



Research Article

Biological evaluation and molecular docking of some newly synthesized 3d-series metal(II) mixed-ligand complexes of fluoro-naphthyl diketone and dithiocarbamate

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Abstract

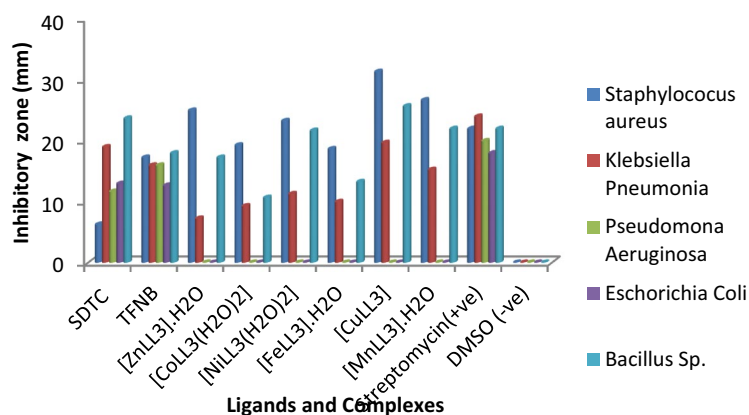
A series of some 3d (Mn, Fe, Co, Ni, Cu and Zn) metal(II) complexes of mixed-ligands-*N,N'*-dimethyldithiocarbamate (SDTC) and 4,4,4-trifluoro-1-(2-naphthyl)-1,3-butanedione (TFNB) have been synthesized and presented for antioxidant, antibacterial and antifungal studies. The complexes were examined for their in-vitro antioxidant potentials by employing ferrous ion chelating and DPPH scavenging methods, while the in-vitro antimicrobial screening of the unbound ligands and their mixed metal(II) complexes against bacteria- *Staphylococcus aureus*, *Bacillus cereus* (Gram (+ve)), *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Escherichia coli* (Gram (-ve)), and fungi- *Aspergillus niger*, *Aspergillus flavous*, *Fusarium species* using agar and disc diffusion methods respectively. The studies revealed that Co(II) complex had the highest antioxidant potential with the percentage scavenging inhibition of 75.04%. The antimicrobial screening of the complexes against the bacterial microbes showed that Cu(II) complex had the best activity with inhibitory zone range of 19.7–31.3 mm; while Fe(II) complex possesses highest fungicidal activities within the inhibitory zone range of 28.7–38.0 mm; compared to other complexes against the fungi strains. Molecular docking approach indicated that Cu(II) complex had higher binding affinity with π -sulphur and Van der Waals interactions.

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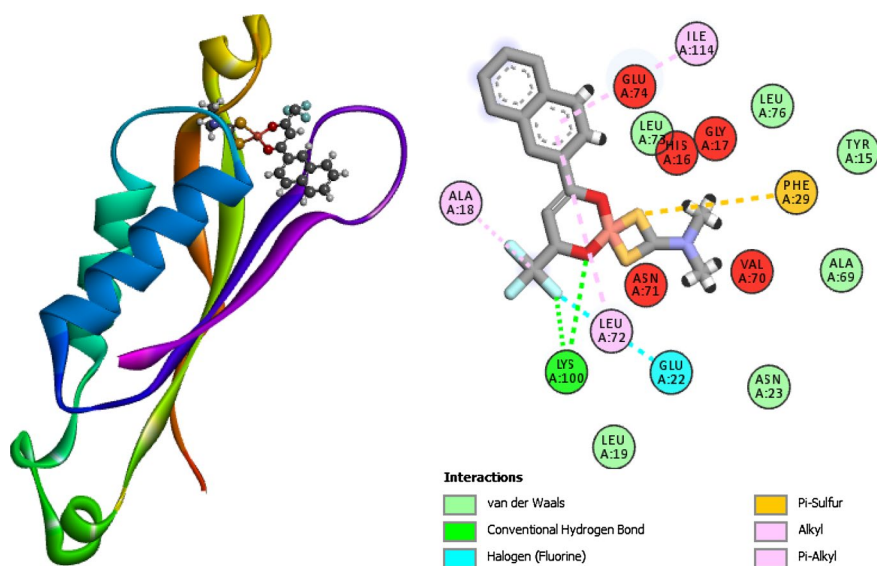


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Graphical abstract



Antibacterial activity of the test compounds represented on Histogram



3-D and 2-D bonding interactions inside the active pocket of Staphylococcus aureus-Cu complex (with the highest binding affinity)

Keywords Microbes · Antioxidant potentials · Toxic · Molecular docking · Binding affinity

1 Introduction

Most of the 3d series (first row transition metals) of the transition elements have been found so important and useful in biological systems. Naturally, many enzymes found in the human body systems, which serve as catalyst for the processes of life are products of coordination compounds/complexes. They consist of one or two transition metals as the center ion. For instance, the mono-nuclear thiolate complex $[\text{Fe}(\text{Cys})_4]$ [1] found in rubredoxins (Rd)

present in bacteria, rhombic iron-sulphur $[2\text{Fe}-2\text{S}]$ clusters found in ferredoxins (Fd) and type I blue copper proteins are essential as electron transfer within the body system [2], while carboxypeptidase which contain zinc metal (Zn) ion centre is a type of coordination compound that behaves as an enzyme and catalyses digestion processes. Other iron (Fe) ion center containing enzymes-haemoglobin or myoglobin and copper (Cu) ion center-haemocyanin are in control of storage and transportation of oxygen, whereas, cobalt (Co) ion center- vitamin B_{12}

cobalamin coenzyme functions as promoter of more than a few molecular conversions within the body systems of mammal [3]. Moreover, chloroplast and chlorophyll (green pigment) formations that are responsible for the processes of food synthesis (photosynthesis) in plants are made up of manganese (Mn) and magnesium (Mg) ion centers [4].

