SYNTHESIS, SPECTRAL CHARACTERIZATION AND ANTIMICROBIAL ACTIVITIES OF BIS(CYCLOPENTADIENYL)TITANIUM(IV) COMPLEXES WITH SCHIFF BASES DERIVED FROM 5-(SUBSTITUTED ARYL)-2-HYDRAZINO-1, 3, 4-OXADIAZOLE AND INDOLINE-2, 3-DIONE

Anupama Srivastava¹, Shilpi Srivastava², Om. P. Pandey¹ and Soumitra K. Sengupta¹
1. Department of Chemistry, D.D. U Gorakhpur University Gorakhpur, India, Pin- 273009.
2. Department of Chemistry, Indira Gandhi National Tribal University, Amarkantak- 484886 India.

Abstract
Titanium(IV) complexes of type[\(\eta^5\text{-C}_5\text{H}_5\text{TiCl(L)}\)] have been synthesized by the reactions of bis(cyclopentadienyl)titanium(IV)dichloride with Schiff bases (LH) derived by the condensation of 5-(substituted aryl)-2-hydrazino-1,3,4-oxadiazole and indoline-2,3-dione in tetrahydrofuran in the presence of triethylamine. All these complexes are soluble in PhNO₂, DMF and DMSO. The complexes were characterized by elemental analyses, electrical conductance, magnetic susceptibility, UV-Vis, IR, \(^1\)H NMR, \(^{13}\)C NMR, XRD and SEM spectral techniques. Low molar conductance values indicate that they are non-electrolytes. The spectral data indicate 5-coordinate geometry for the complexes. XRD pattern indicate that the complexes have monoclinic crystal system and particle sizes were found 49.36 nm (nano-size). In vitro antifungal activity of synthesized compounds was evaluated against fungi Aspergillus niger, Aspergillus flavus, Colletotrichum falcatum and In vitro antibacterial activity was determined by screening the compounds against gram negative (P. aeruginosa, S. typhi) and gram positive (S. aureus and B. subtilis) bacterial strains using minimum inhibition concentration method (MIC) by serial dilution technique. The titanocene(IV) complexes have higher antimicrobial effect than the parent Schiff bases.

Introduction:
Over the past several years, there has been a substantial interest in the application of titanium complexes in biological applications. As a material titanium is extensively used as disinfectant [1], antibiotic [2], biological sensor [3], tumor cell killing agent [4] and gene.

Targeting device [5]. It is an effective antimicrobial agent that kill bacterial cell in water due to the generation of reactive oxygen species [6] which decomposes the cell of bacteria, fungi, algae and viruses due to the oxophilic nature and formation of strong bonds with various biological molecules. The titanium(IV) species are also useful as anticancer agent [7]. It was reported that photoexcitedanatase TiO₂ particles could effectively induces cytotoxicity against HeLa cancer cells[8]. These photoexcitedanatase TiO₂ particles will effectively damage the human colon.
cancer cell[4]. Due to the lower toxicity and less acute side effects exhibited by the titanium(IV) materials, these are found to be highly attractive in various therapeutic applications.

On the other hand, oxadiazoles are an important type of oxygen and nitrogen containing aromatic heterocyclic compounds, possess desirable electronic and charge-transport properties and the various functional groups are easily introduced into the structurally rigid oxadiazole ring. These characteristics resulted in the extensive potential applications of oxadiazole based derivatives in the field of medicinal chemistry. 1,3,4-Oxadiazole derivatives have been found to exhibit diverse biological activities such as antibacterial [9], antifungal [10], anti-inflammatory [11], antioxidant and antihypertensive [12]. The widespread use of 1,3,4-oxadiazoles as a scaffold in medicinal chemistry establishes this moiety as an important bio-active class of heterocycles.

The present paper includes the synthesis, characterization and antimicrobial activities of bis(cyclopentadienyl)titanium(IV) complexes with Schiff bases derived from 5-(substituted aryl)-2-hydrazino-1,3,4-oxadiazoles.

