- methyl-2(1H)-quinolone. Hydrazone complexes were subjected to elemental analysis, UV visible, magnetic susceptibility, FTIR, 1H NMR spectra, mass spectra, thermal analysis, XRD analysis and antimicrobial activity. IR spectra indicate that free ligand exist in the hydrazo-ketone form in solid states. The ligand behaves as a neutral tridentate with coordination involving the carbonyl of 2(1H) quinolone, hydrazone nitrogen and keto oxygen of amide group that is ONO donor sites. The magnetic and spectral data indicate octahedral geometry for all complexes. The molar conductivity values indicating non electrolytic nature. The mass spectra and analytical data the stiochitometry of metal complex has been found to be the 2:1 ligand to metal ratio. Ea, ΔS, ΔH and ΔG parameters were evaluated for thermal decomposition stages of complexsing Horowitz-Metzer and Coats-Redferm methods. X-ray diffraction data suggests triclinic structure of Cu(II) complex. The ligand and their metal chealets have been screened for their antibacterial activity using the Agar cup method at fixed concentration of 1% against microbial strains, E.coli, S. typhi, S. aureus, B. subtilis. The antibacterial screening of ligand and it's complex illustrates that ligand and complex seems to be inert towards the gram positive bacteria E. coli and S. typhi The complex show higher activity than ligand against gram negative bacteria S. aureus and B. subtilis. Antifungal activity of ligand and complex were tested in vitro against fungi that is A. niger, P. chrysogenum, f. moniliforme, A. flavus by poison plate method using potato dextrose agar medium at fixed (1%) concentration. Ligand does not show fungal activity but it's Cu(II) complex show better activity. It suggests that the incorporation of metal ion in the ligand results in increasing the antimicrobial activity.

KEYWORDS: ONO donar ligand, octahedral complexes, 1H NMR, Mass, TG-DTA, p-XRD, Biological activity.

I. INTRODUCTION

Schiff base hydrazones are obtained by condensation of aldehydes or ketones with acid hydrazides or hydrazines. They are versatile ligands in coordination chemistry because their wide range of applications [1-5] in catalysis, medicine, corrosion and analytical chemistry as well as functional materials [6]. Synthetic flexibility of these Schiff base hydrazones occupy special place because transition metal complexes of these ligands developed due to chelating capability. Metal complexes of hydrazones proved to have potential applications in luminescence probes [7] and molecular Sensor [8]. In continuation of these studies [9-12] using hydrazone ligand bearing ONO donar set, here we report the synthesis, spectroscopic, thermogravimeric and p-XRD analysis of Cu(II) complex using tridentate Schiff base like hydrazone ligand (E)-4-hydroxy-N'-(1-(4-hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3yl)ethylidene)benzohydrazide, derived from the condensation of 3-acetyl-4-hydroxy-1- methyl-2(1H)-quinolone and 4-hydroxybenzhydrazide.

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II. EXPERIMENTAL

2.1. Materials and Methods

All the chemical are of analytical grades. 1-methyl aniline, diethyl malonate, diphenyl ether, n-butanol, acetic acid, 4-hydroxybenzhydrazide and metal nitrate salts. All chemicals were perched from SD fine chemicals. Solvents were dried and distilled before use according to standard methods [13]. The precursor 3-acetyl-4-hydroxy-1-methyl-2*(1H)*-quinolone was prepared by standard method [14]. The metal nitrates were used in hydrated form. Elemental analyses (C,H,N,O,) were performed on Perkin Elmer-2400. IR spectra were recorded on FTIR Spectrophotometer model RZXC Perkin Elmer in the range (400-4000 cm^{-1}), ^{1}H NMR spectra were recorded on Bruker Avance II at 400 M_{HZ} using teramethyl silane as an internal standard. Electronic spectra were recorded using Shimadzu-1800 spectrophotometer using DMSO as a solvent. The LC-MS spectra were recorded on a Waters, Q-TOF Micro Mass (LC-MS). Conductance were measured on Elico cm-180 Conductometer using $10^{-3}M$ solution in DMSO. Room temperature magnetic data were collected on a Guoys balance using mercury (II) tetrathiocynato cobaltacetate (II) as a calibrant. Diamagnetic contributions were estimated for each compound by using Pascal's constants. The TG-DTA analysis of Cu(II) complex was performed in an inert nitrogen atmosphere on Perkin Elmer STA 6000. The heating rate was 10˚/min and flow rate of nitrogen 50 ml/min. The reference substance used was α Al_2O_3 in platinum crucible and sample weighed in the range of 4-12 mg. P-XRD studies were carried out with a Bruker AXS D8 Advance was recorded employing Cu k radiation (λ= 1.541 A˚) in the range 0-60˚.

2.2. Antimicrobial activity

The antibacterial activity were performed against microbial strains, *E. coli, S. typhi, S. aureus, B. subtilis* by agar-cup method at fixed concentration of 1% in DMSO. In this method test was performed on nutrient agar cup of 10 mm diameter were borered in the agar plate with stirile cork borer. All solutions were prepared in DMSO (1%) was added on cup, one cup blank DMSO and other for standard reference. The plates were incubated for 24 h at 37˚C. The diameters of zones of inhibition for all test compounds were measured and the results compared with penicillium of the same concentration as that of the test compounds under identical conditions.

Antifungal activity of the compounds was evaluated against fungi that is *A. niger*, *P. chrysogenum*, *f. moniliforme, A. flavus* by poison plate method using potato dextrose agar medium at fixed (1%) concentration. The plates were incubated at 37˚C for 48 h. The diameters of the zone of inhibition for all the test compounds were measured and results compared with standard drug Grisofulvin of same concentration under identical conditions.

