



**SYNTHESIS, SPECTRAL CHARACTERIZATION AND ANTIMICROBIAL
STUDIES OF NANO-SIZED ORGANOTITANIUM (IV) COMPLEXES WITH
SCHIFF BASES DERIVED FROM 5-(SUBSTITUTED ARYL)-2-HYDRAZINO-1, 3,
4-OXADIAZOLE AND INDOLINE-2, 3-DIONE**

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Abstract

*Titanium (IV) complexes of type $[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}(\text{L})]$ 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 impendence of triethylamine. All these complexes are soluble in PhNO_2 , DMF and DMSO. The complexes were characterized by elemental analyses, electrical conductance, magnetic susceptibility, UV-Vis, IR, ^1H NMR, ^{13}C NMR and XRD spectral techniques. Low molar conductance values indicate non-electrolytic nature of the complexes. The spectral data indicate 5-coordinate geometry for the complexes. XRD pattern evince that the complexes have monoclinic crystal system and particle sizes were found in the range 42.32 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.cereus*) bacterial strains using minimum inhibition concentration method (MIC) by serial dilution technique. The titanocene (IV) complexes have higher antimicrobial impact than the parent Schiff bases.*

Keywords: Titanocene, IR, NMR, XRD, Antimicrobial



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Introduction

There has been an adequate interest in the application of titanium complexes in biological applications. The material titanium is spaciouly used as disinfectant [1], antibiotic [2], biological sensor [3], tumor cell killing agent [4] and gene targeting device [5]. It is an efficacious 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 several biological molecules [7,8].

On the other hand, 1,3,4-Oxadiazole derivatives have been found to demonstrate miscellaneous biological activities such as antibacterial [9], antifungal [10], anti-inflammatory [11] antioxidant and antihypertensive [12]. The prevalent use of 1,3,4-oxadiazoles as a scaffold in medicinal chemistry underlay this moiety as an vital bio-active class of heterocycles.

The present paper comprise 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.

1. Experimental

2.1 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 illuminated methods [13]. Bis(cyclopentadienyl)titanium(IV) chloride was buy up from Aldrich. The ligands were prepared as reported in literature [14].

2.2 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. ¹H and ¹³CNMR spectra were recorded by a Bruker Avance III, 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 calibrant. 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.

2.3 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 stirred for *ca* 10–12 h at room temperature. The coloured complexes, so obtained, were recrystallized from a mixture of dimethylformamide and etherdried in vacuo.

The physical properties and analytical data of the complexes are given in **Table 1**.

2.4 Biological activity study

2.4.1 Bio safety during the antibacterial and antifungal activity

The antimicrobial properties of the Schiff bases (L¹H–L⁴H) and thereorganotitanium(IV) complexes were tested against three fungal strains *Aspergillus flavus*, *Aspergillus niger*, *Colletotrichum falcatum* and four bacteria namely *Bacillus cereus*, *Pseudomonas aeruginosa*, *Salmonella typhi* and *Streptococcus aureus*. Bacteria/fungi are potentially perilous 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.

2.5 Antimicrobial studies

2.5.1 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.cereus* 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 compounds were dissolved in 1mL of DMSO separately to prepare stock solution. From stock solution, different concentrations 100, 50, 25, 12.5, 6.25, 3.12, 1.625 and 0.81µg/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. The results of the antibacterial studies were summarized in **Table 6**.

2.5.2 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 (5µg) 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, 1.62 and 0.81µg/mL. Petri dishes were inoculated with 1.5×10^4 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 results of the antifungal studies were summarized in **Table-7**.

2. 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 colored amorphous products of type $[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl(L)}]$, (II) as shown in **Figure-1**.

