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# Synthesis, spectroscopic studies and biological aspects of bis(cyclopentadienyl)titanium(IV) complexes with 4-amino-5-(nicotinic/picolinic/isonicotinic/indole-3-propyl/indole-3-ethyl)-3-mercapto-1,2,4-triazole

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Titanium(IV) complexes of type $[(\eta^5\text{-}C_5H_5)_2TiCl(L)]$ have been synthesized by the reactions of bis(cyclopentadienyl)-titanium(IV)dichloride with ligand (LH) derived from condensation of (nicotinic/picolinic/isonicotinic/indole-3-propyl/indole-3-ethyl)carboxylic acid and thiocarbohydrazide in dry tetrahydrofuran in the presence of triethylamine. All these complexes are soluble in $PhNO_2$, DMF and DMSO. The complexes are characterized by elemental analyses, electrical conductance, magnetic susceptibility, UV-Vis, IR, $^1H$ NMR, $^{13}C$ NMR, XRD and SEM spectral techniques. Low molar conductance values indicate that they are non-electrolytes. The spectral data indicate five-coordinate geometry for the complexes. XRD pattern indicate that the complexes have monoclinic crystal system and particle sizes were found at *ca.* 57.71 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 titanium(IV) complexes have higher antimicrobial effect than the parent Schiff bases.

Keywords: Titanocene, 1,2,4-triazole, NMR, IR, XRD, SEM, antimicrobial.

## 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 antibiotic[1], biological sensor[2], tumor cell killing agent[3] and gene targeting device[4]. It is an effective antimicrobial agent that kill bacterial cell in water due to the generation of reactive oxygen species[5] 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[6]. It was reported that photoexcited anatase $TiO_2$ particles could effectively induces cytotoxicity against HeLa cancer cells[7]. These photoexcited anatase $TiO_2$ particles will effectively damage the human colon carcinoma cell[3]. 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, large number of ring containing 1,2,4-triazoles have been incorporated in to a wide variety of therapeutically interesting drug candidates including antiinflammatory[8], CNS stimulants, antidepressant, anticonvulsant, anti-anxiety, antiasthmatic[9], antibacterial[10], antitubercular[11], anticancer[12], antiproliferative, antiulcerogenicity[13]. This moiety was found in potent agonist and antagonist receptor ligand[14], in HIV-1 protease inhibitors[15] and in thrombin inhibitors[16]. Triazole derivatives competitively inhibit lanosterol 14$\alpha$-demethylase (CYP51), a key enzyme in sterol biosynthesis of fungi. Based on structure of the active site of CYP51 and the extensive investigation of azole antifungals triazole inhibitors are able to fit in the active site by H-bonding, hydrophobic interaction and $\pi$–$\pi$ stacking within the heme environment of the enzyme[17]. 1,2,4-Triazole is an antifungal scaffold because of its high potency and low toxicity[18]. Hence many potent antifungal compounds were developed in recent past by bioisosteric replacement of imidazole moiety with triazole[19]. The widespread use of 1,2,4-triazoles as a scaffold in medicinal chemistry establishes this moiety as an

important bioactive class of heterocycles.

The present paper includes the synthesis, characterization and antimicrobial activities of bis(cyclopentadienyl)-titanium(IV) complexes with ligands 4-amino-5-(nicotinic/picolinic/isonicotinic/indole-3-propyl/Indole-3-ethyl)-3-mercapto-1,2,4-triazole.

## 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 $Et_3N$ was purified by published methods[20]. Bis(cyclopentadienyl)-titanium(IV) chloride was purchased from Aldrich. The ligands were prepared as reported in literature[21,22].

*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 $TiO_2$. $^1H$ and $^{13}C$ NMR spectra were recorded by a Bruker Avance III, 400 MHz. Chemical shifts are reported in ppm and are referenced to TMS. Infrared spectra (4000–200 $cm^{-1}$) 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 vapour. The magnetic susceptibility at room temperature was measured by Gouy's method using $Hg[Co(NCS)_4]$ as callibrant. 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 Bruker AXS D8 Advance X-ray powder diffractometer.

*Synthesis of titanium(IV) complexes:* A mixture of bis(cyclopentadienyl)titanium(IV) (60 mmol) and appropriate ligand 4-amino-5-(nicotinic/picolinic/isonicotinic/indole-3-propyl/indole-3-ethyl)-3-mercapto-1,2,4-triazole (60 mmol) was dissolved in dry tetrahydrofuran (15 $cm^3$). To the resulting clear solution, triethylamine (60 mmol) was added and the mixture was refluxed for *ca.* 10–12 h at room temperature. The coloured complexes, so obtained, were recrystallized from a mixture of dimethylformamide and ether dried *in vacuo*.