2.3. Synthesis of ligand:

The equimolar mixture of 3-acetyl-4-hydroxy-1-methyl-2(1*H*)-quinolone (0.01 mol) and 4-hydroxybenzhydrazide (0.01 mol) in methanol (30mL) were refluxed in the presence of catalytic amount of glacial acetic acid (5-10 drops) for 3 hours on rotaheating mantal. The reaction mixture was then cooled to room temperature and the solid compound formed was filtered. It was then washed with methanol and dried and recrystallized from mixture of ethanol-DMF. (Yield 85%, M.p. 230˚C).

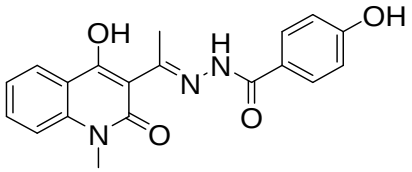

Fig. 1 structure of ligand

2.4. Synthesis of metal complex

Synthesis of Cu(II) metal complex. The metal complex by adding to the hot solution of ligand in methanol (0.02 mol in 25mL), hot methanolic solution of metal salt (0.01 mol in 25 mL) was added drop wise. To this reaction mixture, 10% methanolic ammonia was added to adjust the pH of solution to 7.5 to 8.5. The reaction mixture stirred for 3-5 hours in warm condition on magnetic stirrer to get complex in solid form. The solid complex was filtered off, washed several times with methanol and dried in vacuum over $CaCl_2$.

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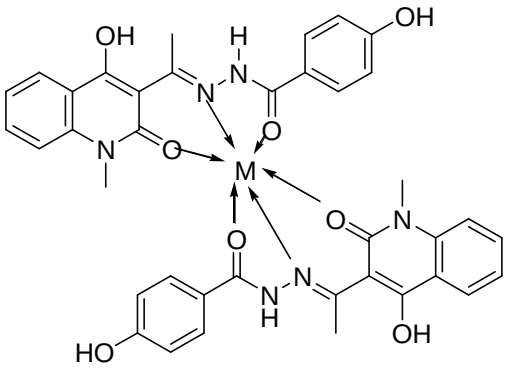

Where M= Cu(II)

Fig. 2 structure of metal complex

III. RESULTS AND DISCUSSION

The Schiff base is soluble in DMF, DMSO and insoluble in common organic solvents. The synthesis of ligand is checked by elemental analysis, FT-IR, ^{1}HNMR and LC-Mass. The physical characteristics of the Schiff base and its metal complex are given in **Table 1**. The metal complex is soluble in ethanol, methanol and water. The elemental analysis data of the Schiff base and its metal complex is consistent with the calculated results from the empirical formula represent in Fig 2.

3.1. Conductivity measurements

The molar conductivity values for freshly prepared DMSO (10^{-3}M) solution of the complex molar indicate that complex is non electrolytic in nature [15].

Table 1 : Physical, Analytical Data of Ligand and its Metal Complexes

Compound	Mol. formula	Colour	M.P. ˚C	Mol. .Wt	C% Found (Calculated)	H% Found (Calculated)	N% Found (Calculated)	O% Found (Calculated)	Metal Found (Calculated)	$\mu_{(eff)}$ B.M.	Molar conductance Ohm^{-1} cm^{2} mol^{-1}
HL	($C_{19}H_{17}N_3O_4$)	white	230	351	64.91 (64.96)	5.58 (4.87)	10.04 (11.95)	18.04 (18.21)	--	--	---
(CuL_2)	($C_{38}H_{34}N_6O_8$ Cu)	Green	>250	766.2	59.96 (59.42)	4.15 (4.46)	11.47 (10.96)	16.35 (16.69)	7.89 (8.28)	1.81	4.1

3.2. Magnetic and Electronic Spectral studies

The electronic spectra of ligand and Cu(II) complex was recorded in DMSO solution 10^{-3}M molar concentration. The electronic spectrum of ligand exhibits three absorption transitions at 357.5 nm (27972 cm^{-1}), 289.5 nm (34542 cm^{-1}) and 261.5 nm (38240 cm^{-1}) assigned to the n-π* and π-π* transitions of azomethine, 2-quinolone and 4-hydroxy group respectively.

The Cu(II) complex displayed bands at 376.5 nm (26560 cm^{-1}) and 285 nm (38240 cm^{-1}) which may be assigned to $^{2}B_{1g} \rightarrow {}^{2}E_g$ transitions and charge transfer band respectively [16,17]. Cu(II) shows magnetic moment 1.79 B.M. shows distorted octahedral geometry [18].

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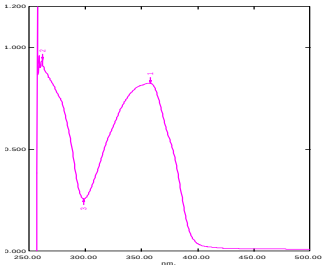

Fig.3 UV spectra of ligand.

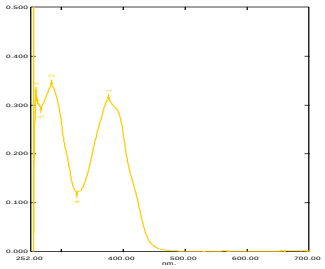

Fig. 4 UV spectra of Cu(II) complex.

3.3. Infrared spectra

IR spectral data of ligand and Cu(II) metal complex are given in **Table 2**. The spectra of ligand dispaly bands in the region 3333, 3178, 1634, 1587, 1610, 1176, 754 cm^{-1} due to enolic -OH group of 4-hydroxy-2(1*H*)-quinolone, -NH strech of hydrazone, >C=O (quinolone), >C=N (azomethine), >C=O (amide), aromatic -OH and -NH out of plane bend respectively. The careful investigation of the spectra of the complex and ligand indicate that the bands of -OH, -NH are present in the spectra of complex indicating non coordination with metal ion. They observed at lower frequency in complex may due to its presence in chelate system rather than the open system of the ligand. In complex there is presence of strong sharp band at 1163 cm^{-1} -OH group substitution on aromatic ring this band observed at same stretching frequency as observed in ligand. The bands of >C=O (quinolone), >C=N (azomethine), >C=O (amide) are shifted to lower frequencies by 36 cm^{-1}, 85 cm^{-1} and 51 cm^{-1} respectively on complexation due to their participation in the mode of coordination. This behavior indicates that ligand behaves as neutral tridentate ligand. In Cu(II) complex the bands at 525 $cm^{-1,}$ 466 cm^{-1} which are not present in the spectra of the free Schiff base Hydrazones are assigned to (M-O) and (M-N) bonding [19].