**Experimental**

**Materials and Reagents:**

All reactions were carried out under strictly anhydrous conditions. Glass apparatus with interchangeable quick fit joints were used throughout. THF was dried by heating under reflux over Na wire. The Et₃N was purified by published methods [13]. Bis(cyclopentadienyl)titanium(IV) chloride was purchased from Aldrich. The ligands were prepared as reported in literature [14].

**Instruments**

Elemental analysis was measured with Elementar Vario EL III. Titanium was estimated gravimetrically as its oxide. The known weight of the compound was added in concentrated nitric acid and heated up to a small volume. Then the solution was diluted with distilled water and titanium precipitated as its hydrated oxide by adding ammonia solution. This precipitate was collected on Whatmann filter paper no. 41, washed with distilled water and ignited in a silica crucible to TiO₂. H and ¹³CNMR spectra were recorded by a BrukerAvanceIII, 400MHz. Chemical shifts are reported in ppm and are referenced to TMS. Infrared spectra (4000-200cm⁻¹) of the ligands and complexes were recorded as KBr pellets on a Nicolet-5700 FTIR Spectrophotometer. Progress of reaction and purity of the compounds were confirmed by pre-coated TLC plates (Merck, 60F-254) and spots were visualized using iodine vapors. The magnetic susceptibility at room temperature was measured by Gouy's method using Hg[Co(NCS)₄] as celebrant. Electronic spectra of the complexes were recorded on Beckmann DU-2 spectrophotometer and Cϕ10 spectrophotometer instruments using DMSO as a solvent. Conductance measurements were recorded in DMSO using Toshniwal conductivity bridge model no. c/01/01, provided with a dip type conductivity cell fitted with Pt electrodes. XRD of complexes recorded on BrukerAXS D8 Advance X-ray powder diffractometer.

**Synthesis of titanium(IV) complexes**

A mixture of bis(cyclopentadienyl)titanium(IV) chloride (60 mmol) and appropriate Schiff base derived from 5-(substituted aryl)-2-hydrazino-1,3,4-oxadiazole and indoline-2,3-dione (60mmol) was dissolved in dry tetrahydrofuran (30 cm³). To the resulting clear solution, triethylamine (60 mmol) was added and the mixture was refluxed for ca10–12 h at room temperature. The coloured complexes, so obtained, were recrystallized from a mixture of dimethylformamide andetherdried in vacuo.

The synthetic route for the preparation of ligands and their corresponding bis(cyclopentadienyl)titanium(IV) complexes is given in Figure1.

**Biological activity study**

Bio safety during the antibacterial and antifungal activity.

The antimicrobial properties of the Schiff bases (L¹H–L⁴H) and there titanium(IV) complexes were tested against three fungal strains Aspergillus flavus, Aspergillus niger, Colletotrichum falcatum and four bacteria namely Bacillus subtilis, Pseudomonas aeruginosa, Salmonella typhi and Streptococcus aureus. Bacteria/fungi are potentially hazardous and care should be taken while working with them. Standard bio safety lab techniques were followed while handling bacteria /fungi and various media. Gloves were used during all experimentation, and any accidental spills were immediately sterilized using 70% isopropanol/water followed by bleach. The work area was also
sterilized with 70% isopropanol/water after completion of work unused media and bacteria suspensions were first deactivated with commercial bleach for 1 h before being disposed in biosafety bags. All material that had come in contact with bacteria (pipette tips tubes, plates, etc.) was also thrown in biosafety bags in tightly closed bins. Bio safety bags were autoclaved for 2 h before final disposal.