The synthetic route for the preparation of ligands and their corresponding bis(cyclopentadienyl)titanium(IV) complexes is given in Fig. 1.

*Biological activity study:*

*Bio safety during the antibacterial and antifungal activity:* The antimicrobial properties of the Schiff bases ($L^1H$-$L^5H$) and there corresponding 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% isopropenol/water followed by bleach. The work area was also sterilized with 70% isopropenol/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 bio safety bages in tightly closed bins. Bio safety bages 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 subcultured 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 (6.0 mm in diameter) were placed on

the nutrient agar plates. Five milligrams of each test compounds were dissolved in 1 mL of DMSO separately to prepare stock solution. From stock solution, different concentrations 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 bacterial growth. Ciprofloxacin was designated in our experiment as a control drug.

*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 1 mL of DMSO, and solution was diluted with water (9 mL). 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. Petri dishes were inoculated with $1.5\times10^4$ colony forming units (CFU) and incubated at 37°C for 26 h. The MICs in μg/mL were noted. To ensure that 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 result of the antimicrobial studies was summarized in Table 3.

*Chemistry:*

[$(\eta^5\text{-}C_5H_5)_2$Ti)$L^1$]: Yellow color solid; m.p. (°C): 178, yield (%): 72 (stirring method) 10 h, analyses (%) found (calcd. for $C_{17}H_{16}N_5STiCl$): C, 50.05 (50.29); H, 3.88 (3.90); N, 17.06 (17.20); S, 7.80 (7.88); Cl, 8.45 (8.69); Ti, 11.66 (11.89); mol. wt. found (calcd.): 405.23 (405.56); IR (KBr, $cm^{-1}$): 2988m (νC-H aromatic), 2940s (νC-H aliphatic), 1630s (νC=N triazole), 462m (νTi-N), 384m (νTi-S), 1369s (ν sk triazole ring), 612s (νC-S), 1572m (νN-N=C), 3418b ($\nu NH_2$ group),1162 (νN-N), 3105m, 1460m, 1042m, 834w (ν $\eta^5$-$C_5H_5$); $^1$H NMR (δ): 5.70 (s $\eta^5$-$C_5H_5$), 7.45–8.92m (nicotinic ring), 12.3s (2H) ($NH_2$ group); $^{13}$C NMR (δ): 116 ($\eta^5$-$C_5H_5$), 120–155 (nicotinic ring), 147, 152 (triazole ring).

[$(\eta^5\text{-}C_5H_5)_2$Ti)$L^2$]: Dirty yellow color solid; m.p. (°C): 184; yield (%): 78 (stirring method) 11 h, analyses (%) found (calcd. for $C_{17}H_{16}N_5STiCl$): C, 50.24 (50.32); H, 3.85 (3.94); N, 17.14 (17.23); S, 7.76 (7.88); Cl, 8.53 (8.70); Ti, 11.62 (11.82); mol. wt. found (calcd.): 405.34 (405.56); IR (KBr, $cm^{-1}$): 2987m, (νC-H aromatic), 2933s (νC-H aliphatic), 1628s (νC=N triazole), 460m (νTi-N), 382m (νTi-S), 1367s (ν sk of triazole ring), 609s (νC-S), 1570m (νN-N=C), 3417b ($\nu NH_2$ group), 1160 (νN-N), 3102m, 1457m, 1040m, 830w (ν $\eta^5$-$C_5H_5$); $^1$H NMR (δ): 5.78s ($\eta^5$-$C_5H_5$), 7.28–8.73m (picolinic ring), 12.8s (2H) ($NH_2$ group), $^{13}$C NMR (δ): 115.7 ($\eta^5$-$C_5H_5$), 123–148 (picolinic ring), 147, 152 (triazole ring).

[$(\eta^5\text{-}C_5H_5)_2$Ti)$L^3$]: Light brown color solid; m.p. (°C): 186; yield (%): 74 (stirring method) 10 h, analyses (%) found (calcd. for $C_{17}H_{16}N_5STiCl$): C, 50.04 (50.22); H, 3.82 (3.90); N, 17.09 (17.20); S, 7.26 (7.84); Cl, 8.49 (8.67); Ti, 11.65 (11.79); mol. wt. found (calcd.): 405.59 (405.70); IR (KBr, $cm^{-1}$): 2985m, (νC-H aromatic), 2935s (νC-H aliphatic), 1626s (νC=N triazole), 457m (νTi-N), 382m (νTi-S), 1364s (ν sk of triazole ring), 603s (νC-S), 1569m (νN-N=C), 3421b ($\nu NH_2$ group), 1159 (νN-N), 3104m, 1455m, 1039m, 832w (ν $\eta^5$-$C_5H_5$); $^1$H NMR (δ): 5.64s ($\eta^5$-$C_5H_5$),7.54–8.76m (4H) (isonicotinic ring), 13.3s (2H) ($NH_2$ group); $^{13}$C NMR (δ): 115.5 ($\eta^5$-$C_5H_5$), (122–150) (isonicotinic ring), 147, 152 (triazole ring).