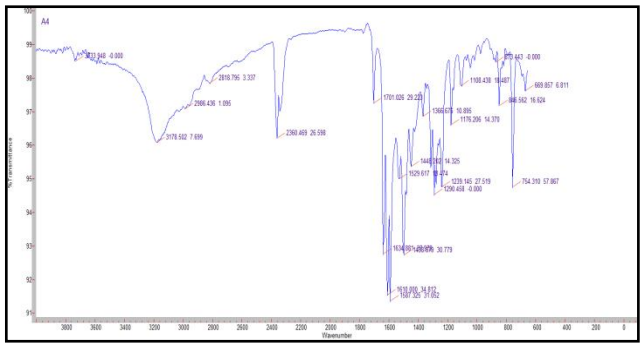

Fig.5 IR spectra of ligand

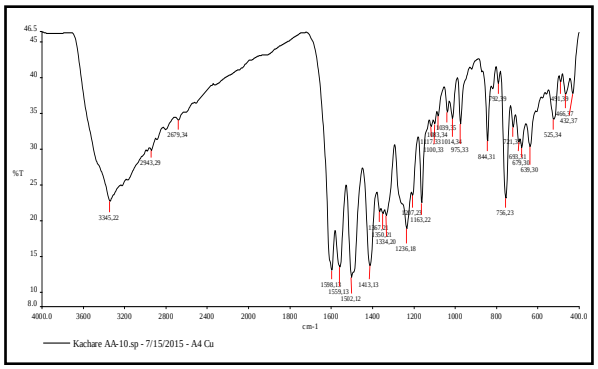

Fig.6 IR spectra of Cu(II) Complex

Table 2
Salient Features of IR Spectral Data of Ligands.
(Assignment of band frequencies to bond vibration modes)

Ligands	υ(OH) Enolic	υ (NH) Hydrazone	υ (C=O) Quinolone	υ (C=N) Azomethine	υ (C=O) amide carbonyl	υ (OH)	υ (-NH) out of plane
Ligand	3333 (b)	3178 (b)	1634 (s)	1587 (b)	1610	1176 (s)	754 (s)
CuL_2	3345 (m)	3205 (s)	1598 (s)	1502 (s)	1559 (s)	1163 (s)	756 (s)

3.4. The ^{1}H-NMR Spectra of Ligand and Complex

^{1}H- NMR Spectra of ligand and Cu(II) complex were recorded in DMSO over the range 0-20 δ ppm. In ligand signals at 2.74 δ ppm. (s,3H, N=C-CH_3) assigned to azomethine protons, 3.53 δ ppm.(s,3H,N-CH_3), 7.20-8.14 δ ppm (m, 8H, aromatic), 10.23 δ ppm ^{1}H (s 1H -OH substituted on hydrazide)11.29 δ ppm ^{1}H (s broad N-H), 16.76 δ ppm ^{1}H (broad hump, enolic-OH). In ^{1}H NMR spectra of complex indicates presence of broad signal at 10.35 δ ppm due -NH proton

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of hydrazone indicating non enolization of -NH with amide carbonyl. In complex 9.04 δ ppm observed at ^{1}H (s 1H -OH substituted on hydrazide). There is slightly upfield shift due to change of environment of free ligand and complexation of ligand with metal. In Cu(II) complex aromatic frequency observed in the range 8.99-6.58 δ ppm. In complex N-CH_3 signal observed at 3.64 δ ppm. In complex azomethine frequency observed at 2.97 δ ppm. (s,3H, N=C-CH_3) here also upfield shift in frequency observed in complex than ligand. In complex there are upfield shifts in NMR frequency than free ligand indicating formation of complex takes place [19].

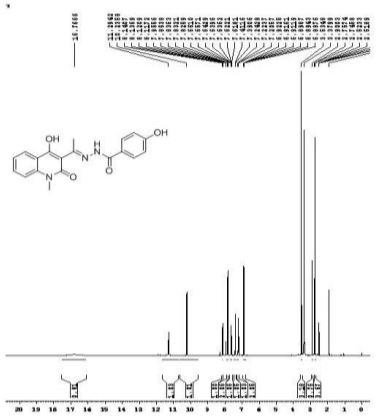

Fig.7 ^{1}H NMR of Ligand

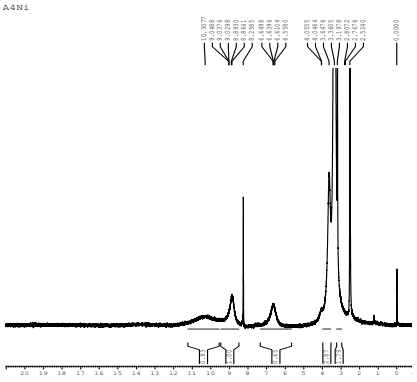

Fig.8 ^{1}H NMR of Cu(II) complex

3.5. Mass spectra of ligand and Cu(II) complex

Mass spectrum of the ligand and complexes supports its proposed formulation. It reveals the molecular ion peak m/z at 352.2, 353.1 a.m.u. due to (M+1) and (M+2) molecular ion peak, consistent with the molecular weight of the ligand. The mass spectra of the Cu(II) complex molecular ion peak observed at 766.07 m/z which is match with their calculated mass.