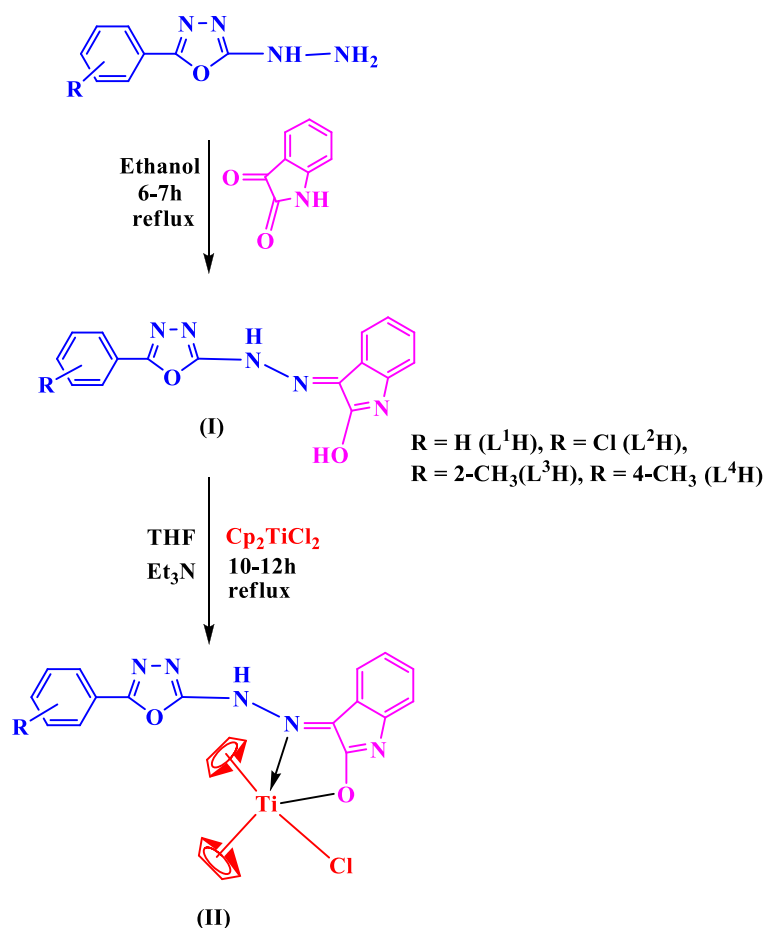


Figure-1: Reaction scheme for the preparation of Schiff bases (I) and their corresponding titanium(IV) complexes (II).

The complexes are soluble in nitrobenzene, dimethylformamide and dimethylsulphoxide. The molar conductance values in DMF are in range of $4\text{-}9\ \text{ohm}^{-1}\text{cm}^2\ \text{mol}^{-1}$ indicating nonelectrolyte behavior in solution. Magnetic susceptibility measurements show their diamagnetic nature.

3.1 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.

3.2 Infrared spectra

The IR spectra provide valuable information regarding the nature of the functional group attached to the metal atom. Schiff bases ($\text{L}^1\text{H}\text{-}\text{L}^4\text{H}$) appear to exist in both keto and enol tautomer forms (**Figure 2**) suggested by a broad band (solution spectra) at $2600\ \text{cm}^{-1}$,

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 1312-1330 cm⁻¹ in the complexes. The coordination through phenolic oxygen further confirmed by the appearance of band at 480-500cm⁻¹ assignable [16] to $\nu(\text{Ti-O})$. The spectra of Schiff bases show a medium band at 3240-3274cm⁻¹ due to $\nu(\text{N-H})$ which remains almost at the same position in complex indicating the non-involvement of N-H group in bond formation. The $\nu(\text{C-O-C})$ vibration appears as a strong band at ca.1080 cm⁻¹ in the free ligands type (L¹H-L⁴H) [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 $\nu(\text{C=N})$ 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 455-463 cm⁻¹ are assigned [19] to $\nu(\text{Ti-N})$. Absorption bands occurring at ca 2978-2996 cm⁻¹ for $\nu(\text{C-H})$, ca 1420 cm⁻¹ for $\nu(\text{C-C})$ 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 ($\eta^5\text{-C}_5\text{H}_5$) group persists in the complexes [20]. The significant IR spectral data of organotitanium (IV) complexes are listed in **Table-2**.

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.