However, chelating ligands and metal complexes comprising atoms with lone pair of electrons such as nitrogen (N), oxygen (O) or sulphur (S) are of exceptional interest because of increase in the coordination fashion in which they are bonded to the central metal ions (structural diversity) and pronounced biological activities they displayed, such as potential drugs [5, 6] and fungicidal agents [7]. β -diketones happened to be one of these promising ligands and several biological activities of their metal complexes such as antioxidant, antibacterial, antifungal and anticancer properties [8–11] have been reported.

Furthermore, dithiocarbamates and their metal complexes have also been reported to possess: antibacteria, antifungal, antioxidant and anticancer activity; and in the industry, they are used as catalyst in the sulphur vulcanization of rubber [12–15]. Nevertheless, the biological evaluation of first row transition metal complexes of mixed-ligands-*N,N'*-dimethyldithiocarbamate (SDTC) and 4,4,4-trifluoro-1-(2-naphthyl)-1,3-butanedione (TFNB) have not been considered and documented. In continuation of our work on these newly synthesized 3d series (Mn, Fe, Co, Ni, Cu and Zn) metal(II) mixed-ligands complexes of dithiocarbamates and β -diketones [16, 17], this paper aim to investigate the biological potency of the transition metal(II) complexes of two ligand systems of *N,N'*-dimethyldithiocarbamate (SDTC) and 4,4,4-trifluoro-1-(2-naphthyl)-1,3-butanedione (TFNB), which might find importance and applications as lead compounds in metal-based chemotherapy/pharmacology as antibacterial,

antifungal and antioxidant agents. Molecular docking studies would also be carried out in order to corroborate the binding affinity of the complexes.

2 Experimental

2.1 Materials and reagents

All the chemicals and solvent used were of analytical grade, obtained from standard commercial groups such as Sigma-Aldrich, Central Drug House (CDH chemicals), British Drug House Chemicals Limited (BDH) and were used as supplied. They include sodium dimethyldithiocarbamate (SDTC), 4,4,4-trifluoro-1-(2-naphthyl)-1,3-butanedione (TFNB), 2,2-diphenyl-1-picrylhydrazyl, ascorbic acid, 1,10-phenanthroline, streptomycin, fluconazole, manganese(II) sulphate monohydrate, iron(II) sulphate heptahydrate, copper(II) sulphate pentahydrate, zinc(II) sulphate heptahydrate, cobalt(II)chloride hexahydrate and nickel(II) chloride hexahydrate. Dimethylsulphoxide (DMSO) solvent was used for the preparation of each concentrations of all the compounds under investigation.

2.2 Synthetic method for the metal(II) complexes

The two ligand system metal(II) complexes were prepared according to published procedure [16] with little modification. Equimolar amounts of 0.60 g (4.189×10^{-3} mol) SDTC and 1.12 g (4.189×10^{-3} mol) TFNB were dissolved in 15 mL 50% ethanol while stirring at room temperature and 0.71–1.20 g (4.189×10^{-3} mol) of the respective metal(II) salts were added slowly and carefully to the mixture, with constant stirring. The resultant coloured homogenous solutions were refluxed for 5 h. The precipitated products

Table 1 Antibacterial activities of the ligands and metal complexes (mm)

Compounds/bacteria	<i>Staphylococcus aureus</i>	<i>Klebsiella pneumonia</i>	<i>Pseudomona aeruginosa</i>	<i>Eschorichia coli</i>	<i>Bacillus sp.</i>
SDTC, L	6.3±0.4	19.0±0.7	11.7±0.4	13.0±0.7	23.7±0.4
TFNB, L ³	17.3±0.9	16.0±0	16.0±0	12.7±0.4	18.0±0
[ZnLL ³].H ₂ O	25.0±0.7	7.3±0.9	No activity	No activity	17.3±0.4
[CoLL ³ (H ₂ O) ₂]	19.3±0.9	9.3±0.9	No activity	No activity	10.7±0.9
[NiLL ³ (H ₂ O) ₂]	23.3±0.9	11.3±0.9	No activity	No activity	21.7±0.4
[FeLL ³].H ₂ O	18.7±0.9	10.0±0	No activity	No activity	13.3±0.9
[CuLL ³]	31.3±0.9	19.7±0.4	No activity	No activity	25.7±0.4
[MnLL ³].H ₂ O	26.7±0.9	15.3±0.9	No activity	No activity	22.0±0
Streptomycin(+ve)	22.0±0	24.0±0	20.0±0	18.0±0	22.0±0
DMSO (–ve)	No activity	No activity	No activity	No activity	No activity

