RESEARCH ARTICLE

Synthesis, Characterization and Biological Activity of a new Ligand 2,5-bis[(2E)-2-(2-bromobenzylidene) hydrazinyl]-1,3,4-thiadiazole with Some Transition Metal Complexes

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ABSTRACT

One of the limitations in curing infection has been considered to be bacterial resistance to a variety of antibiotics. Therefore, such a condition resulted in developing novel anti-microbial agents. Hence, a lot of researchers specially investigated the new 2,5- disubstituted-1,3,4-thiadiazole derivatives, which exhibit alternative biological activities. Then, new transitional metal (Fe(III), Ni(II) as well as Cu(II) complexes of ligand 2,5-bis[(2E)-2-(2-bromobenzylidene)hydrazinyl]-1,3,4-thiadiazole were prepared. All the prepared complexes were diagnosed by IR, elemental analyses, H^1-NMR and mass spectral. The electronic behavior of their link data has been confirmed.It was concluded that ligand had coordination via nitrogen (N) and (NH) atoms, which has been noted in during the study for each complex. Ligand coordinated through the [^{15}NH] and the nitrogen atom of Schiff base [N^3]. This view is more supported by a band's appearance returned to the metal–nitrogen stretching vibration at 540–547 cm^{-1} in the complexes. With regard to the findings obtained, we recommended the tetrahedral geometry for Cu(II) and Ni(II) complexes, whereas Fe(III) complexes were presented octahedral geometrics. All the synthesized complexes have been screened for anti-bacterial by using the spread method and measurement inhibition zone with E-coli and staph aureus (DMSO).

Keywords: Anti-bacterial agents, Anti-microbial agents, Ligand, Thiadiazole derivatives, Transition Metal.

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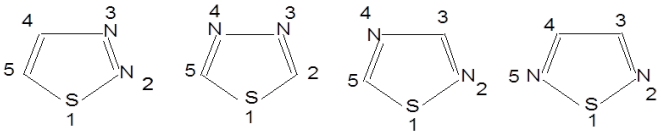
INTRODUCTION

Experts in the field have referred to the prominent contribution of the heterocyclic compounds to the biological processes, in particular, hetero-cycles consisting of N duo to the respective extensive utilization in the medicinal scaffolds for active agents.[1] For example, in the 19th century, Hugo Schiff could present one of the novel groups of organic compounds with diverse utilizations in different areas, which are known as Schiff's bases. Regarding the above-mentioned scientist, a log of authors provided various Schiff bases as well as the respective coordination compounds with transitional elements so that a majority of these prepared complexes showed diverse biological activities.[2] The 1,3,4-thiadiazole nucleus constituting the azole group has been proposed as a flexible pharmacophore, showing diverse biological activities. Thiadiazole represents a group of heterocyclic whose derivatives are crucial in industrial, agriculture, and medicine areas.[3,4] These compounds contain a 5-member di-unsaturated ring structure consisting of two nitrogen atoms and one sulfur atom. Thiadiazole presents almost in four parent compounds shown in Figure 1.

These compounds have a considerable published work and best intensive study.[5,6] 1,3,4-Thiadiazole has been initially illustrated in 1882 by Fischer and then formulated by Busch et al. Emergence of the sulfur medicines as well as the appearance of the mesoionic compounds largely speed up the level of progress in this area.[7] Among the different azole heterocycles, 1,3,4-Thiadiazole as well as the respective derivatives are powerfully attracted by the experts in the field as a result of their high drug and industrial significance. Surprisingly, synthetic publications far outweighs in numbers the cases associated with all other areas. These compounds



1,2,3-Thiadiazole 1,3,4-Thiadiazole 1,2,4-Thiadiazole 1,2,5-Thiadiazol)