**Antimicrobial studies**

**Antibacterial screening**
The antibacterial properties of the ligands and their corresponding titanocene complexes were evaluated *In vitro* against (i) Gram-positive bacteria, *S. aureus*, *B. subtilis* and (ii) Gram-negative bacteria, *P. aeruginosa*, *S. typhi* by disk diffusion method. The bacterial strains were subcultures in broth agar and incubated for 18 h at 37°C, and then freshly prepared bacterial cells were spread onto nutrient agar plate in a laminar flow cabinet. Sterilized paper disks (6.0mm in diameter) were placed on the nutrient agar plates. Five milligrams of each test compound were prepared. Thus, proper amounts of the different concentrations of compounds were pipetted on the blank disks, which were placed on the plates. The plates were incubated at 37°C for 24 h. The MICs, the lowest concentration (µg/mL) of the test compound that result no visible growth on the plate, were recorded. DMSO was used as a solvent control to ensure that the solvent had no effect on bacterial growth. Ciprofloxacin was designated in our experiment as a control drug. The results of the antibacterial studies were summarized in Table 2.

**Antifungal screening**
The ligands and their corresponding titanocene complexes were screened for their antifungal activity against *Aspergillus niger*, *Aspergillus flavus* and *Colletotrichum falcatum* (recultured) in DMSO by serial plate dilution method. Test compound (5 µg) were dissolved in 1mL of DMSO, and solution was diluted with water (9mL). Further progressive dilutions with melted Mueller–Hinton agar were performed to obtain required concentrations of 100, 50, 25, 12.5, 6.25, 3.12 and 1.625 µg/mL of each compound were prepared. Thus, proper amounts of the different concentrations of compounds were pipetted on the blank disks, which were placed on the plates. The plates were incubated at 37°C for 24 h. The MICs, the lowest concentration (µg/mL) of the test compound that result no visible growth on the plate, were recorded. DMSO was used as a solvent control to ensure that the solvent had no effect on fungal growth, a control test was performed with test medium supplemented with DMSO at the same dilutions as used in the experiment. Fluconazole was used as a standard drug. The results of the antifungal studies were summarized in Table 3.

**Chemistry**

[(η⁵-C₅H₅)₂TiCl(η¹)]
Light brown color solid: M.P (°C): 168, yield (%): 76 (stirring method) 10h, conductance(Ohm⁻¹cm²mole⁻¹): 6.2; analyses (%) found (calcld for C₂₆H₃₀N₂O₂TiCl): C-60.33(60.49), H-3.57 (3.89), N-13.59 (13.59), Cl-6.67 (6.78), Ti-9.02(9.13); mol. Wt. found (calcld): 516.57(516.69); Conductance (Ohm⁻¹cm²mole⁻¹) 6.2; IR(KBr, cm⁻¹): 2974m (C-H aromatic), 1605s (ν =C=O), 3248s (ν N-H); 1H NMR(DMSO-d₆, δ, ppm): 6.93(s η¹ - C₅H₅ ), 7.59 - 7.52m (phenyl ring), 12.31s (NH); 13CNMR(DMSO-d₆, δ, ppm): 115.2 (η¹ - C₅H₅ ), 126-149(aromatic ring), 150(C=N),165, 162(oxadiazolering).

[(η⁵-C₅H₅)₂TiCl(η²)]
Brown color solid; M.P (°C): 162, yield (%): 68 (stirring method) 10h, conductance(Ohm⁻¹cm²mole⁻¹): 4.1; analyses (%) found (calcld for C₅₃H₅₉N₄O₂TiCl₃); C-56.42(56.79), H-3.37 (3.49), N-12.69 (12.79), Cl-6.70 (6.74), Ti-8.40(8.56); mol. Wt. found (calcld): 550.47(550.69); Conductance (Ohm⁻¹cm²mole⁻¹) 4.1; IR(KBr, cm⁻¹): 2978m (C-H aromatic), 1600s (ν =C=O), 3240s (ν N-H); 489m (ν Ti-O), 458s (ν Ti-N), 1318s (ν C=O), 1084s(C-O-C), 2987m, 1420m, 1015m, 807m(η²-C₅H₅); 1H NMR(300MHz, DMSO-d₆, δ, ppm): 6.93(s η² - C₅H₅ ), 7.57 - 7.53m (phenyl ring), 12.36s (NH); 13CNMR(DMSO-d₆, δ, ppm): 116 (η² - C₅H₅ ), 130-152(aromatic ring), 153(C=N),159, 165(oxadiazolering).