[$(\eta^5\text{-}C_5H_5)_2$Ti)$L^4$]: Brown color solid; m.p. (°C): 173; yield (%): 68 (stirring method) 12 h, analyses (%) found (calcd. for $C_{22}H_{22}N_5STiCl$): C, 55.94 (56.02); H, 4.52 (4.69); N, 14.74 (14.80); S, 6.68 (6.76); Cl, 7.39 (7.48); Ti, 10.05 (10.12); mol. wt. found (calcd): 471.08 (471.73); IR (KBr, $cm^{-1}$): 2979m, (νC-H aromatic), 2931s (νC-H aliphatic), 1622s (νC=N triazole), 454m (νTi-N), 380m (νTi-S), 1360s (ν sk of triazole ring), 1454s (νC=C), 593s (νC-S), 1567m (ν N-N=C), 3416b ($\nu NH_2$ group ), 1158 (νN-N), 3101m, 1454m, 1038m, 828w (ν $\eta^5$-$C_5H_5$); $^1$H NMR (δ): 5.53s ($\eta^5$-$C_5H_5$), 7.21–7.46m (4H), 6.68s (1H) (for C-H of indole ring), 10.79s (1H) (for N-H of indole ring), 2.57t (2H), 2.78t (2H) (methylene), 13.8s (2H) ($NH_2$ group), $^{13}$C NMR (δ): 115.3 ($\eta^5$-$C_5H_5$), 113–139 (indole ring), 148, 152 (triazole ring), 31–25 (methylene).

[$(\eta^5\text{-}C_5H_5)_2$Ti)$L^5$]: Dirty brown color solid; m.p. (°C): 192; yield (%): 70 (stirring method) 11 h, analyses (%) found (calcd. for $C_{23}H_{24}N_5STiCl$): C, 56.04 (56.88); H, 4.90 (4.95); N, 14.30 (14.39); S, 6.33 (6.58); Cl, 7.18 (7.26); Ti, 9.66 (9.79); mol. wt. found (calcd.): 485.02 (485.85); IR (KBr, $cm^{-1}$): 2978m,

(νC-H aromatic), 2927s (νC-H aliphatic), 1617s (νC=N triazole), 452m (νTi-N), 378m (νTi-S), 1356s (ν sk of triazole ring), 590s (νC-S), 1562m (νN-N=C), 3415b ($\nu NH_2$ group), 1154 (νN-N), 3094m, 1450m, 1032m, 823w (ν $\eta^5$-$C_5H_5$); $^1$H NMR (δ): 5.53s ($\eta^5$-$C_5H_5$), 7.14m (4H), 6.67s (1H) (for C-H of indole ring), 10.42s (1H) (for N-H of indole ring), 2.51t (2H), 2.39t (2H), 1.84q (2H) (for methylene), 13.4s (2H) ($NH_2$ group), $^{13}$C NMR (δ): 115.2s ($\eta^5$-$C_5H_5$), 110–142 (indole ring), 149, 154 (triazole ring), 31–25 (methylene).

## Results and discussion

(Nicotinic/picolinic/isonicotinic/indole-3-propyl/indole-3-ethyl)carboxylic acid reacts with thiocarbohydrazide in ethanol in acidic medium to give ligands (LH) (**I**). These ligands react with bis(cyclopentadienyl)titanium(IV) dichloride to give colored amorphous products of type [($\eta^5$-$C_5H_5$)$_2$TiCl(L)], (**II**) as shown in Fig. 1.

The complexes are soluble in nitrobenzene, dimethyl formamide and dimethylsulphoxide. The molar conductance values in DMF are in range of 8–12 $\Omega^{-1}$ 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 475–436 nm, which was assigned to the charge transfer band and is in accordance with an (n–1)d$^0$ ns $^0$ electronic configuration[23]. One more band was observed at *ca.* 280–318 nm, which may be due to intra-ligand transition.