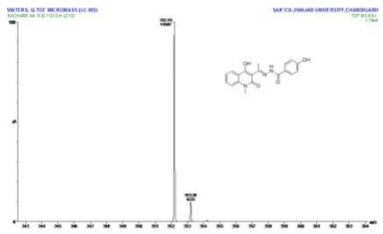

Fig.9 Mass spectra of ligand

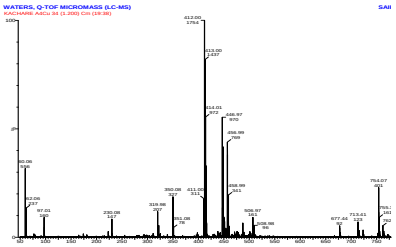

Fig.10 Mass spectra of Cu(II) complex

3.6. Thermogravimetric Studies

The simultaneous TG/DTA analysis of Cu(II) complex was studied

Cu(II) complex of (Fig. 11) decomposes in two steps. It is stable up to 230˚C indicating absence of lattice as well as coordinated water molecules. The complex continues to decompose in a first step up to 350˚C with weight loss of 58% (calc. wt. loss 58.9%) which is confirmed by sharp endothermic peak in DTA curve at 290.94˚C may be due to the decomposition of non coordinated part of the complex. The second step covering the slow step decomposition of the reaction interval 350-750˚C with 30% mass loss corresponds to decomposition of actual coordinated part of the complex and above which the residue attains almost constant weight due to formation of CuO as a final product.

The thermal behavior of copper complex in the present study indicates high thermal stability. Decomposition complex is started at relatively higher temperature (~230˚C), finally giving a metal oxide residue. Thermogram of complex indicate the absence of coordinated as well as lattice water and exhibit higher thermal stability.

The thermal kinetic parameters ΔS, Ea and Z for non- isothermal decomposition of complex have been calculated by Horowitz-Metzer and Coats-Redfern method from TG-DTA curves (Fig.11) and are presented in **Table 3.**

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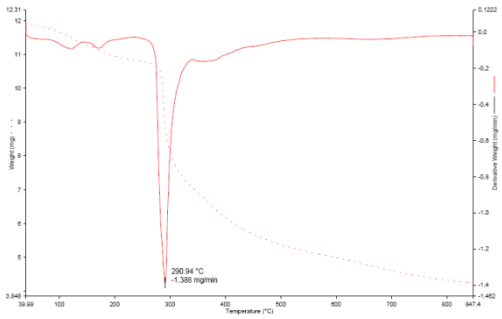

. Fig. 11 TG-DTA Curve of Cu(II) Complex

Table 3. Thermodynamic and Kinetic Parameters

Metal complex	Method	Step	Decomp. Temp.	Order of Reaction	Ea(KJ mol^{-1})	ΔS(KJ mol^{-1})	ΔG(KJ mol^{-1})	Z (S^{-1})	Correlation Coefficient (r)
Cu(II)	**H-M**	I	320	0.55	7.43	-162.68	19.62	41425.71	0.997
	C-R				6.82	-161.7	19.54	46628.83	0.999
	H-M	II	440	0.55	9.68	-171.11	36.39	31330.3	0.999
	C-R				9.95	-170.76	36.33	32685.77	0.997

Generally, with decreasing value of ΔE, the value of Z increases, and higher value of activation energy suggest higher stability [20]. In the present complex, the value of E_a decrease with the increasing value of (Z) i.e. frequency factor indicating that the activated complex have more ordered or more rigid structure than the reactants or intermediate and that the reactions are slower than normal

3.7. X-RAY DIFFRACTION STUDY

The X-ray diffractogram, of Cu(II) complex was scanned in the range 0-60˚ at wavelength 1.54 A˚ The X-ray diffraction pattern of the complex with respect to major peaks having relative intensity greater than 10% have been indexed by using computer program [21]. The above indexing program gives hkl planes, unit cell parameters and volume of the unit cell. The diffractogram and associated data gives 2θ values for each peak, relative intensity and inter planer spacing (d-values). On the basis of X-ray diffraction analysis the standard deviation observed was within the permissible range. The observed density is 0.8251 gcm^{-3} and calculated density is 0.8242 gcm^{-3}. The Cu(II) complex is triclinic lattice type having one atom per unit cell. For this complex lattice parameters are a=22.35 A˚, b=9.01 A˚, c=8.2 A˚, α=95˚, β=110˚, γ= 91.125˚, V=1543 $A^{\circ 3}$. Which satisfies the condition a ≠b ≠ c and α ≠ β≠ γ [22].

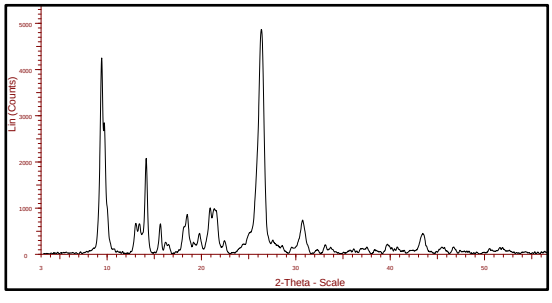

Fig. 12 X-ray Diffractogram of Cu(II) complex

IV. BIOLOGICAL ACTIVITY OF THE COMPOUNDS

4.1. In *vitro* antibacterial activity of the compounds

The antimicrobial activity of the ligand and complex were tested against the standard microbial strains, *Escherishia coli*, *Salmonella typhi*, *staphylococcus aurus*, *Bacillus substilis* by agar cup method at fixed concentration of 1% in

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DMSO. The test was performed on nutrient agar Cup of 10 mm diameter were borered in the agar plate with stirile cork borer. All solutions were prepared in DMSO(1%) was add on cup, One cup for DMSO as blank and other for standard reference penicillium was also placed on the seeded nutrient agar. Then the plates were shifted to incubator at 37˚C and incubated for 24 hours. Activity measured in diameter (mm). The results obtained are presented in **Table 4**

Inspection of the data revealed that complex and ligand lack the activity towards the Gram-negative bacteria *E. coli* and *S. typhi*. On the other hand, ligand and complex shows activity against Gram-positive bacteria *S. aureus* and *B. substilius*.