[(η⁵-C₅H₅)₂TiCl(η³)]
Light yellow color solid; M.P(°C): 193, yield (%): 72 (stirring method) 10h, conductance (Ohm⁻¹cm²mole⁻¹): 5.7; analyses (%) found (calcld for C₅₃H₅₉N₄O₂TiCl₃); C-61.11(61.17), H-4.27 (4.53), N-13.59 (13.64), Cl-6.59 (6.70), Ti-8.82(8.89); mol. Wt. found (calcld): 530.39(530.62); Conductance (Ohm⁻¹cm²mole⁻¹)5.7; IR(KBr, cm⁻¹): 2978m (C-H aromatic), 1610s (ν =C=O), 3248s (ν N-H); 480m (ν Ti-O), 463s (ν Ti-N), 1330s (ν C=O), 1098s(C-O-C), 2996m, 1420m, 1015m, 807m(η³-C₅H₅); 1H NMR(300MHz, DMSO-d₆, δ, ppm): 6.93(s η³-C₅H₅ ), 7.58-7.50m

INT. J. ADV. RES. 9(09), 900-909
(phenyl ring), 12.40 s (NH), 1.07 s (CH$_3$); $^{13}$CNMR(DMSO-d$_6$, $\delta$, ppm): 115.6 (\(\eta^5\)-C$_5$H$_5$), 120-142 (aromatic ring), 9.2 (methyl), 147(C=N), 162, 150 (oxadiazole ring)

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[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl(L)}] ^
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Yellow color solid; M.P(°C): 188, yield (%): 70 (stirring method) 10 h, conductance (Ohm$^{-1}$cm$^2$mole$^{-1}$): 7.3; analyses (%) found (calcd for C$_2$H$_{19}$N$_5$O$_2$TiCl): C-61.04 (61.16), H-4.49 (4.49), N-13.53 (13.65), Cl-6.57 (6.72), Ti-8.68 (8.73); mol. wt. found (calcd): 530.42 (550.74); Conductance (Ohm$^{-1}$cm$^2$mole$^{-1}$) 7.3; IR(KBr, cm$^{-1}$): 2978 m (C-H aromatic), 1610 s (v C=N ring), 3248 s (v N-H group), 480 m (v Ti-O), 463 m (v Ti-N), 1330 s (v C-O), 1098 s (C-O-C), 2996 m, 1420 m, 1015 m, 807 m(\(\eta^5\text{-C}_5\text{H}_5\)), $^{1}$HNMR(300MHz, DMSO-d$_6$, $\delta$, ppm): 6.96 (s \(\eta^5\text{-C}_5\text{H}_5\)), 7.60-7.55 m (phenyl ring), 12.29 s (NH), 1.07 s (CH$_3$); $^{13}$CNMR(DMSO-d$_6$, $\delta$, ppm): 115.8 (\(\eta^5\text{-C}_5\text{H}_5\)), 124-149 (aromatic ring), 9.7 (methyl), 150(C=N), 165, 162 (oxadiazole ring)

Results and Discussion:-
5-(Substituted aryl)-2-hydrazino-1,3,4-oxadiazoles react with indoline-2,3-dione in ethanol in acidic medium to give Schiff base ligands (LH) (I). These ligands react with bis(cyclopentadienyl)titanium(IV) chloride to give color amorphous products of type $\{[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl(L)}]\}$, (II) as shown in Figure 1.

Figure 1:- Reaction scheme for the preparation of Schiff bases (I) and their corresponding titanium(IV) complexes (II).

The complexes are soluble in nitrobenzene, dimethylformamide and dimethylsulphoxide. The molar conductance values in DMF are in range of 4-9 ohm$^{-1}$cm$^2$mol$^{-1}$ indicating nonelectrolyte behavior in solution. Magnetic susceptibility measurements show their diamagnetic nature.
Electronic spectra
The electronic spectra of all the complexes show a single band in the region of 474-428 nm, which is assigned to the charge transfer band and is in accordance with an (n-1)d^0ns^0 electronic configuration \[15\]. One more band was observed at ca 283-315 nm, which may be due to intra-ligand transition.