*Infrared spectra:* The IR spectra provide valuable informations regarding the nature of the functional group attached

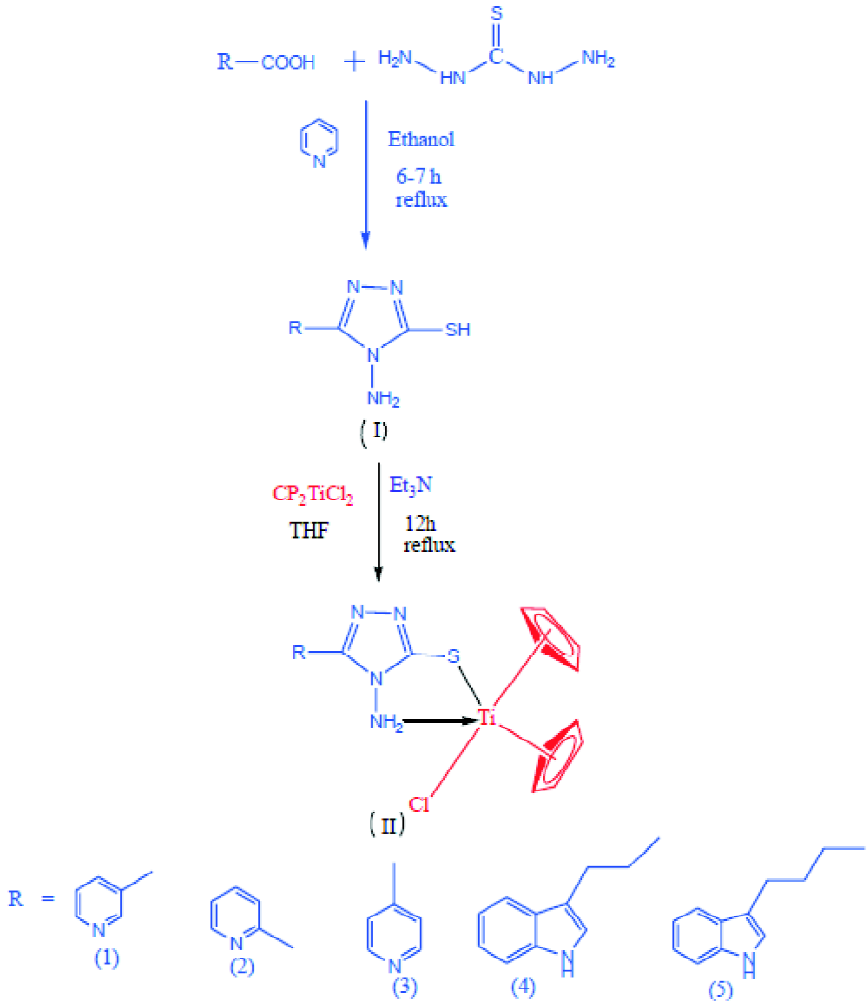


**Fig. 1.** Reaction scheme for the preparation of Schiff bases (I) and their corresponding titanium(IV) complexes (II).

to the metal atom. Ligand appear to exist in both thiol and thione tautomeric forms **(I)** as suggested by a broad band at *ca.* 2700–2600 $cm^{-1}$ assignable to ν(SH).

In complexes (**1**-**5**) ν(SH) band disappears indicating the deprotonation of thiol group and formation of bond between metal and sulphur. This is further confirmed by appearance of new band in complexes at *ca.* $cm^{-1}$, assignable to ν(Ti-S)[25,26]. The spectra of Schiff bases show a broad band at 3230–3274 $cm^{-1}$ due to ν(N–H) which remains almost at the same position in complex indicating the non-involvement of N-H group in bond formation. New bands appear in metal complexes at *ca.* 593–455 $cm^{-1}$ due to ν(Ti-N) vibrations. All ligand and their titanium(IV) complexes show bands at *ca.* 3103–2975 $cm^{-1}$ due to ν(Ar-H), 2939 $cm^{-1}$ for aliphatic hydrogen, 1473–1476 $cm^{-1}$ for (C=C)[28], 1137–1139 for (C-S) stretching. Absorption bands occurring at *ca.* 2978–2996 $cm^{-1}$ for ν(C–H), *ca*. 1420 $cm^{-1}$ for ν(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 ($\eta^5$-$C_5H_5$) group persists in the complexes[25,26].