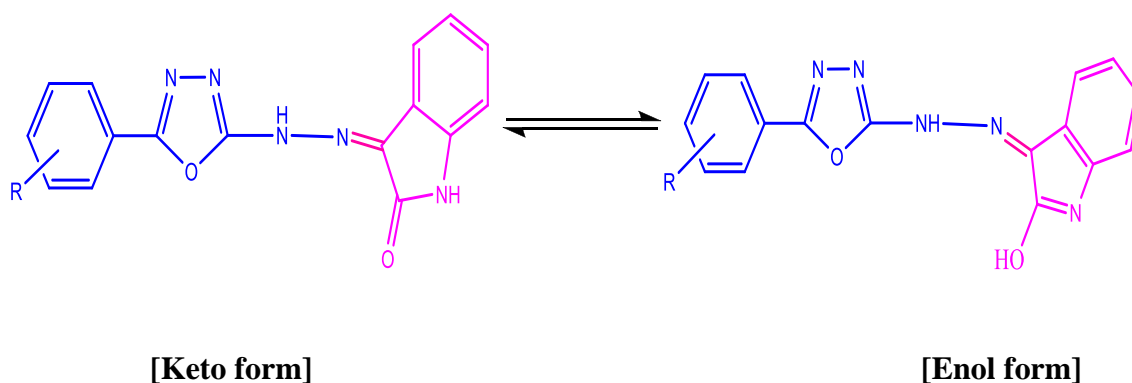


Figure-2 Synthesized Schiff bases in tautomer forms

3.3 ¹H NMR spectra

The proton magnetic resonance spectra of ligand and their corresponding complexes were recorded in DMSO-d₆. The intensities of all the resonance lines 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 demonstrate signals at δ 6.93-6.96 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 (L¹H-L⁴H) exhibit signals at δ 5.52-5.60 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 7.29-7.40 ppm due to aromatic protons in the Schiff bases and their corresponding titanium(IV) complexes. Titanium(IV) complexes also exhibit a signal at δ 1.15-1.30 ppm due to methyl protons. The ¹H NMR spectra of titanium(IV) complexes exhibit signals at δ 12.29-12.32 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. The significant ¹H NMR spectral data of organotitanium (IV) complexes are listed in **Table-3**.

3.4 ¹³C NMR spectra

The ¹³C NMR spectra of these complexes were recorded in DMSO-d₆. Schiff bases derived from indoline-2,3-dione (L¹H-L⁴H) show signals at δ 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 δ 13.5 ppm in ligands (L³H, L⁴H) and their corresponding complexes. Schiff bases of type (L¹H-L⁴H) and their corresponding titanium(IV) complexes show signals at about δ 169 ppm and δ 160 ppm assignable for oxadiazole ring carbons. These signals remain unchanged in their corresponding complexes indicating that oxadiazole ring nitrogen is not participated in bond formation. All complexes show peak at δ 115.2-116 ppm due to cyclopentadienyl group [19]. The signal observed in the region δ 122-152 ppm as a multiplet could be assigned to aromatic carbons of ligands and their corresponding complexes. The significant ¹³C NMR spectral data of organotitanium (IV) complexes are listed in **Table-4**.

3.5 X-Ray powder diffraction

The structural characterization of the complex $[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}(\text{L}^3)]$ 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 $\text{CuK}\alpha_1$ ($\lambda = 1.54056\text{\AA}$) source. The XRD pattern of the complex was given in **Figure 3**. The peaks in the XRD pattern clearly indicate the formation of nano crystals. The crystallite sizes have been calculated using Debye-Scherrer formula [22, 23] given by

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

Where D is the crystallite size, λ is the wavelength of X-ray used; β is the full width at half maximum (FWHM) and θ is the Bragg angle of diffraction. The average crystallite sizes of the complex $[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}(\text{L}^3)]$ was found in the range 42.32-49.36 nm.