Infrared spectra
The IR spectra provide valuable information regarding the nature of the functional group attached to the metal atom. Schiff bases (L^1H-H-L^4H) appear to exist in both keto and enol tautomer forms (Figure 2) suggested by a broad band (solution spectra) at 2600 cm\(^{-1}\) due to intramolecular H-bonded OH group which disappears in their corresponding Ti(IV) complexes indicating the coordination of phenolic oxygen to titanium metal ion through deprotonation. This is further supported by shift in phenolic(C-O) band from 1285 cm\(^{-1}\) (in the free ligand) to 1317-1330 cm\(^{-1}\) in the complexes. The coordination through phenolic oxygen further confirmed by the appearance of band at 480-500 cm\(^{-1}\) assignable \[16\] to \(\nu(Ti-O)\). The spectra of Schiff bases show a medium band at 3230-3274 cm\(^{-1}\) due to \(\nu(N-H)\) which remains almost at the same position in complex indicating the non-involvement of N-H group in bond formation. The \(\nu(C-O-C)\) vibration appears as a strong band at ca.1080 cm\(^{-1}\) in the free ligands type (L^1H-L^4H) \[17\]. The position of which also remains the same in their corresponding complexes, indicating non-coordination of oxadiazole ring oxygen to metal atom. The ligands show one strong intensity band at 1630 cm\(^{-1}\) assignable \[18\] to \(\nu(C=N)\) which shifts to 1610-1600 cm\(^{-1}\) in the complexes. This shift indicates the coordination of azomethine nitrogen to metal ion \[18\]. The bands at 456-463 cm\(^{-1}\) are assigned \[19\] to \(\nu(Ti-N)\). Absorption bands occurring at ca 2978-2996 cm\(^{-1}\) for \(\nu(C-H)\), ca 1420 cm\(^{-1}\) for \(\nu(C-C)\) and ca 1010 and 810 cm\(^{-1}\) for (C-H out-of-plane deformation) in the complexes are due to the cyclopentadienyl rings. These bands are similar to those reported for bis(cyclopentadienyl)titanium(IV) dichloride and their appearance indicates that the (η^5-C_5H_5) group persists in the complexes \[20\].

On the basis of IR data, we conclude that the Schiff base ligands behaves as monobasic, bidentate chelating agent having coordination sites at OH group and one azomethine nitrogen atoms.

\[\text{[Keto form]} \quad \text{[Enol form]}\]

Figure 2: Synthesized Schiff bases in tautomer forms.

H NMR spectra
The proton magnetic resonance spectra of ligand and their corresponding complexes were recorded in DMSO-d_6. The intensities of all the resonancelines were determined by planimetric integration. Coupling between various groups complicates the spectra but a comparison of spectra of ligands with those of the complexes can lead to following conclusions.