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

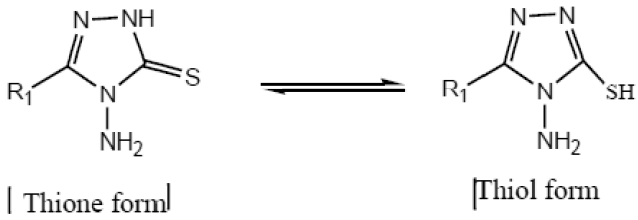


**Fig. 2.** Synthesized Schiff bases in tautomeric forms.

$^1$H NMR: The proton magnetic resonance spectra of ligand and their corresponding complexes were recorded in DMSO-$d_6$ chemical shift for proton in different environments. 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 titanium(IV) complexes exhibit signals at δ 5.35–5.70 assigned to the cyclopentadienyl ring proton and indicate the rapid rotation of the ring about the metal axis (25-26). All ligands exhibits signals at δ 4.2–4.6 due thiol group proton which disappear in corresponding titanium(IV) complexes. This confirms that the thiol group reacted with metal ion via deprotonation. Multiplate δ 6.90–9.15 ppm due to aromatic protons in the ligand and their corresponding titanium(IV) complexes show signals at δ 6.82–8.94 ppm this indicate signal shift downfield slightly upon coordination through metal ion in complexes. Ligands ($L^4$H, $L^5$H) and their corresponding titanium(IV) complexes also exhibit a signals at δ 2.97–2.45 due to methylene protons. The $^1$H NMR spectra of ligand of type ( $L^4$H, $L^5$H) exhibit signals at δ 10.6 due to NH group of indole ring and their corresponding titanium(IV) complexes exhibit signals at δ 10.79 this indicate signal shift downfield only slightly upon coordination through metal ion in complexes.

$^{13}$C NMR spectra: The $^{13}$C NMR spectra of ligand and their corresponding complexes were recorded in DMSO-$d_6$. Ligands ($L^4$H, $L^5$H) and complexes show singlet at δ 31.2 and 25.6 ppm may be assigned to methylene carbons respectively. For triazole ring carbons, two signals appear at δ 158.4, 157.3 which remain unchanged in their corresponding complexes (**1**-**5**) indicating that triazole ring carbons are not participated in bond formation[24]. All complexes show peak at δ 115.2–116 ppm due to cyclopentadienyl group[25–27]. The signal observed in the region δ 122.5–152.4 ppm as a multiplet could be assigned to aromatic carbons of ligands and their corresponding complexes.

SEM: The morphology and particle size of the titanium(IV) complexes were investigated using SEM. Fig. 3 depicts the SEM images of the synthesised 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 irregular of many 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 titanium(IV) complex [($\eta^5$-$C_5H_5$)$_2$TiCl($L^5$)] with a particle size of 57.77 nm. Complex [($\eta^5$-$C_5H_5$)$_2$TiCl($L^2$)] has a well-arranged microgranular with cuboid shape structure. The image of complex [($\eta^5$-$C_5H_5$)$_2$TiCl($L^3$)] shows a granular-like

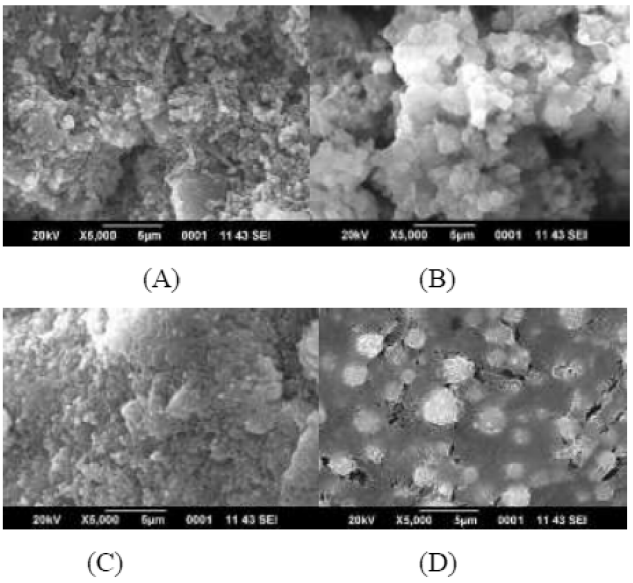


**Fig. 3.** SEM images of (A) [$(\eta^5$-$C_5H_5)_2TiCl(L^1)$], (B) [$(\eta^5$-$C_5H_5)_2TiCl(L^2)$], (C) [$(\eta^5$-$C_5H_5)_2TiCl(L^3)$], and (D) [$(\eta^5$-$C_5H_5)_2TiCl(L_5)$] complexes.

micro-shaped structure. However, complex [$(\eta^5$-$C_5H_5)_2TiCl(L^1)$] has granular-shaped morphology with micro and nanometric particle size.