Average zone of inhibition (mm) of the three values were presented with average deviation, while streptomycin was a positive reference standard and DMSO as a negative control

Table 2 Antifungal activities of ligands and metal complexes (mm)

Compounds/bacteria	<i>Aspergillus niger</i>	<i>Aspergillus flavous</i>	<i>Fusarium species</i>
SDTC, L	35.3 ± 0.9	28.0 ± 0	30.7 ± 0.9
TFNB, L ³	30.0 ± 0	32.7 ± 0.9	30.3 ± 0.4
[ZnLL ³]-H ₂ O	33.3 ± 0.9	23.3 ± 0.9	34.0 ± 0
[CoLL ³ (H ₂ O) ₂]	R	R	32.0 ± 0
[NiLL ³ (H ₂ O) ₂]	R	R	36.0 ± 0
[FeLL ³]-H ₂ O	36.0 ± 0	28.7 ± 0.9	38.0 ± 0
[CuLL ³]	R	R	36.0 ± 0
[MnLL ³]-H ₂ O	29.7 ± 0.4	10.0 ± 0	38.0 ± 0
Fluconazole(+ ve)	15.3 ± 0.9	11.0 ± 0.7	14.0 ± 1.3
DMSO (-ve)	R	R	R

Average zone of inhibition (mm) of the three values were presented with average deviation, while fluconazole was a positive reference standard and DMSO as a negative control. R implies Resistance

were separated by filtration, washed with the starting solvent and diethyl ether, and dried over silical gel.

2.3 Antioxidant studies

The antioxidant activity of the test compounds were determined by two different antioxidant assays- ferrous ion chelating activity and DPPH free radical scavenging ability.

2.3.1 Ferrous ion (Fe²⁺) chelating capacity

The antioxidant activity of the mixed ligands metal(II) complexes were determined by ferrous ion chelating ability according to published procedure [18]. The stock solution of the metal(II) mixed-ligand complexes was prepared by dissolution of appropriate amounts (1.0 mg) of each complexes in 1.0 mL DMSO. In the same manner, 50 mg of 1,10-Phenanthroline and 11 mg of FeSO₄·7H₂O were separately dissolved in 100 mL DMSO. The same proportion, 1.0 mL each of the three solutions were carefully and thoroughly mixed together, stirred mechanically for 4–6 min, with the addition of 2.0 mL DMSO. The homogenous mixture was incubated (stored in the dark cupboard) practically for 16 min at room temperature, and the absorbance of each sample mixture solution was detected spectrophotometrically at 550 nm. The mixture of 1 mL FeSO₄·7H₂O, 1 mL 1,10-Phenanthroline and 2 mL DMSO solutions represented the control or blank, while the standard was ascorbic acid. The basis for evaluation was carried out in triple identical parts and ferrous ion chelating activity measured as percentage scavenging inhibition was stated and calculated as:

$$\% \text{ ferrous scavenging inhibition} = \frac{A_{\alpha} - A_{\epsilon}}{A_{\alpha}} \times \frac{100}{1}$$

From the expression:

A_α denotes absorbance of control or blank solution, while

A_ε denotes absorbance of sample solution and also absorbance of standard solution separately.

2.3.2 DPPH Scavenging Activity

The assay was carried out according to published procedure [19], with little adjustment. The DPPH (2,2-diphenyl-1-picrylhydrazyl) assay, has been the easiest and broadly employed method of determining the free radical scavenging potential of antioxidant substances or compounds, which is based on the reduction of a stable free DPPH radical, resulted on the decrease of absorbance and lowering of colour (purple → yellow) caused by antioxidants. Various concentrations (100 µg/mL, 200 µg/mL, 300 µg/mL, 400 µg/mL and 500 µg/mL) from 1.0 mg of each complexes in 1.0 mL DMSO of the test complexes were prepared and 25 mg/L of DPPH with DMSO solvent was also prepared. The 1.0 mL test complexes and 3.0 mL DPPH solution was completely mixed together and placed in the dark for 1,800 s at 25 °C. After incubation, the absorbance of each mixture of test compounds plus DPPH solution was measured spectrophotometrically against the blank and standard solutions at 517 nm. The test complexes was completely absent in the control or blank solution.