The complexes exhibit signals at δ 6.90-6.65 assigned to the cyclopentadienyl ring proton and indicate the rapid rotation of the ring about the metal axis \[19\]. Schiff bases derived from indoline-2,3-dione of type (L^1H-L^4H) exhibit signals at δ5.52-5.60 ppm due to an indoline-2, 3-dione NH proton \[18\]. In titanium (IV) complexes indoline-2, 3-dione NH peak disappears. This confirms that the enol form (OH) of Schiff base reacted with metal ion via deprotonation. Multiplet is observed at δ 7.39-7.60 ppm due to aromatic protons in the Schiff bases and their corresponding titanium(IV) complexes. Schiff bases and their corresponding titanium(IV) complexes also exhibit a signal at δ 1.15-1.30 ppm due to methyl protons. The \(^{1}H\) NMR spectra of Schiff bases of type (L^1H-L^4H) exhibit signals at δ11.75-11.98 ppm due to NH of azomethine \(18\). In titanium(IV) complexes this signal shifts downfield. The downfield shift indicates the deshielding effect due to the coordination of azomethine nitrogen to central metal ion.
C NMR spectra
The $^{13}$C NMR spectra of these complexes were recorded in DMSO-d$_6$. Schiff bases derived from indoline-2,3-dione (L$^1$H-L$^4$H) show signals at $\delta$156-147 ppm for their azomethine carbons and they shift downfield in their corresponding titanium(IV) complexes due to the coordination through azomethine nitrogens [21]. For methyl carbon a signal appears at $\delta$ 13.5 ppm in ligands (L$^1$H, L$^4$H) and their corresponding complexes. Schiff bases of type (L$^1$H-L$^4$H) and their corresponding titanium(IV) complexes show signals at about $\delta$ 169 ppm and $\delta$ 160 ppm assignable for oxadiazole ring carbons. These signals remain unchanged in their corresponding complexes indicating that oxadiazole ring nitrogen are not participated in bond formation. All complexes show peak at $\delta$ 115.2-116 ppm due to cyclopentadienyl group [19]. The signal observed in the region $\delta$ 122-152 ppm as a multiplet could be assigned to aromatic carbons of ligands and their corresponding complexes.

X-Ray powder diffraction
The structural characterization of the complex[($\eta^5$-C$_5$H$_5$)$_2$TiCl(L$_3^3$)] was carried out from the analysis of X-Ray powder diffraction (XRD) pattern obtained using an X-ray powder diffractometer (Bruker AXS D8 Advance) with CuK$\alpha_1$ ($\lambda = 1.54056\ \text{Å}$) source. The XRD pattern of the complex was given in Figure 3. The peaks in the XRD pattern clearly indicate the formation of nanocrystals. The crystallite sizes have been calculated using Debye-Scherer formula[22,23] given by

$$D = \frac{0.94\lambda}{\beta \cos \theta}$$

Where D is the crystallite size, $\lambda$ is the wavelength of X-ray used; $\beta$ is the full width at half maximum (FWHM) and $\theta$ is the Bragg angle of diffraction. The average crystallite sizes of the complex[($\eta^5$-C$_5$H$_5$)$_2$TiCl(L$_3^3$)] was found to be 49.36 nm.

The indexing of the powder patterns for each complex was carried out using the program N-TREOR. The Miller indices (hkl) relate the peak positions or d-spacing to the lattice parameters by an equation specific to the crystal system. The initial unit cell (lattice) parameter was also determined by N-TREOR[24]. These unit cell parameters were refined from the regression analysis and the best crystal system and space group was assigned using CHEKCELL[25] program. It was found that the complex[($\eta^5$-C$_5$H$_5$)$_2$TiCl(L$_3^3$)] reveal monoclinic crystal systems with the most probable space groups P2$_1$/c. The lattice parameters and observed & calculated X-ray diffraction data for the complex[($\eta^5$-C$_5$H$_5$)$_2$TiCl(L$_3^3$)] have been shown in Table 1.

![Figure-3](image-url)
Scanning Electron Microscope (SEM)
The morphology and particle size of the titanium(IV) complex was investigated using SEM. Figure 4 depicts the SEM images of the synthesized titanium(IV) complexes at low and high magnification. We note that there are well-arranged nanostructures of the synthesized complexes in the micrographs. The micrographs show that the particles have irregularly small cuboids and granular with homogeneous phase. This leads us to believe that we are dealing with nanoscale materials. A granular shape is observed in $\left[(η^5-C_5H_5)_2TiCl(L^4)\right]$ complex with a particle size of 67.71 nm.