X-Ray diffraction study: X-Ray powder diffraction pattern of one representative titanium(IV) complex is given in Fig. 4. The structural characterization of the complex 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 Cu K$\alpha$ (k = 1.54056 Å) source. The XRD pattern clearly indicates the formation of nanocrystal. The crystallite size have been calculated by using Debye-Scherer formula[29,30] given as

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

where $D$ is the crystallite size, $\lambda$ is the wavelength of X-ray used; $\beta$ is the full width at half maximum (FWHM) and is the Bragg angle of diffraction. The average crystallite sizes of the titanium(IV) complex was found to be 57.71 nm range.

The indexing of the powder patterns for titanium(IV) complex was carried out using the program N-TREOR. The Miller indices (*hkl*) relate the peak positions or *d*-spacings to the lattice parameters by an equation specific to the crystal system. The initial unit cell (lattice) parameters were also determined by N-TREOR[31]. These unit cell parameters were refined from the regression analysis and the best crystal system and space group were assigned using CHEKCELL[32] program. It was found that the complex [$(\eta^5$-$C_5H_5)_2TiCl(L^2)$] reveal monoclinic crystal systems with the most probable space P21/n. The lattice parameters and observed and calculated X-ray diffraction data for the titanium(IV) complexes have been shown in Table 1.

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 favours the

**Table 1.** The unit cell parameters and observed and calculated X-ray diffraction data of [$(\eta^5$-$C_5H_5)_2TiCl(L^3)$] complex

$a$ = 10.09209 Å, $b$ = 11.58679 Å, $c$ = 9.66536 Å, $\beta$ = 100.4924 , cell vol = 1111.2418 Å$^3$

| Sr. No. | $d$ (obs) | $d$ (calcd.) | $\Delta$ ($d$) | $I/I_m\times100$ | 2$\theta$ (obs) | 2$\theta$ (calcd.) | $\Delta$ (2$\theta$) | $h\,k\,l$ |
|---|---|---|---|---|---|---|---|---|
| 1. | 3.68571 | 3.68272 | 0.00298 | `23.4545 | 24.127 | 24.147 | –0.020 | –2 2 1 |
| 2. | 3.31584 | 3.31711 | –0.00127 | 36.9127 | 26.866 | 26.855 | 0.011 | –3 0 1 |
| 3. | 2.86217 | 2.86254 | –0.00037 | 73.9393 | 31.225 | 31.221 | 0.004 | 3 1 1 |
| 4. | 2.53027 | 2.52953 | 0.00074 | 32.3030 | 35.448 | 35.459 | –0.011 | –3 0 3 |
| 5. | 2.44826 | 2.44643 | 0.00183 | 27.0303 | 36.677 | 36.705 | –0.028 | –1 4 2 |
| 6. | 2.21288 | 2.21369 | –0.00081 | 11.7449 | 40.742 | 40.726 | 0.016 | –1 5 1 |
| 7. | 2.11078 | 2.11214 | –0.00135 | 20.8484 | 42.807 | 42.778 | 0.029 | –3 3 3 |
| 8. | 1.59568 | 1.59551 | 0.00016 | 8.4242 | 57.729 | 57.736 | –0.007 | –6 2 2 |