Table 4: Report for Antibacterial testing.

Medium - Nutrient Agar Method- Agar cup method
Dose of compound - 1% cup size - 10 mm

compound	*Bacillus subtilis* (mm)	*Stapylococcus aureus* (mm)	*Escherichia coli* (mm)	*Salmonella typhi* (mm)
Ligand(L)	14	12	--	--
(CuL_2)	25	21	--	--
Penicillium	14 mm	20 mm	36 mm	28 mm

4.2. *In vitro* antifungal activity of the compounds

Compound were screened in vitro against *Aspergillus niger*, *Penicilium chrysogenum*, *fusarium moneliforme*, *Aspergillus flavus*, by poison plate method with potato dextrose agar media. The compound were tested at the 1% concentration in DMSO and compared with control.

Gresiofulvin was prepared as standard reference plate. The fungal suspension was spot inoculated on the plates prepared using compound with nicrome wire loop. The plates were incubated at room temperature for 48 hours. The results obtained are presented in **Table 5**. Ligand does not show antifungal activity but it's complex shows appreciable activity. Antifungal activity of complex increased several times on being coordinated with metal ions. Cu(II) complex shows more than 90% reduction of fungal growth for all fungi.

Table 5 : Report for Antifungal testing

Compound	*Aspergillus niger*	*Penicillium chrysoganum*	*Fusarium Moniliforme*	*Aspergillus flavus*
Ligand	+ve	+ve	+ve	+ve
(CuL_2)	RG	-ve	-ve	-ve
Grisefulvin	-ve	-ve	-ve	-ve

Legends- + ve - Growth -(Antifungal Activity absent)
-ve - No growth (More than 90 % reduction in growth Antifungal activity present)
RG - Reduced Growth.

V. CONCLUSION

In the light of above discussion we have proposed octahedral geometry for both complex. On the basis of physicochemical and spectral data discussed above, one can assume that the ligand behaves as, ONO tridentate, coordinating via quinolone carbonyl, azomethine nitrogen and amide oxygen in complex. The mass spectra of ligand and its metal complex are in great accordance with calculated and observed. Thermogravimeric studies of Cu((II) complex revealed that complex is rigid and stable. p-XRD study of Cu((II) complex shows triclinic lattice type. The complex is biologically active and having greater activity compared to free ligand.

VI. ACKNOWLEDGEMENTS

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Synthesis, Characterization and Antimicrobial study of Manganese (II) Complex of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl) prop-2-en-1-one

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ABSTRACT

The synthesis of Manganese (II) metal complex **1** has been synthesized by using novel (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one ligand. The ligand was prepared by the Claisen-Schmidt condensation method of 2,6-dihydroxy acetophenone and 2-furaldehyde. The structure of the complex has been characterized by the analytical data, conductivity measurement, magnetic moment, UV-Vis spectra, and thermal studies. Analytical data shows 1:2 stoichiometry and the magnetic moment, TG-DTA suggests that Mn(II) complex has octahedral geometry. The presence of coordinated water molecules in Mn (II) complex **1** is confirmed by thermal studies. The conductivity data revels that the complex is non electrolyte. Antimicrobial study of complex with selected bacterial strain and fungal strain carried out and the results have been compared with commercial standards. The Mn (II) complex **1** shows moderate to good Antibacterial and Antifungal activity.

Keywords: Antimicrobial activities, TG-DTA study, Physico-chemical property, Magnetic Susceptibility and Conductivity.

I. INTRODUCTION

Chalcones and their metal complexes play an important role in modern coordination chemistry. These compounds possessing novel structural features, interesting spectral and magnetic properties, have been observed of intensive research due to their importance in medical, agriculture, analytical, biological and industrial fields. In recent years a number of β-dicarbonyl compounds in which the carbonyl function bonded to olefinic linkage have gained considerable importance mainly because of the fact that such compounds are structurally related to the active chemical constituents of several traditional medicinal plants[1-3].

Chalcones constitute an important group of natural products, which has two aromatic rings joined by α, β unsaturated carbonyl system. The name chalcone is given by Kostanecki and Tambar [4]. The metal complexes

possess interesting biochemical properties, such as antitumor, antioxidant, and antimalerial, anti-fungal and antimicrobial activities [5]. The magnetic moment, TG-DTA supports the octahedral geometry of the metal complex of chalcone.

II. MATERIALS AND METHODS

2.1. Synthesis of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl) prop-2-en-1-one ligand:

The reagents used for preparation of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl) prop-2-en-1-one are of A.R. grade. A mixture of 2,6-dihydroxy acetophenone (0.01 mol) and 2-furaldehyde (0.01 mol) are dissolved in ethanol (20 mL) and then solution of potassium hydroxide 10 mL (15%) were added to it. The mixture was stirred for overnight. The progress of the reaction was monitored by TLC. It was then poured on ice cold water and acidified with dilute HCl. The coffee brown solid was precipitates, filtered and washed with water and recrystallized from ethanol to give the chalcone [6].

2.2. Synthesis of Metal Complex:

The solution of 0.02 mole of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one was taken in round bottom flask containing 30 ml of anhydrous methanolic solution and boiled for 10 minutes. A hot solution of 0.01 mole, of Manganese Acetate in 20 ml of methanol was added drop wise to the solution of the chalcone of 5-methylfurfural to this reaction mixture, 10% alcoholic ammonia was added up to slightly alkaline pH. The complex was precipitated at 8 pH range. The pH 8-10 range was definite for these complexes [7]. The content was stirred on magnetic stirrer for one hour. The solid metal complex separated out and washed with methanol three to four times. The melting point of the complex was determined by Thiele's melting apparatus. The reactions of formation of Mn (II) complex **1** is shown in **Figure-1**.