![SEM images of titanium(IV) complexes](image)

Antimicrobial activity
The Schiff bases are found to be biologically active and their corresponding titanium(IV) complexes show significantly enhanced antibacterial (Table 2) and antifungal (Table 3) activities. As chelation increases, bacterial and fungal growth inhibition also increases. Actual mechanism of increased activity of complexes is not certain but factors like solubility, dipole moment and cell permeability mechanism and their enzymatic action may be the possible reason. According to Overtone’s concept of cell permeability, the lipid membrane surrounding the cell favors the passage of lipid-soluble materials, making the solubility an important factor controlling the antimicrobial activity [26]. Tweedy’s chelation theory the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of $\pi$-electrons over the whole chelate ring and enhances the lipophilicity of the hetero chelates. The increased lipophilicity enhances the penetration of the hetero chelates into lipid membranes and blocks the metal binding sites in the enzymes of microorganisms. These hetero chelates also disturb the respiration process of the cell and block the synthesis of proteins, which actually restricts further growth of the organisms. Furthermore, the mode of action comprising the compounds may involve the formation of hydrogen bond through the azomethine/carbonyl/amine group with the active center of cell constituents and interferences forced with the normal cell process [27]. In antifungal activity all ligands and titanium(IV) complexes are found to be more active against A. niger (Figure6). It is found that substitution in the ligands increases the activity against bacteria and fungi. 2-chloro substituted ligands/compounds are more active than the other substituted ligands/compounds. Due to
the chelating properties of 2-chloro group, antibacterial and antifungal activity increases. The complexes \([\eta^5\text{-C}_5\text{H}_{5}\text{TiCl}(L^3)]\) is more active against all bacteria and fungi due to the chelation of ligands. In antibacterial activity, all Schiff bases and titanium(IV) complexes are more active against *S. aureus* (Figure 5).

Table-1: The unit cell parameters and observed & calculated X-Ray diffraction data of \([\eta^5\text{-C}_5\text{H}_{5}\text{TiCl}(L^3)]\) complex.

| S. N. | d(obs) | d(calc) | \(\Delta(d)\) | \(I/I_m\times100\) | 2 \(\theta\) (obs) | 2 \(\theta\) (calc) | \(\Delta(2\theta)\) | h k l |
|-------|--------|---------|----------------|-----------------|-----------------|-----------------|-----------------|-----|
| 1     | 7.19085| 7.17660 | 0.01425        | 10.3012         | 12.299          | 12.323          | -0.025          | -1 1 1 |
| 2     | 4.17896| 4.18272 | -0.00376       | 7.6807          | 21.244          | 21.225          | 0.019           | -2 0 2 |
| 3     | 3.54710| 3.55353 | -0.00643       | 35.8433         | 25.085          | 25.039          | 0.046           | 2 3 1 |
| 4     | 3.30969| 3.30770 | 0.00200        | 100             | 26.917          | 26.933          | -0.017          | 2 3 1 |
| 5     | 3.24292| 3.24144 | 0.00148        | 29.2771         | 27.482          | 27.495          | -0.013          | -1 1 3 |
| 6     | 2.69133| 2.68877 | 0.00256        | 6.9879          | 33.263          | 33.295          | 0.033           | 0 3 3 |
| 7     | 2.53756| 2.54034 | -0.00278       | 1.7710          | 35.343          | 35.303          | 0.040           | 1 3 3 |
| 8     | 2.23666| 2.23602 | 0.00064        | 32.2289         | 40.290          | 40.302          | -0.012          | 1 6 1 |
| 9     | 2.16428| 2.16372 | 0.00056        | 5.6325          | 41.699          | 41.710          | -0.011          | 2 3 4 |
| 10    | 2.08592| 2.08655 | -0.00062       | 24.4277         | 43.343          | 43.329          | 0.014           | -5 1 3 |
| 11    | 1.80130| 1.80079 | 0.00052        | 28.5843         | 50.635          | 50.650          | -0.016          | 6 2 1 |
| 12    | 1.70300| 1.70273 | 0.00027        | 26.4156         | 53.785          | 53.794          | 0.009           | -6 4 2 |
| 13    | 1.63707| 1.63749 | -0.00042       | 15.3614         | 56.138          | 56.122          | 0.015           | 4 5 3 |

Table-2: Antibacterial Activity of Schiff bases and their corresponding of titanium(IV) complexes.