Figure 1

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enjoy highly different biological features,[8,9] like anti-fungal,[10] anti-inflammatory,[11] anti-bacterial,[12] anti-parasitic,[13] anti-oxidant, anti-depressant,[14] as well as anti-convulsant,[15] anti-convulsant, anticancer,[16] antitumoral agents[17] and diuretic,[12] In fact, urea has been the first synthesized organic compound. Its' artificial synthesis was done in a synthetic laboratory by Wohler in 1828. It has been synthesized in the bodies of numerous organisms as a portion of the urea cycle. Its generation takes place in the liver and is observed in the mammals' urine. Moreover, it is dissolved in the plants, blood, bird, yeast, and several micro-organisms.[18] However, microbial resistance to the medicines has been considered one of medicinal chemistry concerns, probably because of the gene transfer or excess consumption of the drugs. During the last years, drug resistance enhanced in detecting the hospital-acquired infections resulted from multi-drug resistant strains so that such a condition has been regarded as one of the public health problems. In fact, drug resistance endangers treating infectious illnesses and this simultaneously triggers searching for novel bio-active materials. Therefore, researchers largely considered anti-fungal and anti-bacterial features related to the thiadiazole nucleus and thus diverse synthetic procedures have been presented to produce thiadiazole derivatives.[19-21] In addition, their utilization as viscosity stabilizers in the rubber processing has been reported,[22] additives to produce lithium battery electrodes[23] dyes[24] as well as to-electronic substances.[25] Moreover, utilizations of the 1,3,4-thiadiazole derivatives, especially 2,5-dimercapto-1,3,4-thiadiazoles have been reported as the lubricants.[26]

EXPERIMENTAL

Materials

According to the research design, each chemical used has been of reagent grade. We used Hydrazine hydrate (BDH), absolute ethanol (BDH), Hydrochloride acid(BDH), Sodium hydroxide,2-Bromobenzaldehyde and carbon disulfide (BDH) ed. All the metal chlorides ($NiCl_2.6H_2O$, $CuCl_2.6H_20$, $FeCl_{3.}6H_2O$) were purchased from BDH fine chemicals.

Analytical Methods and Physicalmmeasurements

The fourier-transform infrared spectroscopy (FTIR) ispectra in the range 200-4000 cm^{-1} were registered as CsI discussing a Shimadzui FTIR spectrophotometer, Elemental) C, H and Ni (analysis which was conducted on a thermo-finigan flash analyzer. The proton nuclear magnetic resonance (^{1}H-NMR) spectra were registered on quicksilver -300BB nuclear magnetic resonance (NMR) 300ispectrometer, return to the internal standard tetramethylsilane (TMS)i, d6-DMSO used as solvents. Mass spectra have been registered in the rangef (0-800) m/e onma 5973 networkp mass selective detector. Melting points were Identified in open capillary tube byusing any electro thermal melting point/SMP3I apparatus.

Preparation of the ligand

New ligand 2,5-bis[(2E)-2-(2-bromobenzylidene) hydrazinyl]-1,3,4-thiadiazole (Schemep1) wasiprepared asifollows:

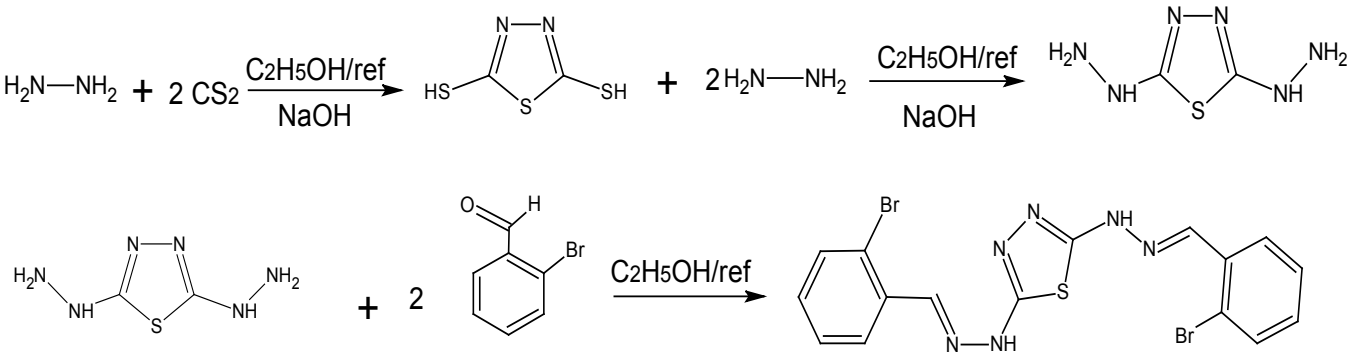
A mixture of 0.32 mol of Hydrazine hydrate and 0.6 mol of sodium hydroxide was dissolved in 200 mL absolute ethanol it this solution 0.26 mol of carbon disulfide was added gradually. The resulting mixture was heated under reflux for 16 hours. The resultant mixture was concentrated and carefully acidified with hydrochloric acid HCl (10%) to give a yellow precipitate. The product was filtered and washed with cold water, recrystallized from ethanol to give the desirediproduct5-Amino-1,3,4-thiadiazole-2-thiol (A_1)mas yellow crystals,[27] yield (76%), m.p. 162-164C.

A mixture (A_1) (0.04 mol), as well as Hydrazine hydrate (0.1 mol) dissolved in ethanol (100 mL), has been heated under reflux for 10 hours until the emission of hydrogen disulfide gas is over. The result antimixture [B] was concentrated and the white crystals separated was filtered and recrystallized from ethanol. Yield: (66 %), m. p. 173-175°C.

A mixture (B) (0.01 mol) and 2-Bromo benzaldehyde (0.02 mol) dissolved in ethanol (25 mL) was heated under reflux for 3 hours; the resultant mixture Ligand was concentrated, and the yellow crystals which separated filtered and recrystallized from ethanol (Scheme 1).

Preparation of Complexes

The Fe(III), Ni(II), and Cu(II) complexes were synthesized by mix (0.01 mol) from ligand with (0.01 mol) from salts ($FeCl_3.6H_2O$), ($NiCl_2.6H_2O$), ($CuCl_2.6H_2O$)h in (50ml) ethanol absolute and refluxed for 2 hours .then the precipitate has been filtered and rinsed many times with ethanol. After that, the resultant solids separated dried in air.



2,5-bis[(2*E*)-2-(2-bromobenzylidene)hydrazinyl]-1,3,4-thiadiazole

Scheme 1: Preparation of ligand

RESULTS AND DISCUSSION

The ligand and its complexes were checked by TLC, elemental analysis shown are (CHN) in Table 1, Physical properties, molar conductance and the melting point of all the compounds synthesized are tabulated in Table 2.

The FT-IR Spectral

FT-IR spectrum for the free ligand showed five major bandsiat 3362 cm^{-1}, 2824 cm^{-1}, 1566 cm^{-1}, (1369, 1307) cm^{-1} and 1045 cm^{-1} returned to iυ (N-H), υ(C–H),[22,23] (C=N),[24,25] asymmetrical (C-S-Cm), msymmetrical (C-S-C) and structure movement respectivelyh.[21,26] New bands were appeared at the (540–547 cm^{-1} and (254-273)cm^{-1} regionrefers to coordinate(M-N) and (M-Cl) respectively .this refers that the coordinate happend throughatoms (Cl) and (N) The IRidata for the ligandiandits complexesiare exhibited in Table 3 and Figure 4-6.

Nucleari Magnetic Resonance

The data of H^1-NMR for the ligand showed good solubility in DMSO. The H^1–NMRspectral data gave another confirmation for their suggested structure of the ligand. Theispectrashowed signals at (3.8 ppm) and (5.7 ppm) due to (CH) and (NH)[28-27] (respectively another multiple signal at chemical shift (δ) at range (7.5–8.03 ppm) due to the aromatic ring protons.[29,30] The H^1-NMRiof the ligand shown in Figure 7.