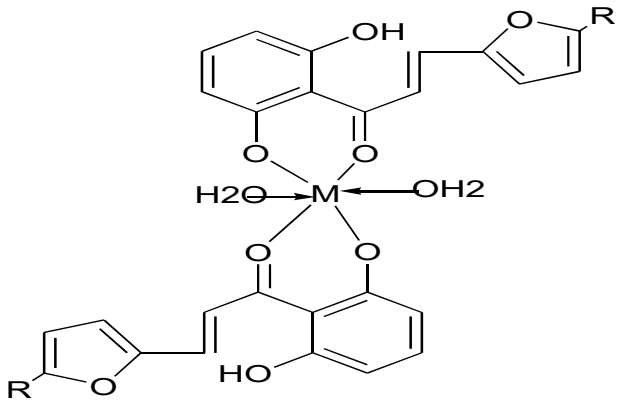

Figure-1: Metal complex **1** of Manganese (II) with (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one
R= -H, M= Mn(II)

III. RESULTS AND DISCUSSION

3.1. Physical parameters:

Metal complex **1** of Manganese (II) with (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one was brown in color. The complex was precipitated at 8 pH range, having Melting point 320°C. The complex is insoluble in water and soluble in DMSO, DMF [8].

3.2. CHO analysis:

The carbon, hydrogen, oxygen, Manganese metal percentage in Mn (II) complex **1** of chalcone measured at SAIF Cochin, Kerala. The calculated and measured values of CHO analysis are matching and are given in the **Table-1**.

Table-1: Study CHO analysis of synthesized Mn (II) complex **1**

Metal complex	Chemical formula	Mol. Wt.	Elemental analysis : % found (calculated)						
			C	H	N	O	S	X(Br)	M
Mn (II) Complex	$[C_{26}H_{22}O_{10}Mn]$	549	56.84 (64.33)	4.03 (4.57)	-	29.12 (19.78)	-	-	9.99 (11.32)

3.3. Magnetic susceptibility, solution conductivity and electronic absorption spectral data Magnetic susceptibility:

The magnetic moment of Mn (II) complex **1** in the present investigation are in the range which is almost close to the spin only value of 5.92 B.M. These values are in good agreement with the moment reported for mononuclear high spin octahedral Mn (II) complex **1** by earlier workers [9].

Table-2: Study magnetic susceptibility, solution conductivity and electronic absorption of synthesized Mn (II) complex 1 of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one

Mn(II) Complex	Molar Conductance Ohm^{-1} cm^{2}mol^{-1}	μ_{eff} (B.M.)	Absorption Maxima cm^{-1} (nm)		
			$^6A_{1g} \rightarrow {}^4T_{2g}$ (G)	$^6A_{1g} \rightarrow {}^4A_{1g}$ (G), ^4E_g	Charge Transfer
1	2.12	5.86	24937(401)	28571(350)	32154(311)

Solution conductivity and electronic absorption spectral data:

The solution conductivities of 10^{-3} M solution of metal complex in DMSO were measured on EQUIPTRONICS digital conductivity meter EQ - 660 with 20 μΩ to 200 μΩ at 298K temperature. They are insoluble in water and soluble in DMSO, DMF. The low solution conductivity of 10^{-3} M solutions of Mn (II) complex **1** in DMSO indicates their non-electrolytic nature.

Figure-2.

Figure-2: Electronic absorption spectrum of Mn (II) complex **1** of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one

The electronic absorption spectra of Mn(II) complex **1** **Table-1:** Study CHO analysis synthesized Mn (II) complex **1** were showed three bands at 19,120 to 25000 cm^{-1}, 25125 to 27700 cm^{-1}, and 28993 to 30581 cm^{-1} assignable to $^6A_{1g} \rightarrow {}^4T_{2g}(G)$, $^6A_{1g} \rightarrow {}^4E_{1g}$ or $^6A_{1g} \rightarrow {}^4T_{1g}$ (G) and charge transfer indicating octahedral geometry around the metal ion [10-11].

3.4. Infra-red spectrum:

The IR spectrum of α, β-unsaturated carbonyl group has characteristic bands of chalcone at prominent bands between 1625 to 1650 cm^{-1}. The characteristic peaks in infra red spectrum give the presence of particular functional group. The region at which other absorption bands appear depends on the type of aromatic / hetero-aromatic rings as well as the substituent present on these rings. The infrared spectrum of Mn (II) complex **1** of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one was recorded on a Perkin- Elmer Spectrum RX-IFTIR Spectrophotometer in the range 4000-400 cm^{-1} (**Table-2**) using potassium bromide pellet at CIL, Chandigarh, Punjab. The stretching frequency of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one is represented in table number (2) and the IR spectrum in **Figure-3.**