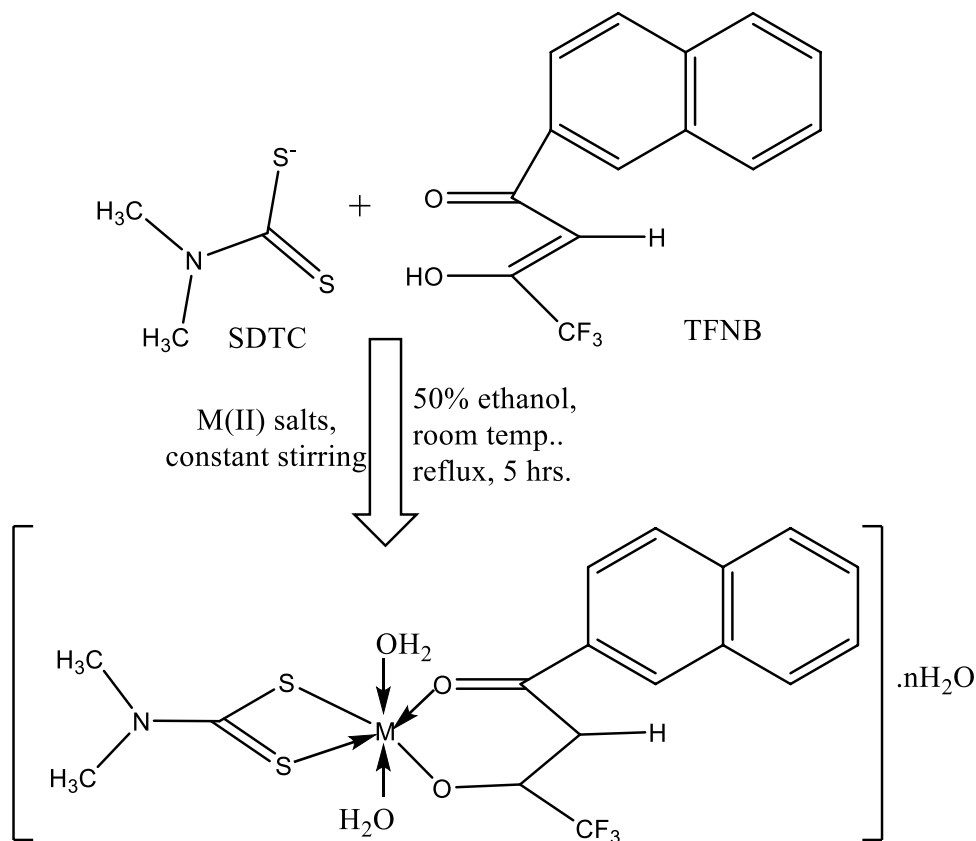
The percentage DPPH scavenging effect is calculated using the equation:

DPPH scavenging effect (%) or Percent inhibition

$$= A_0 - A_1 / A_0 \times 100.$$

where A₀ is the Absorbance of control reaction and A₁ is the Absorbance in presence of test or standard sample.

Scheme 1 Formation of the complexes from the starting ligands and the hydrated metal(II) salts



- a) 4-coordinate $M-2H_2O = Fe, Mn, Zn$ when $n = 1$ and Cu when $n = 0$
 b) 6-coordinate $M = Co, Ni$ when $n = 0$

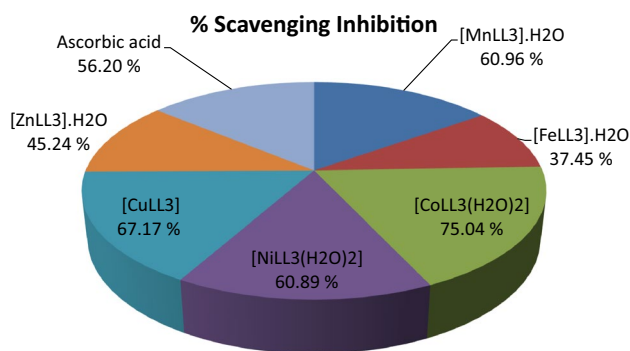


Fig. 1 Antioxidant activity of the complexes showing their percentage ferrous scavenging inhibition

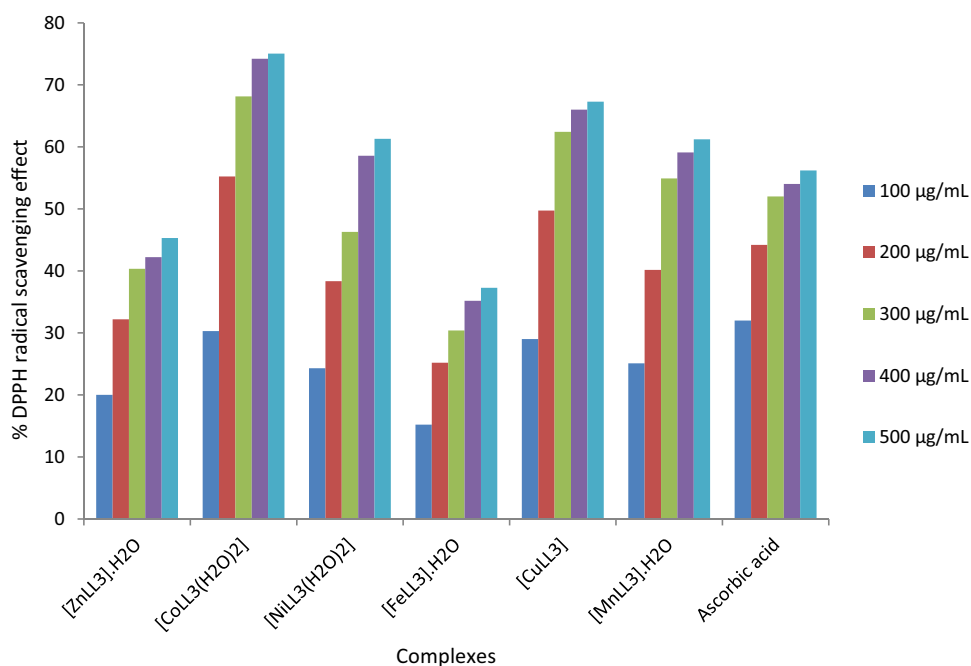
2.4 Antimicrobial studies

All the metal(II) mixed-ligand complexes were screened for their in-vitro antibacterial and antifungal activities using agar diffusion and disc diffusion methods respectively.