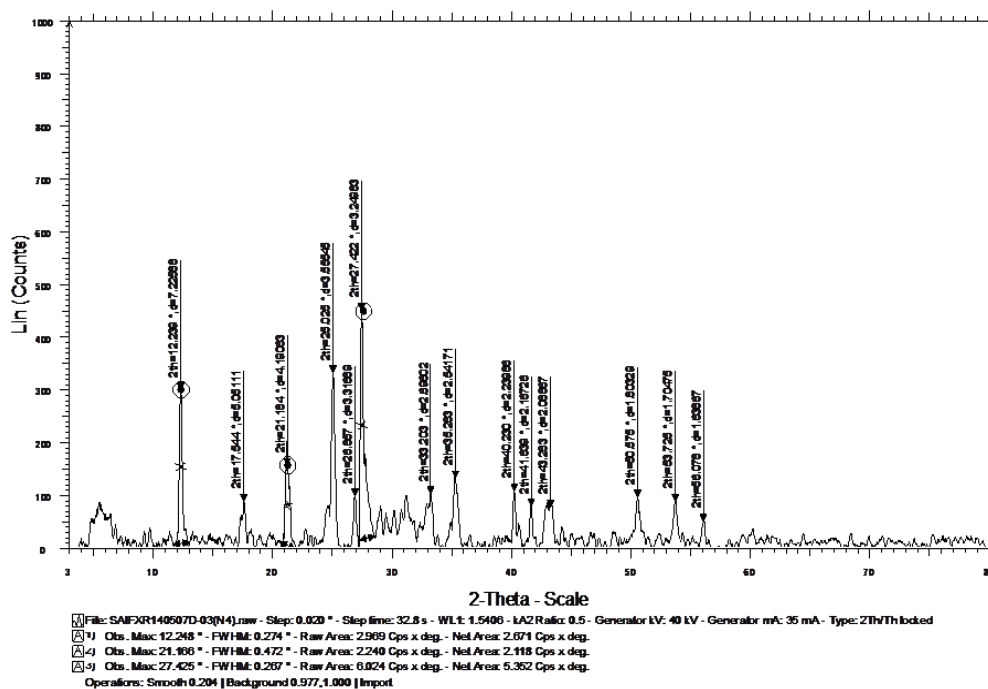


Figure- 3 A representative XRD spectra of complex $[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}(\text{L}^3)]$

3.6 Antimicrobial activity

The Schiff bases are found to be biologically active and their corresponding organotitanium(IV) complexes show significantly enhanced antibacterial (**Table 5**) and antifungal (**Table 6**) 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 [24]. 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 π -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 [25]. In antifungal activity all ligands and titanium(IV) complexes are found to be more active against *A. flavus* (**Figure 5**). 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 $[(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}(\text{L}^2)]$ 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 4**).

Conclusion

Schiff bases ($\text{L}^1\text{H}-\text{L}^4\text{H}$) 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, ^1H NMR, ^{13}C NMR and XRD. All these data puts together leads us to propose the structure of titanium(IV) complexes. 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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Table-1 Physical properties and analytical data of organotitanium (IV) complexes of 5-(substituted aryl)-2-hydrazino-1,3,4- oxadiazole Schiff bases.

S. No.	Complexes	Empirical formula	Color	Yield	Conductance (Ohm ⁻¹ cm ² mole ⁻¹)	Analysis (%) Found(Calculated)			
						Ti	C	H	N
1	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ¹)]	(C ₂₆ H ₂₀ N ₅ O ₂ TiCl)	Light brown	74	6.2	9.10(9.13)	60.43(60.49)	3.57(3.89)	13.39(13.59)
2	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ²)]	(C ₂₇ H ₂₂ N ₅ O ₂ TiCl)	Brown	63	4.1	8.86(8.95)	61.12(61.19)	4.16(4.22)	13.18(13.25)
3	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ³)]	(C ₂₇ H ₂₂ N ₅ O ₂ TiCl)	Light brown	70	5.7	8.82(8.89)	61.11(61.17)	4.27(4.53)	13.59(13.64)
4	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ⁴)]	(C ₂₆ H ₁₉ N ₅ O ₂ TiCl ₂)	Light yellow	56	7.3	8.56(8.73)	56.74(56.86)	3.46(3.49)	12.53(12.65)

Table-2 Significant IR spectral band of organotitanium (IV) complexes of 5-(substituted aryl)-2-hydrazino-1,3,4- oxadiazole Schiff bases.

S. No	Complexes	ν(C=N)	ν(N-H)	ν(Ti-O)	ν(Ti-N)	ν(C-O)	ν(C-O-C)	ν (η ⁵ -C ₅ H ₅)
1	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ¹)]	1605s	3248m	489m	458m	1318s	1084m	2978 m, 1420 m, 1010 m, 803 w
2	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ²)]	1600s	3240m	480m	455m	1312s	1080m	2988m, 1420 m, 1006 m, 810 w
3	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ³)]	1610s	3274m	500m	463m	1330s	1098m	2996m, 1420 m, 1015 m, 807 w
4	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ⁴)]	1608s	3260m	493m	460m	1326s	1092m	2984m, 1420 m, 1012 m, 800 w

Table -3 ¹HNMR spectral data of titanium(IV) complexes of 5-(substituted aryl)-2-hydrazino-1,3,4- oxadiazole Schiff bases.

S.No.	Complexes	(η ⁵ -C ₅ H ₅)	Aromatic Ring (m)	-NH (hydrazino) (s)	Methyl group
1	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ¹)]	6.93s	7.59-7.52m	12.31	-
2	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ²)]	6.93s	7.57-7.53m	12.36	-
3	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ³)]	6.93s	7.58-7.50m	12.40	-
4	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ⁴)]	6.96s	7.60-7.55m	12.29	1.07

Table-4 ¹³C NMR spectral data of Ti (IV) complexes of 5-(substituted aryl)-2-hydrazino-1,3,4-oxadiazoleSchiff bases.