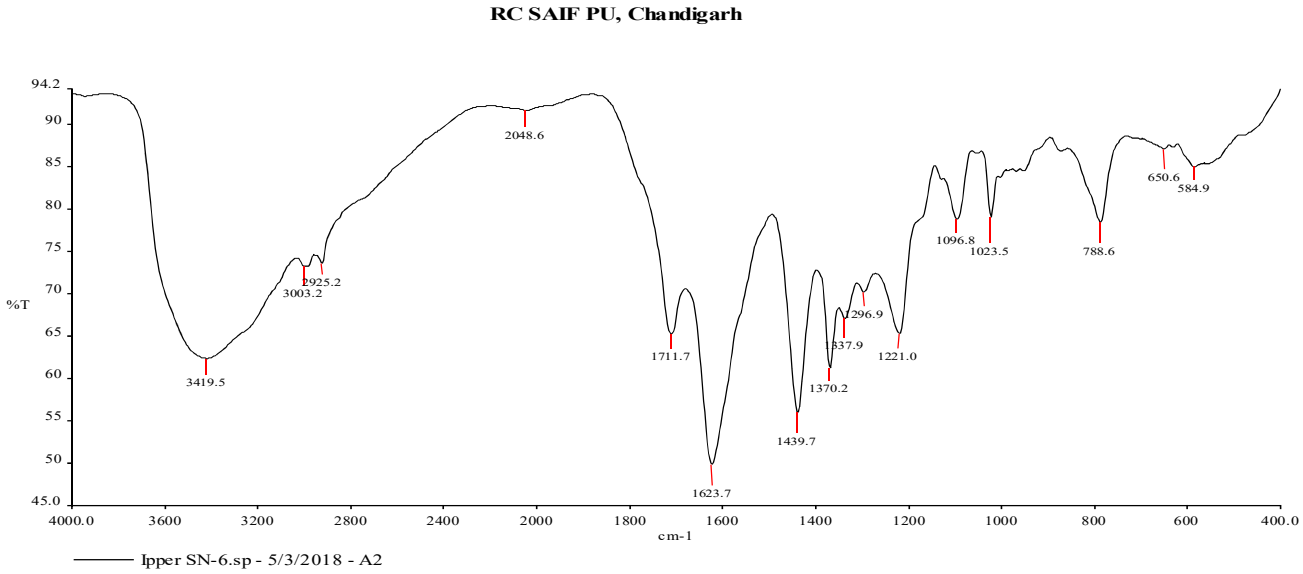

Figure-3: IR spectrum of Mn (II) complex **1** of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one

Table-3: IR spectral data of Mn (II) complex **1** of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one

Molecule	υ(OH) Enolic	(-CO-CH=CH-) α,β-unsaturated carbonyl group	Carbonyl group (-C=O in pyron ring)	(C-O-C) Stretching Frequency	(C=C) Stretching Frequency	Aromatic Ring (C=C) Stretching Frequency	Ar-H Stretching Frequency	$-NO_2$ stretching frequency
Ligand	3420	1652	-	1096	1575	1457	2920	-

3.5. Thermal analysis Mn (II) complex 1 of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one

The simultaneous thermo gravimetric, differential thermal analysis of Mn (II) complex **1** of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one was performed in an inert nitrogen atmosphere on Perkin Elmer STA

6000 at SAIF, Cochin, Kerala. The heating rate was 10˚/min and flow rate of nitrogen 50 ml/min. The reference substance used was α Al_2O_3 in platinum crucible and sample weighted in the range of 4-12 mg. The thermogram of Mn (II) complex (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one is presented in figure-2. This curve reveals that there is presence of lattice as well as coordinated water in the complex.

The thermogram of Mn (II) complex **1** of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one shows first weight loss at 60˚C indicating presence of lattice water. The second loss due to the coordinated water molecule liberated, from the complex. The anhydrous compound undergoes four step decomposition. In the first two steps, decomposition occurs due to loss of non-coordinated part of ligand. The first step shows decomposition within a temperature of range from 240-330˚C with mass loss of 39.29%, which is supported by a sharp an endothermic peak at 259˚C in DTA curve. It may be due to half decomposition of non-coordinated part of ligand. In the second step, decomposition observed at about 350-400˚C with the weight loss of 33.78% in TG curve. This is supported by an endothermic peak at 380˚C. This may be due to decomposition of remaining coordinated part of ligand. Beyond 600˚C there is a formation of MnO as indicated by constant weight loss of in TG-DTA curve.

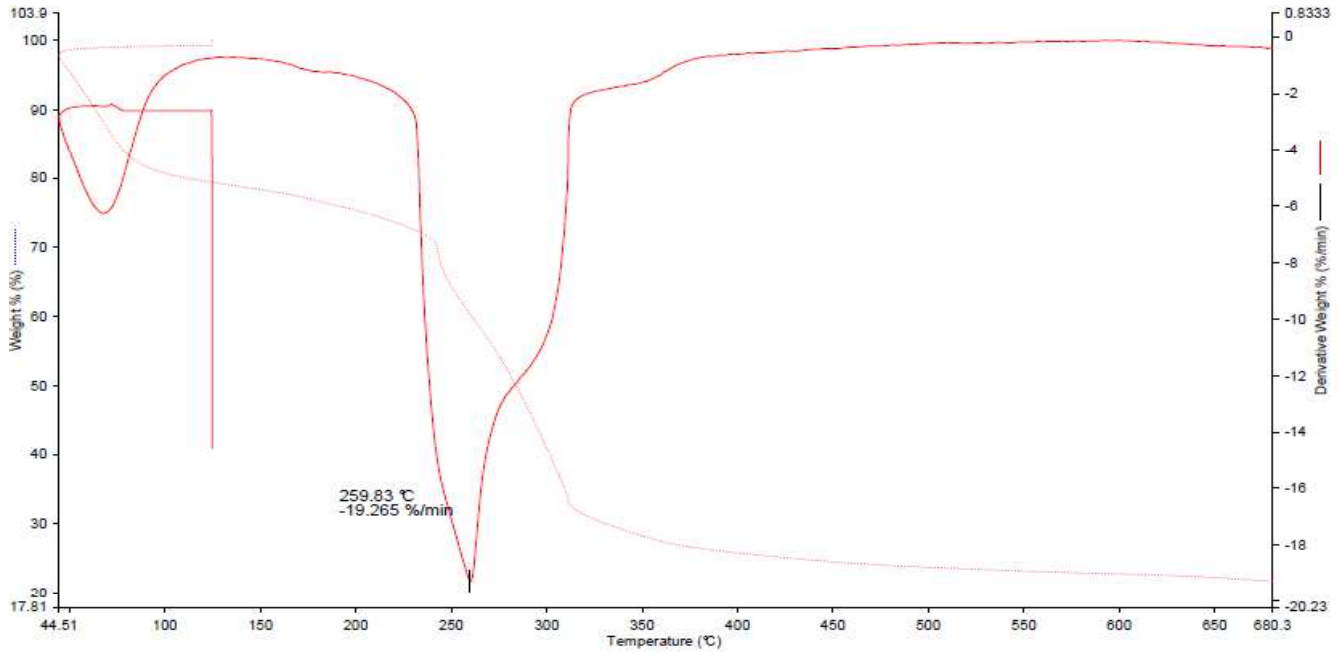

Figure-4: TG-DTA curve of Mn (II) complex **1** of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one