Theimass Spectra

mmThe mass spectra of the ligand shown molecular.ion $[M]^{+.}$ peak at(478) m/z Which.is match the molecular[formula[$C_{16}H_{12}N_2rBS_6]^{+.}$k,The other peaks are due to the fragments like $[C_{16}H_{12}N_2rB_5]^{+.}$at (432) m/z,$[C_{16}H_{12}NrBS_6]^{+.}$= (399) m/z, $[C_{16}H_{12}NrB_6]^{+.}$= (368) m/z, $[C_{16}H_{12}NrB_5]^{+.}$= (354) m/z, $[C_{16}H_{12}NrBS_5]^{+.}$= (386)m/z $[C_{10}H_8NrBS_6]^{+.}$ = (323)m/z,

Table 1: Elemental analysis for the ligand

Experimental			*Theoretical*		
C%	H%	N%	C%	H%	N%
40.119	2.598	17.61	40.02	2.52	17.5

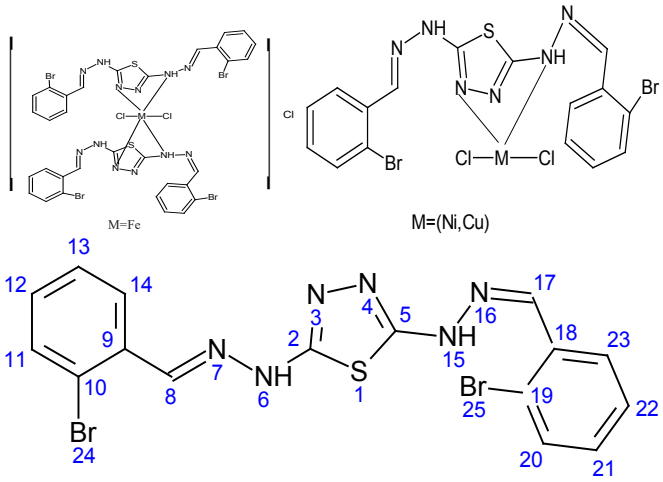


Figure 2: The stereochemistry of the ligand

Figure 3: Antibacterial activity (inhibition zone)

Table 2: Physical features, conductance data of the ligand and its complexe

No	*Compound*	*Molecularformula*	*Color*	*Λ Scm2 mol-1*	*Melting Point*
1	Ligand	$_2rBS_6N_{12}H_{16}C$	Yellow	–	235–237
3	$[Fe(L)_2Cl_2]Cl$	Cl3 ($_2rBS_6N_{12}H_{16}C$)Fe	Dark yellow	40.8	294–296
5	$[Ni(L)Cl_2]$	Cl2($_2rBS_6N_{12}H_{16}C$)Ni	Light green	10.05	263–265
6	$[Cu(L)\ Cl_2]$	Cl2($_2rBS_6N_{12}H_{16}C$) Cu	Dark green	9.8	278–276

Table 3: The IR data of the ligand and its metal complexes

NO	*Compound*	*vN -H*	*vC- H aromatic*	*vC- Haliphatic*	*vC=N*	*v C-S-C*	*Structure movement*	*M-Nv*	*M-Cl v*
L	$_2rBS_6N_{12}H_{16}C$	3362	3151	2824	1566	1369asy 1307sy	1045	.....	.....
1	$[Cu(L)\ Cl_2]$	3316	3151	2924	1570	1373asy 1307sy	1049	543	262
2	$[Fe(L)_2Cl_2]Cl$	3371	3189	2958	1576	1378asy 1317sy	1058	540	273
3	$[Ni(L)\ Cl_2]$	3321	3135	2932	1552	1368sy 1314sy	1052	547	254