S.No.	Complexes	(η ⁵ -C ₅ H ₅)	Aromatic ring	Methyl group	-C=N (Azomethine)	oxadiazole ring
1	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ¹)]	115.2	126-149	----	150	165, 162
2	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ²)]	116.0	130-152	----	153	169, 165
3	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ³)]	115.6	120-142	9.2	147	162,150
4	[(η ⁵ -C ₅ H ₅) ₂ TiCl(L ⁴)]	115.8	124-149	9.7	150	165, 162

Table-5 Antibacterial Activity of Schiff bases and their corresponding of titanium(IV) complexes of 5-(substituted aryl)-2-hydrazino-1,3,4- oxadiazole Schiff bases.

S. N.	Complexes	Antibacterial (MIC, $\mu\text{g/ml}$)			
		S. aureus	B. cereus	P. aeruginosa	S. typhi
1	L ¹ H	3.12	6.25	25	25
2	[[η^5 -C ₅ H ₅] ₂ TiCl(L ¹)]	1.62	3.12	12.5	12.5
3	L ² H	1.62	1.62	3.12	6.25
4	[[η^5 -C ₅ H ₅] ₂ TiCl(L ²)]	0.81	0.81	1.62	3.12
5	L ³ H	6.25	12.5	25	12.5
6	[[η^5 -C ₅ H ₅] ₂ TiCl(L ³)]	3.12	6.25	12.5	6.25
7	L ⁴ H	6.25	6.25	12.5	25
8	[[η^5 -C ₅ H ₅] ₂ TiCl(L ⁴)]	3.12	3.12	6.25	12.5
9	ciprofloxacin (standard)	1.62	1.62	3.12	3.12

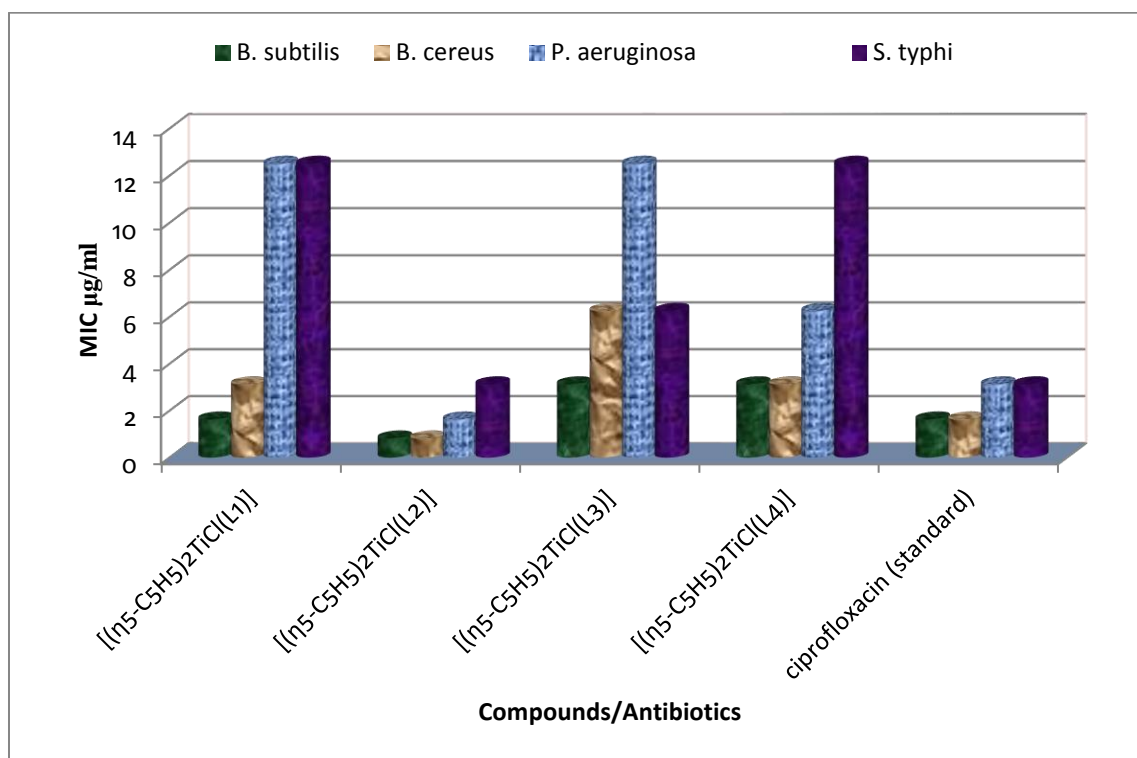


Figure-4 Antibacterial activity of synthesized compounds and standard drug

Table-6 Antifungal Activity of Schiff bases and their corresponding organotitanium (IV) complexes of 5-(substituted aryl)-2-hydrazino-1,3,4- oxadiazole Schiff bases.