3.6. Thermodynamic and Kinetic Parameters

Akahira [12], first introduced that decomposition and kinetic studies of thermal reactions are useful in determining thermodynamic and kinetic parameters like free energy, entropy change, activation energy, pre-exponential factor. Thermal decomposition studies of materials are useful in predicting thermal stability (**Table-3**).

The negative values of the entropy of activation (ΔS) indicate that the metal complex is thermally stable. ΔG is positive for the complexes revealing that the free energy of the final residue is higher than that of the initial complex, and all decomposition steps are non-spontaneous processes. Also, the value of free energy of activation, ΔG increases significantly for the subsequent decomposition stages of a given complex [13]

Table-3: Thermodynamic and Kinetic Parameters of Mn (II) complex 1 of (E)-3-(furan-2-yl)-1-(2,6-dihydroxyphenyl)prop-2-en-1-one

Metal complex	Method	Step	Decomp. Temp.	Order of Reaction	Ea(KJ mol^{-1})	ΔS(KJ mol^{-1})	ΔG(KJ mol^{-1})	Z (S^{-1})	Correlation Coefficient (r)
Mn (II) complex	H-M C-R	I	300	0.5	26.84 21.75	-153.91 -97.64	37.80 28.70	112973.9 98100737	0.907 0.989
	H-M C-R	II	450	0.5	6.73 4.09	-172.89 -83.66	19.06 9.96	11545.4 527754555.2	0.999 0.997

3.7. Antimicrobial activity:

Antimicrobial activity was assayed by cup plate agar diffusion method by measuring inhibition zones in mm. In vitro antimicrobial activity of all synthesized compounds and standard have been evaluated against strains of The fungal toxicity of Mn (II) complex **1** was studied *in vitro* against *Aspergillus niger* ATCC 16404, *Saccharomyces cerevisiae* ATCC 9763, *Candida albicans* ATCC10231 fungal pathogens at fixed 1% concentration.

The antibacterial activity of Mn (II) complex **1** was studied, for evaluating antibacterial activity Gram positive and Gram negative bacterial pathogens were used. *Staphylococcus aureus* ATCC 6538, *Bacillus megaterium* ATCC 2326, *Bacillus subtilis* ATCC 6633 were Gram positive pathogens used in this study. *Escherichia coli* ATCC8739, *Salmonella typhi* ATCC9207, *Shigella boydii* ATCC 12034, *Enterobacter aerogenes* ATCC13048, *Pseudomonas aerogenosa* ATCC9027, *Salmonella abony* NCTC6017 were the Gram-negative pathogens used in this study.

From the results of antimicrobial activity of ligands and complex it is clear that the complex shows enhanced activity than ligand. The increase in antimicrobial activity is due to faster diffusion of metal complexes as a whole through the cell membrane or due to the combined activity of the metal and ligands [14].

IV. CONCLUSION

The Mn (II) complex **1** was colored, soluble in most of the organic solvent. The stoichiometry ratios of the metal complexes are obtained has been found to be 1:2.Solution conductivity of this metal complex reveals non-electrolytic nature. The electronic spectral data, magnetic moment, TG-DTA suggests that Mn (II) has Octahedral geometry. The CHO analysis gives C, H, and O percentage in the metal complex. From the antimicrobial activity of ligand and complex it is clear that the complex shows enhanced antimicrobial activity than ligand.

V. ACKNOWLEDGEMENT

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Chalcone Biological Significance and Synthesis A Review

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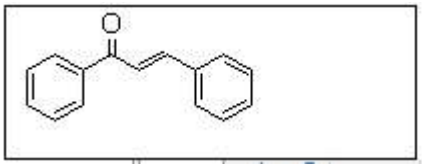
ABSTRACT

Chalcone is an aromatic ketone that forms the central core of many important biological compounds. The biogenetic building blocks of favonoids and isofavonoids, which are abundant in plants, are called chalcones. Chalcones are active lead molecules in the search for new drugs in medicinal chemistry. Here, we review the biological significance and synthesis of natural and synthetic chalcones.

Keywords: Chalcones, Antibacterial activity, Antidiabetic activity, Claisen–Schmidt condensation, Witting reaction

I. INTRODUCTION

Chalcones are the building blocks of several natural compounds.[1-2] The word "chalcone" is derived from the Greek word "chalcos", meaning "bronze", which results from the colors of most natural chalcones.[3] Chalcones are 1, 3-diaryl-2-propen-1-ones with various substitution patterns that exist in cis and trans isomeric forms, with the trans form being thermodynamically advantageous.They are represented as



On their aryl rings, they have different substituents. Some of these substitutes affect the biological properties that chalcones have. However, the key pharmacophore is believed to be the, α,β -unsaturated ketone moiety.[4] Naturally occurring chalcones and their synthetic analogues have been documented to comprise a wide range the biological activity. They are therefore high in demand as the starting components in the synthesis of a number of different heterocyclic compounds. Chalcones have been utilized as medicine for thousands of years to treat a variety of pharmacological conditions through the use of plants and herbs. There are many chalcone-containing drugs that have received clinical use approval. Metochalcone was previously employed as a choleretic medication, whereas sofalcone was used as an antiulcer and mucoprotective medicine (Figure 1)[5, 6]