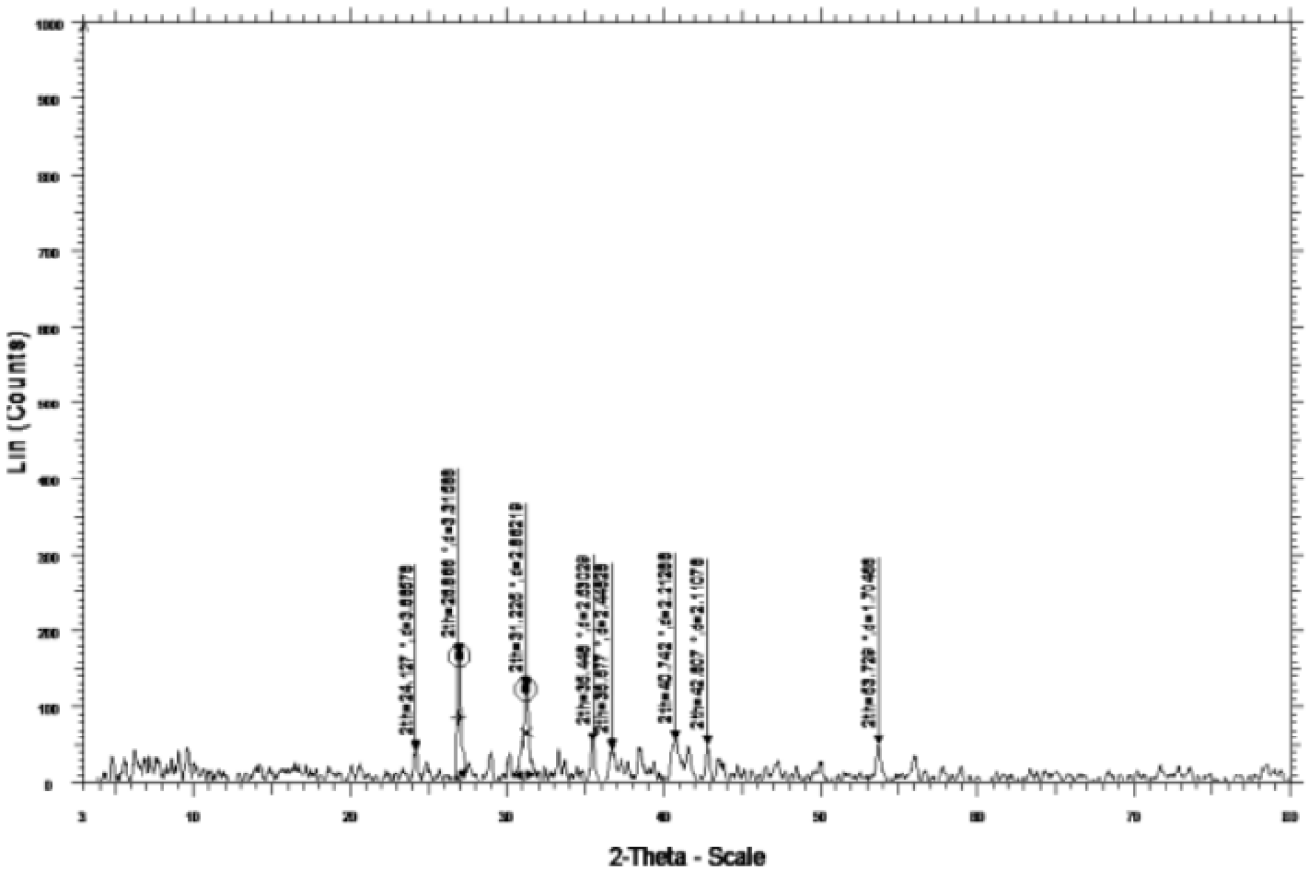


**Fig. 4.** A representative XRD spectra of complex $[(\eta^5\text{-}C_5H_5)_2TiCl(L^5)]$.

**Table 2.** Antibacterial activity of Schiff base and their respective of Ti(IV) complexes of 4-amino-5-(nicotinic/picolinic/isonicotinic/indole-3-propyl/indole-3-ethyl)-3-mercapto-1,2,4-triazole Schiff bases

| Sr. No. | | Antibacterial (MIC, μg/ml) | | | |
|---|---|---|---|---|---|
| | Compound | *S. aureus* | *B. subtilis* | *P. aeruginosa* | *S. typhi* |
| 1. | $L^1H$ | 3.12 | 6.25 | 6.25 | 25 |
| 2. | $[(\eta^5\text{-}C_5H_5)_2TiClL^1]$ | 1.62 | 3.12 | 3.12 | 6.12 |
| 3. | $L^2H$ | 12.5 | 25 | 25 | 50 |
| 4. | $[(\eta^5\text{-}C_5H_5)_2TiClL^2]$ | 6.25 | 12.5 | 12.5 | 25 |
| 5. | $L^3H$ | 12.5 | 25 | 50 | 50 |
| 6. | $[(\eta^5\text{-}C_5H_5)_2TiClL^3]$ | 6.25 | 12.5 | 25 | 25 |
| 7. | $L^4H$ | 3.12 | 6.25 | 6.25 | 12.5 |
| 8. | $[(\eta^5\text{-}C_5H_5)_2TiClL^4]$ | 1.62 | 3.12 | 3.12 | 12.5 |
| 9. | $L^5H$ | 6.25 | 12 | 12.5 | 25 |
| 10. | $[(\eta^5\text{-}C_5H_5)_2TiClL^5]$ | 3.12 | 6.25 | 6.25 | 12.5 |
| 11. | Ciprofloxacin (standard) | 1.62 | 1.62 | 1.62 | 1.62 |

passage of lipid-soluble materials, making the solubility an important factor controlling the antimicrobial activity[33]. Tweedy's chelation theory the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand

**Table 3.** Antifungal activity of ligand and their respective of Ti(IV) complexes of 4-amino-5-(nicotinic/picolinic/isonicotinic/indole-3-propyl/indole-3-ethyl)-3-mercapto-1,2,4-triazole

| Sr. No. | Complexes | Antifungal (MIC, μg/ml) *A. niger* | *A. flavus* | *C. falcatum* |
|---|---|---|---|---|
| 1. | $L^1H$ | 3.12 | 6.25 | 25 |
| 2. | $[(\eta^5\text{-}C_5H_5)_2TiClL^1]$ | 3.12 | 3.12 | 12.5 |
| 3. | $L^2H$ | 6.12 | 12.5 | 50 |
| 4. | $[(\eta^5\text{-}C_5H_5)_2TiClL^2]$ | 3.12 | 6.25 | 12.5 |
| 5. | $L^3H$ | 6.25 | 25 | 12.5 |
| 6. | $[(\eta^5\text{-}C_5H_5)_2TiClL^3]$ | 3.12 | 12.5 | 6.25 |
| 7. | $L^4H$ | 3.12 | 6.25 | 6.25 |
| 8. | $[(\eta^5\text{-}C_5H_5)_2TiClL^4]$ | 1.62 | 3.12 | 3.12 |
| 9. | $L^5H$ | 6.25 | 6.25 | 12.5 |
| 10. | $[(\eta^5\text{-}C_5H_5)_2TiClL^5]$ | 1.62 | 3.12 | 6.25 |
| 11. | Fluconazole (standard) | 1.62 | 1.62 | 1.62 |

orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π-electrons over the whole chelate ring and enhances the lipophilicity of the hetero chelates. Furthermore, the mode of action comprising the compounds may involve the formation of hydrogen bond through the azomethine/carbonyl/amine group with the active centre of cell constituents and interferences forced with the normal cell process[34]. In antibacterial activity all ligands and titanium(IV) complexes are found to be more active against *S. aureus* (Fig. 5). It is found that substitution in the ligands increases the activity against bacteria and fungi. Indole substituted ligands/compounds are more active than the other substituted ligands/compounds. Due to the chelating properties of indole group, antibacterial and antifungal activity increases. The complexes $[(\eta^5\text{-}C_5H_5)_2TiCl(L^4)]$ is more active against all bacteria and fungi due to the chelation of ligands. In antifungal activity, all Schiff bases and titanium(IV) complexes are more active against *A. niger* (Fig. 6).

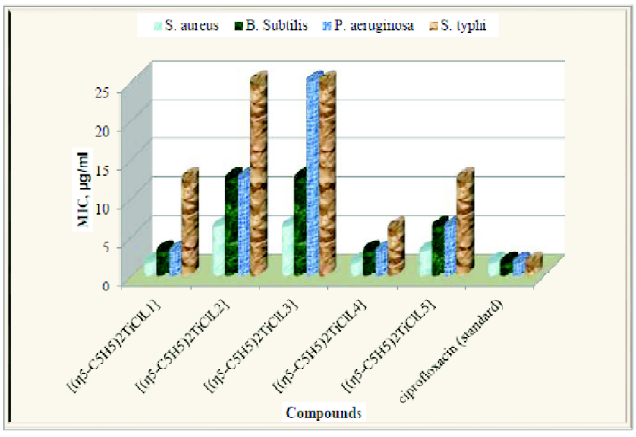


**Fig. 5.** Antibacterial activity of synthesized compounds and standard drug.

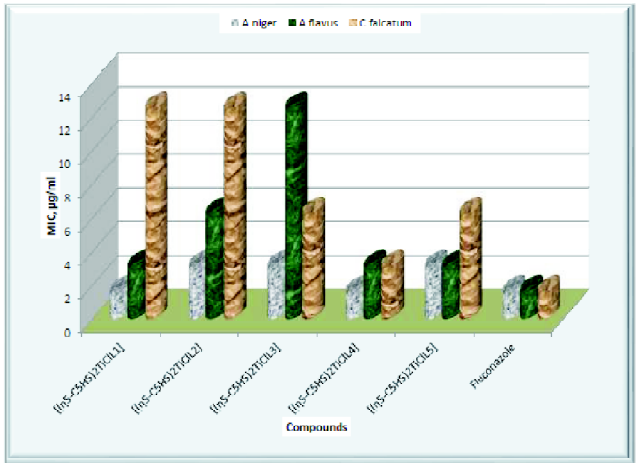


**Fig. 6.** Antifungal activity of synthesized compounds and standard drug.

## Conclusion

Schiff bases ($L^1H$-$L^5H$) are monobasic, bidentate ligands coordinating through amine nitrogen and sulphur atom (NS 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, $^1H$ NMR, $^{13}C$ NMR, XRD and SEM. All these data puts together leads us to propose the structure of titanium(IV) complexes shown in Fig. 1. Scanning electron microscope image showed that titanium complexes look like a nanocrystals and their sizes are 57.71 nm. Antifungal and antibacterial activities of the ligands and corresponding complexes have also been evaluated which showed that the activities increase on chelation.

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