S.N	Complexes	Antifungal (MIC, $\mu\text{g/ml}$)		
		<i>A. flavus</i>	<i>B. niger</i>	<i>C.falcatum</i>
1	L ¹ H	1.62	25	25
2	[(η^5 -C ₅ H ₅) ₂ TiCl(L ¹)]	0.81	6.25	12.5
3	L ² H	3.12	6.25	6.25
4	[(η^5 -C ₅ H ₅) ₂ TiCl(L ²)]	0.81	3.12	3.12
5	L ³ H	6.25	6.25	12.5
6	[(η^5 -C ₅ H ₅) ₂ TiCl(L ³)]	3.12	3.12	6.25
7	L ⁴ H	6.25	6.25	12.5
8	[(η^5 -C ₅ H ₅) ₂ TiCl(L ⁴)]	3.12	3.12	6.25
9	fluconazole (standard)	1.62	1.62	1.62

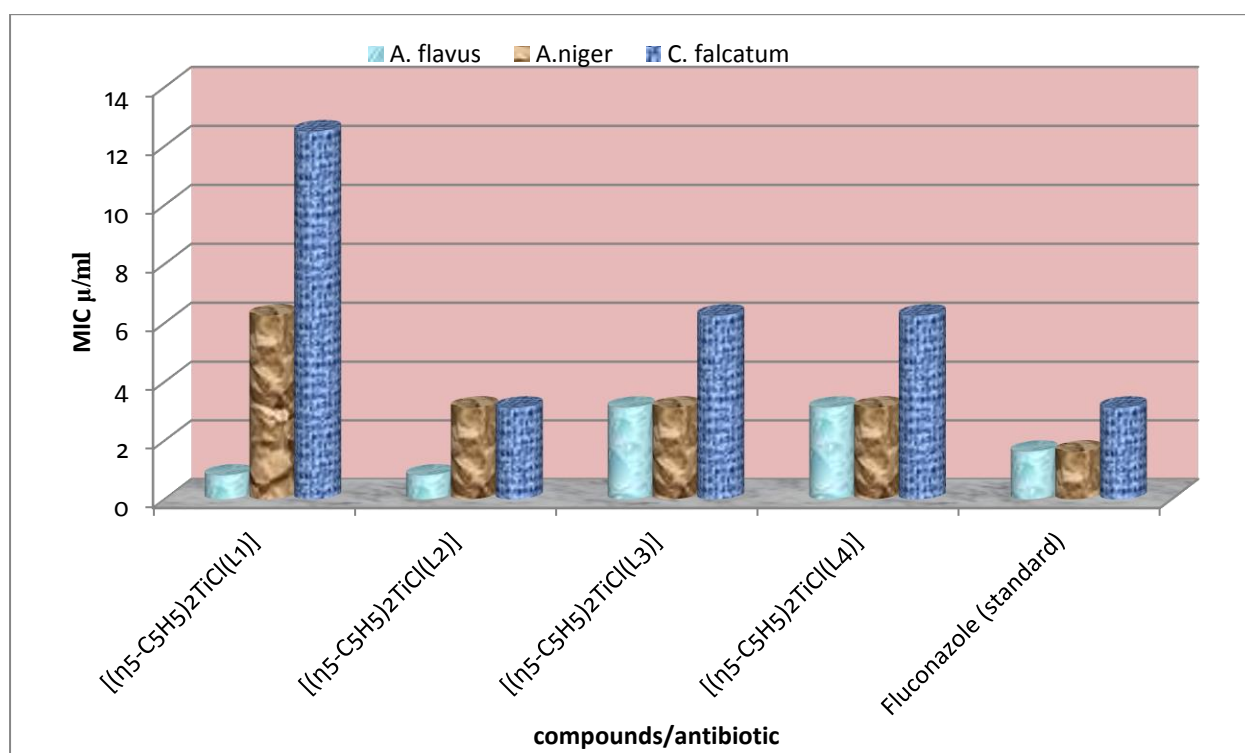


Figure-5 Antifungal activity of synthesized compounds and standard drugs