| S. N. | Complexes | Antibacterial(MIC, \(\mu g/ml\)) |
|-------|-----------|---------------------------------|
|       |           | *S. aureus* | *B. subtilis* | *P. aeruginosa* | *S. typhi* |
| 1     | L\(^1\)H  | 6.25        | 6.25          | 12.5            | 12.5       |
| 2     | \([\eta^5\text{-C}_5\text{H}_{5}\text{TiCl}(L^1)]\)| 3.12        | 3.12          | 12.5            | 12.5       |
| 3     | L\(^2\)H  | 3.12        | 3.12          | 6.25            | 6.25       |
| 4     | \([\eta^5\text{-C}_5\text{H}_{5}\text{TiCl}(L^2)]\)| 1.62        | 1.62          | 3.12            | 3.12       |
| 5     | L\(^3\)H  | 6.25        | 12.5          | 25              | 12.5       |
| 6     | \([\eta^5\text{-C}_5\text{H}_{5}\text{TiCl}(L^3)]\)| 3.12        | 6.25          | 12.5            | 6.25       |
| 7     | L\(^4\)H  | 6.25        | 6.25          | 25              | 25         |
| 8     | \([\eta^5\text{-C}_5\text{H}_{5}\text{TiCl}(L^4)]\)| 3.12        | 3.12          | 6.25            | 12.5       |
| 9     | ciprofloxacin (standard) | 1.62 | 1.62 | 3.12 | 3.12 |

Figure 5: Antibacterial activity of synthesized compounds and standard drug.
Table 3: Antifungal Activity of Schiff bases and their corresponding titanium(IV) complexes.

| S.N | Complexes                                      | Antifungal (MIC, $\mu g/ml$) |
|-----|------------------------------------------------|-----------------------------|
|     |                                                | $A.\text{niger}$ | $A.\text{flavus}$ | $C.\text{falcatum}$ |
| 1   | $L^1H$                                         | 6.25                       | 25               | 25               |
| 2   | $[\eta^2\cdot C_5H_5\cdot TiCl(L^1)]$         | 3.12                       | 6.25             | 12.5             |
| 3   | $L^2H$                                         | 3.12                       | 3.12             | 6.25             |
| 4   | $[\eta^2\cdot C_5H_5\cdot TiCl(L^3)]$         | 1.62                       | 1.62             | 3.12             |
| 5   | $L^3H$                                         | 6.25                       | 6.25             | 12.5             |
| 6   | $[\eta^2\cdot C_5H_5\cdot TiCl(L^3)]$         | 3.12                       | 3.12             | 6.25             |
| 7   | $L^4H$                                         | 6.25                       | 6.25             | 12.5             |
| 8   | $[\eta^2\cdot C_5H_5\cdot TiCl(L^4)]$         | 3.12                       | 3.12             | 6.25             |
| 9   | fluconazole (standard)                         | 1.62                       | 1.62             | 1.62             |

Figure 6: Antifungal activity of synthesized compounds and standard drug.

Conclusion:
Schiff bases ($L^1H$–$L^4H$) are monobasic, bidentate ligands coordinating through azomethine nitrogen and oxygen atom (NO donor). The complexes are soluble in PhNO$_2$, DMF and DMSO. The structures of Schiff bases and complexes have been established by elemental analysis and spectral studies IR, $^1$H NMR, $^{13}$C NMR, XRD and SEM. All these data puts together leads us to propose the structure of titanium(IV) complexes shown in Figure 1. Scanning electron microscope image showed that titanium complexes look like a nanocrystals and their sizes are 67.71 nm. Antifungal and antibacterial activities of the ligands and corresponding complexes have also been evaluated which showed that the activities increase on chelation.
Acknowledgements:-
The authors are thankful to the SAIF STIC Cochin for providing IR, $^{1}$HNMR, $^{13}$CNMR, XRD and SEM data. We thank the DRDO for financial support. Authors are also thankful to Department of Biotechnology, D.D.U Gorakhpur University, Gorakhpur for help in evaluating antibacterial studies.

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