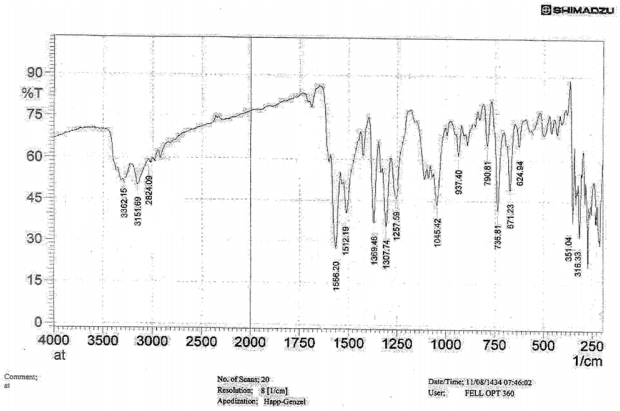


Figure 4: IR spectra of Ligand $_2$r B S $_6$N $_{12}$H$_{16}$ C

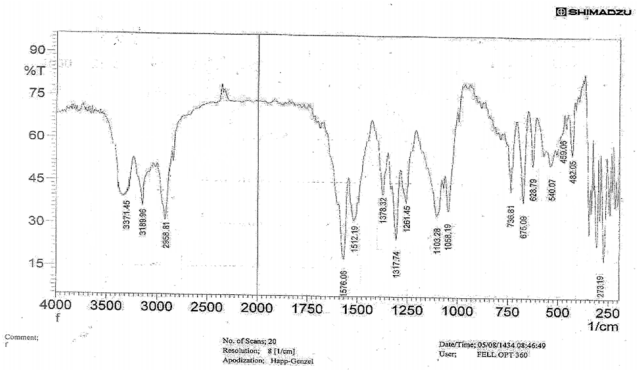


Figure 5: IR spectra of $[Fe(L)_2Cl_2]$

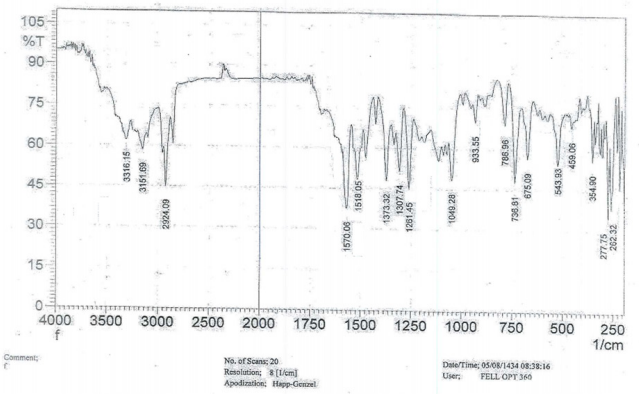


Figure 6: IR spectra of $[Cu(L)_2Cl_2]$

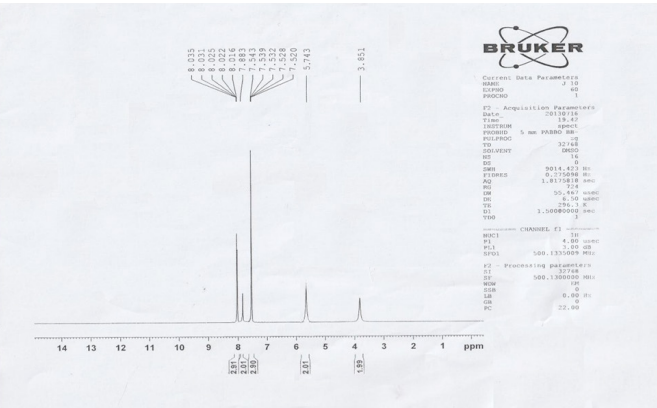
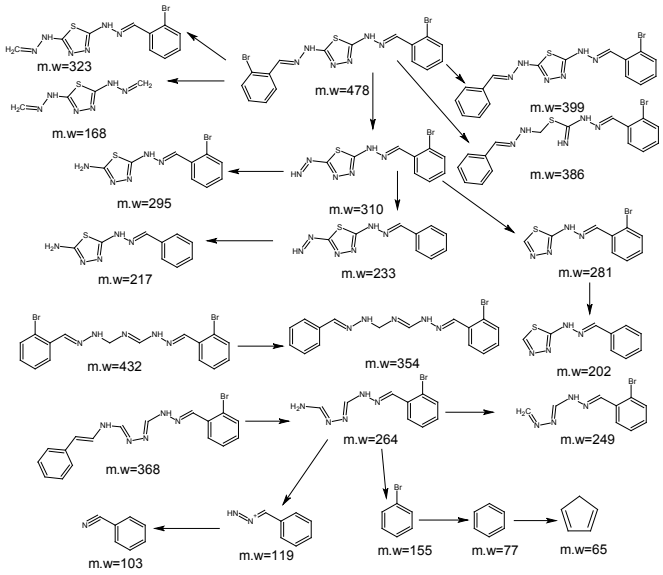