2.4.1 Antibacterial assay

Agar diffusion method [18] was employed to evaluate the in vitro antibacterial activities of the metal complexes. The five laboratory clinical bacteria strains used for the screening consist of two Gram (+ve) bacteria, viz., *Staphylococcus aureus* and *Bacillus cereus* and three Gram(-ve) bacteria, namely, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Escherichia coli*. In a petri dish, the agar's surface was evenly inoculated with 0.3 mL of 1,080 min old test bacteria culture. 7 mm diameter wells were punched in the solidified agar inside plates, using a sterile cork borer, and metal complexes/ ligands dissolved in DMSO (100 µg per milliliter solution of each compound) were dropped into the wells and allowed to stand for almost 30 min on the bench. The inoculated plates were incubated at 37 °C for a day, after which the inhibitory zones were measured in millimeter (mm), which invariably correspond to the measure of antibacterial activities. Streptomycin was used as the positive reference standard drugs for the test bacteria, while DMSO was used as the negative control. The experiments were conducted in triplicates and the average zone

Fig. 2 Percentage DPPH radical scavenging activity of the complexes at various concentrations



of inhibition with the average deviation for the test compounds against bacteria is presented in Table 1.

2.4.2 Antifungal Screening

Disc diffusion method [20] was used to estimate the in-vitro antifungal activities of the metal(II) mixed-ligand complexes. Three different microbes (fungi) were used for the screening. They are: *Aspergillus niger*, *Aspergillus flavus* and *Fusarium species*. Potato dextrose agar (PDA) was employed to measure the effect of the test complexes on the fungi. 1 mL conidial suspension from each fungal isolate was poured into 90 mm petri dish of 20 mL PDA, and left to** dry with removal of excess suspension. A 6 mm diameter sterile test discs were infused with 15 µL of each test compound solution (100 microgramme per milliliter of complex dissolved in DMSO) to get 100 µg/disc in triplicates. The standard or reference drug used was fluconazole in the same concentration per disc while negative control was DMSO. The incubation of all plates at room temperature took 24 h, after which the inhibition region of fungal growth was measured in millimeter. The average zone of inhibition with the average deviation of the test complexes against the fungi is presented in Table 2.

2.5 Molecular Docking method

The docking approach was employed to investigate the inhibition potentials by calculated binding energies. The 3D structures of proteins were downloaded from Protein data bank (PDB). The proteins of *Bacillus cereus*,

Staphylococcus aureus, *Escherichia coli*, and *Pseudomonas aeruginosa* were identified with their PDB codes; 5NCD (resolution 2.45 Å [21], 2DHN (2.2 Å resolution) [22], 1wxh (1.97 Å resolution) [23], and 2w7q (1.88 Å resolution) [24], respectively. The AutoDock tools [25] was applied to determine the grid box and the grid spacing X = 25, Y = 25, Z = 25 with 1.00 Å was used [26]. Gasteiger charges were added using the AutoDock tools graphical user interface from MGL Tools [27]. Lamarckian genetic algorithm was employed in the search for the optimum binding site for the ligands. The compounds were optimized prior to docking using Gaussian 09, [28] to obtain a minimal structures.

3 Results and discussion

3.1 General structure of the ligands and synthesized complexes

A schematic study of the reactions of the two ligands, SDTC and TFNB with the respective metal(II) salts in 1:1:1 molar ratio in EtOH have been prepared and presented below (Scheme 1).

3.2 Biological studies

3.2.1 Antioxidant studies

Ferrous ion chelating and DPPH free radical scavenging assays were employed to determine the antioxidant activities of all the metal(II) mixed-ligand complexes under

investigation. In ferrous ion chelating method, a red coloured complex of [(1,10-phen)Fe]²⁺ was formed from reaction of FeSO₄·7H₂O and 1,10-phenanthroline, prior to the assay. There was a reduction in colour of this complex formation when in contact with a reducing agent, resulting in lowering of absorbance. This absorbance measurement permits the evaluation of the metal ion chelating potential of the complexes, since chelating activity of a substance has been known to be an important basis for antioxidant proficiency [29]. Ferrous ion (Fe²⁺) easily allow reactive oxygen species (ROS) production in mammal's systems through Fenton reaction- Fe²⁺ + H₂O₂ → Fe³⁺ + ·OH + OH⁻; thus stimulate lipid peroxidation and decomposition of lipid hydroperoxidation into alkoxy and peroxy radicals [30].