Figure 7: H^1-NMR spectra of the ligand$_2$r B S $_6$N $_{12}$H$_{16}$ C



Scheme 2: Frigment of ligand

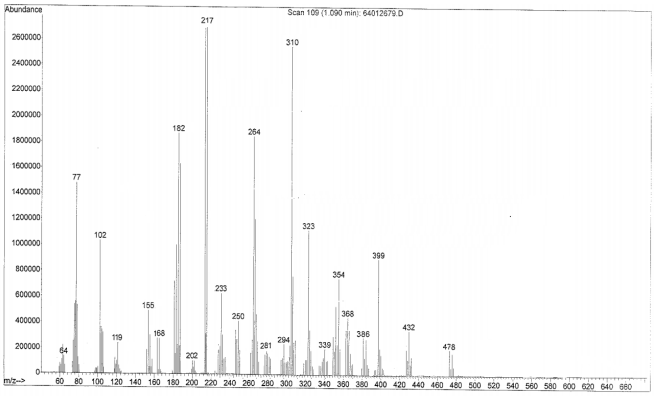


Figure 8: Mass spectra of ligand

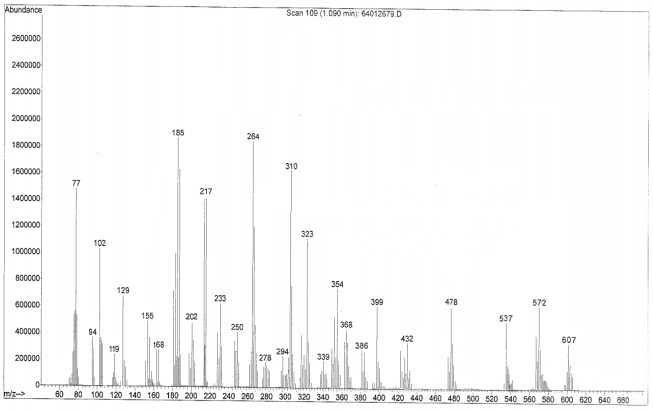


Figure 9: Mass spectra of [Ni L Cl2]

$[C_9H_7NrBS_6]^{+\cdot}$ = (310)m/z and $[C_9H_6NrBS_5]^{+\cdot}$ = (295) m/z, $[C_9H_6NrBS_4]^{+\cdot}$= (281)m/z,$[C_9H_7NrB_5]^{+\cdot}$= (264) m/z, $[C_9H_6NrB_4]^{+\cdot}$= (249)m/z, $[C_9H_9NS_6]^{+\cdot}$= (233)m/z, $[C_9H_7NS_5]^{+\cdot}$= (217)m/z, $[C_6HrB_5]^{+\cdot}$= (155)m/z, $[C_4H_4NS_6]^{+\cdot}$= (168)m/z, $[C_7H_7N_2]^{+\cdot}$= (119)m/z, $[C_7H_5N]^{+\cdot}$= (103)m/z, $[C_6H_6]^{+\cdot}$= (77) m/z, $[C_5H_5]^{+\cdot}$= (65)m/z as shown in Figure 8 and Scheme 2.