The DPPH (2,2-diphenyl-1-picrylhydrazyl) assay method is based on the reduction of a stable free radical, DPPH. The free radical DPPH with an odd electron gives a maximum absorption at 517 nm (purple colour). When antioxidants react with DPPH, it becomes paired off in the presence of a hydrogen donor (e.g., a free radical scavenging antioxidant), reduced to the DPPH-H and as a result the

absorbance decreased from the DPPH free radical to the DPPH-H form, causing decolorization (that is purple → yellow colour) with respect to the number of electrons captured. The more the decolorization, the more is the reducing ability. When a solution of free radical DPPH (K*) is mixed with that of a substance that can donate a hydrogen atom (AH), then the occurrence of reduced form of non radical (diphenylpicrylhydrazine (KH), with the disappearance of the violet colour, even though residual pale yellow colour from the picryl group persist [31].

In this study, the percentage ferrous scavenging inhibition of all the compounds are shown in Figs. 1 while 2 illustrates the percentage DPPH free radical scavenging activity of the synthesized complexes as compared with the standard ascorbic acid at various concentrations of 100 µg/mL, 200 µg/mL, 300 µg/mL, 400 µg/mL and 500 µg/mL.

The results revealed that Co(II) complex had the highest percentage scavenging inhibition of 75.04% while Fe(II) complex had the lowest activity of 37.45%. The Ni(II), Mn(II) and Cu(II) complexes also had inhibitory activity in

Fig. 3 Antibacterial activity of the test compounds represented on Histogram

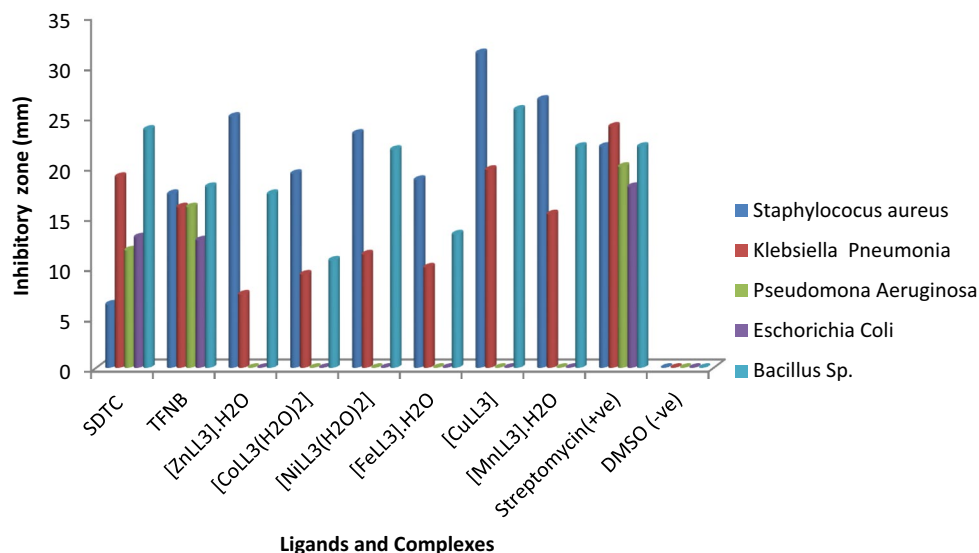


Table 3 Binding free energies (ΔG) of compounds with different targets obtained after molecular docking using AutoDock 1.5.4

Compounds/bacteria	<i>Staphylococcus aureus</i>	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	<i>Escherichia coli</i>	<i>Bacillus sp.</i>
[ZnLL ³].H ₂ O	5.8	5.5	–	–	7.8
[CoLL ³ (H ₂ O) ₂]	10.8	6.7	–	–	5.8
[NiLL ³ (H ₂ O) ₂]	9.8	8.4	–	0.8	7.7
[FeLL ³].H ₂ O	8.6	6.6	1.4	1.2	6.7
[CuLL ³]	12.6	10.4	1.8	2.0	11.4
[MnLL ³].H ₂ O	7.7	9.3	1.6	2.5	9.5

L = SDTC, L³ = TFNB

Fig. 4 Histogram representation of antifungal activity of the compounds

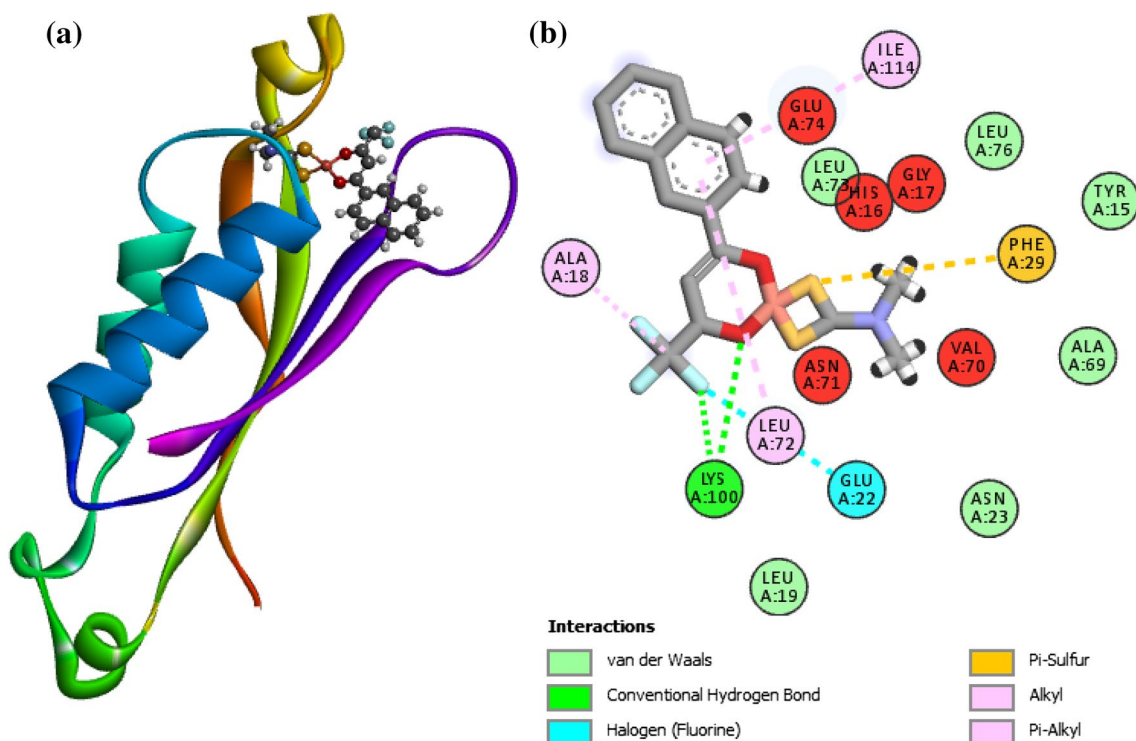
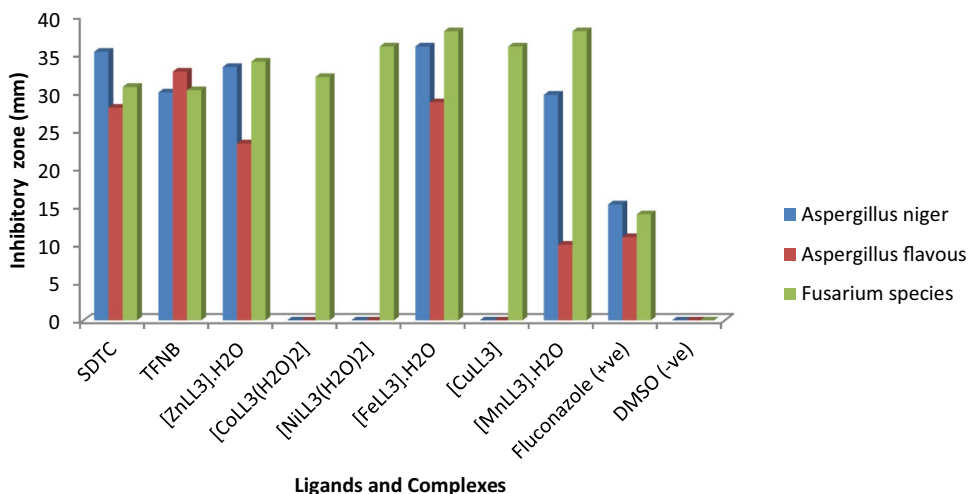


Fig. 5 3-D (a) and 2-D (b) bonding interactions inside the active pocket of *Staphylococcus aureus*-Cu complex (with the highest binding affinity)

the range 60.89—67.17%; which was also higher than the 56.2% activity of the positive standard, ascorbic acid.

Thus, the Co(II), Cu(II), Mn(II) and Ni(II) complexes of SDTC and TFNB might find application in the medical field as therapeutic agents in treatment of some neurodegenerative or heart diseases and cancer [32, 33].

3.2.2 Antibacterial studies

The antimicrobial activities of the ligands and the synthesized mixed ligand metal(II) complexes as were screened in vitro against diverse bacteria and fungi strains are shown in Tables 1 and 2 respectively.

In general, the antibacterial screening data reveal that all the compounds were active against *Staphylococcus aureus*, *Klebsiella pneumonia* and *Bacillus species* with zones

of inhibition ranging in between 6.3 and 31.3 mm. Also, all the metal complexes were active against *Staphylococcus aureus* with greater inhibitory values (18.7–31.3 mm), than their respective ligands (6.3 and 17.3 mm). This expectation is traceable to chelation theory effect [34], which decreases the polarity of the metal atom due to partial sharing of its charge with donor groups of the ligand and the possibility of π -electron delocalization over the whole chelate rings, leading to increase in lipophilic character that allows permeation into the bacterial membrane's lipid layers. The ligands were more sensitive against *K. pneumonia* than the complexes, except Cu(II) complex with zone of inhibition values 19.7 mm. In addition, Copper(II) complex had the highest inhibitory zone value of 25.7 mm against *B. species* compared to other compounds and even the reference drug, streptomycin with 22.0 mm (Table 1). The higher value exhibited by copper complex may be attributed to the bioactivity and biotoxicity of Cu^{2+} metal in coordination with the ligands, leading to easy penetration into the cell-lipid membrane, which obstruct and destroy the respiration process of the test organism [35]. The Cu(II) complex in comparison to all other complexes, is more toxic and effective towards the microbes- *S. aureus*, *B. species*, and *K. pneumonia* with inhibitory zone values of 31.3, 25.7 and 19.7 mm respectively, and to the standard (streptomycin) with respective inhibition values of 22.0, 22.0 and 24.0 mm. Result of this kind, in which test compounds have greater antibacterial efficacy than the standard- streptomycin has been reported [36–38].