The mass spectra of the complex $[Cu(L)Cl_2]$ shown the peak of a molecular ion at 612 m/z that has been equivalent to

Table 4: Anti-bacterial screening data of the ligand and its metal complexes

Compound n	*Escherichia coli Inhibition zone (mm)*	*Staphylococcus Aurensk Inhibition zone (mm) n*
L= $_2$r B S $_6$N $_{12}$H$_{16}$ C	13	15
=E[Fe(L)2Cl2]Cl	31	29
=A[Ni(L)Cl2]	20	27
=D[Cu(L) Cl2]	33	23
Ciprofloxacin	30	25

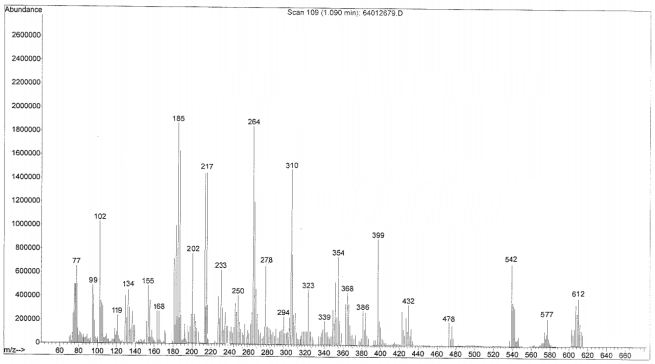


Figure 10: Mass spectra of [Cu LCl$_2$]

the molecular mass of Ni(II) complex. As seen, the complex showed the other fragmentation peaks at 577 m/z and 542 m/z due to lasso one and two of chlorine atoms, respectively. The complex spectrum shown another fragment ion 1 peaks at 134 m/z due to [Cu Cl$_2$]$^{+\cdot}$ and (99) due to [Cu Cl]$^{+\cdot}$the mass 9 spectra of the1complexes shown 2 in Figure 10.

The mass spectral of the complexn [Fe(L)$_2$Cl$_2$]Cl shows the peak of a molecular ion at 1117 m/z which is equivalent to the molecular mass of Fe(III) complex. This complex has shown another fragmentation peaks at 1082 m/z, 1047 m/z as well as 1012 m/z due to]lossione, two and three of chlorine atoms Sequentially .thejcomplex spectrum shown another fragmentation peak at 534 m/z due to [Fe (L)]$^+$.

Spectral and analytical data (^{1}H NMR,IR, mass spectra) of each synthesized compound have been consistent with this new structure.

Biological Activity

By a perspective for exploring possible achievement of the biologically beneficial complexes consisting of 1,3,4-thiadiazole ring system, the biological activities make us for preparing a novel series consisting of uniting. The anti-bacterial activity for ligand and its complexes have been assessed via agar well diffusion. Two types of bacteria have been used, gram-negative bacteria as Escherichia Coli (E. Coli) and gram-positive bacteria staphylococcus,These types of bacteria were chosen because of their importance in the medical field as they cause many different diseases, using Ciprofloxacin as standard drug. The inhibition zone was measured in millimeters methyl sulfoxide (DMSO) used as a solvent. Nutrient agar was used as a culture medium, using a disk susceptibility test. These techniques include the exposure of an inhibition zone to the spread of bacteria on an agar plate. The agar dishes were put in the incubator at 37°C for 24 hours.[31,32]

The anti-bacterial data of ligand and the respective metal complexes have been tabulated Table 4 and shown in. Figure 3.

CONCLUSION

The ligand 2,5-bis[(2E)-2-(2-bromobenzylidene)hydrazinyl]-1,3,4-thiadiazole has been successfully synthesized. The elemental analysis, 1H NMR, IR and mass spectral observations suggest the tetrahedral geometry was proposed for Ni(II), Cu (II). octahedral geometry for the Fe(III).

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