In contrast, only the ligands and streptomycin (the reference standard) were active against *P. aeruginosa* and *E. coli* with inhibitory zones limits of 11.7–20.0 mm, while no activity was observed for all the metal(II) mixed ligand complexes against these two bacteria strains. This inactivity of the complexes might be traced to the probability of lipophobic nature [39] of complexes or the antibiotic resistance and the process of efflux pump development by these bacteria which did not allow the complexes to permeate via their lipid membrane [40].

The order of increasing activities of the compounds against each bacterial strains is as follows:

S. aureus: SDTC < TFNB < Fe^{2+} < Co^{2+} < streptomycin < Ni^{2+} < Zn^{2+} < Mn^{2+} < Cu^{2+}
K. pneumonia: Zn^{2+} < Co^{2+} < Fe^{2+} < Ni^{2+} < Mn^{2+} < TFNB < SDTC < Cu^{2+} < streptomycin.
P. aeruginosa: (Zn^{2+} , Co^{2+} , Fe^{2+} , Ni^{2+} , Mn^{2+} , Cu^{2+})* < SDTC < TFNB < streptomycin.
E. coli: (Zn^{2+} , Co^{2+} , Fe^{2+} , Ni^{2+} , Mn^{2+} , Cu^{2+})* < TFNB < SDTC < streptomycin.
B. species: Co^{2+} < Fe^{2+} < Zn^{2+} < TFNB < Mn^{2+} = streptomycin < Ni^{2+} < SDTC < Cu^{2+}

The results revealed that Cu(II) complex had highest antibacterial activities compared to other complexes against the bacterial strains (Fig. 3).

3.2.3 Antifungal studies

The antifungal studies showed that the ligands and some complexes that were active against the three fungi- *Aspergillus niger*, *Aspergillus flavous* and *Fusarium species* in most cases, possess almost two and half times potency (23.3–38.0 mm) compared to the standard fluconazole (11.0–15.3 mm), except only Mn(II) complex with (10.0 mm) zone of inhibition very close to that of fluconazole (11.0 mm) against *Aspergillus flavous*. The mixed-ligand complexes of Cu(II), Co(II) and Ni(II) were resistant to the *Aspergillus niger*, and *Aspergillus flavous*. Interestingly, all the compounds were more active (30.3–38.0 mm) compared to the reference drug (14.0 mm) against *Fusarium species*, with the chelates having larger values of inhibition in the range 32.0–38.0 mm than the ligands with inhibitory zone values range 30.3–30.7 mm, corroborating effect of Tweedy's chelation theory [18, 41]. The fungicidal activities of the compounds against each class of the fungi strains is given in the following order as:

A. niger: Fe^{2+} > SDTC > Zn^{2+} > TFNB > Mn^{2+} > fluconazole.
A. flavous: TFNB > Fe^{2+} > SDTC > Zn^{2+} > fluconazole > Mn^{2+}
F. species: Fe^{2+} = Mn^{2+} > Cu^{2+} = Ni^{2+} > Zn^{2+} > Co^{2+} > SDTC > TFNB > fluconazole.

The results revealed Fe(II) complex to be the best with highest fungicidal activities compared to other complexes against the three fungi (Fig. 4).

3.3 Molecular docking

Molecular docking studies was performed in this study showing the potential interaction between complexes and targets as seen in Table 3. Complexes with the best binding conformation are presented in Fig. 4. Results revealed that, in complex *S. aureus*, $[\text{CuLL}^3]$ and $[\text{CoLL}^3(\text{H}_2\text{O})_2]$ displayed the highest binding ability with the highest binding energy of –12.6 and 10.8 kcal/mol respectively, when compared to other complexes (Table 1). It was also observed that the good binding affinity was evident in the interaction with binding site residues indicating hydrogen bonding, π -interactions (π -sulfur and π -alkyl) and Van der Waals interactions (Fig. 5b).

4 Conclusion

In this work, we have presented the antibacterial, antifungal and antioxidant studies of the synthesized two ligands system metal(II) complexes of SDTC and TFNB. The antioxidant studies showed that most of the complexes could be potential antioxidant agents in the increasing order: Ni(II) < Mn(II) < Cu(II) < Co(II). The in-vitro antibacterial screening results revealed that the tested compounds were more active against the Gram(+ve) than the Gram(-ve) bacterial strains and Cu(II) complex of the mixed ligands displayed greatest toxicity and effectiveness towards the bacterial strains. Furthermore, the molecular docking studies corroborated the good complex-target interactions of the complexes, mostly, against *S. aureus*, *K. pneumonia* and *B. species* with significant binding potentials showing Cu(II) complex as the highest.

Finally, the antifungal studies indicated that Fe(II) complex had the best and highest fungicidal activities against the three fungi strains.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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