Research Article

# Synthesis, Characterization and Antimicrobial Activity Study of new Metal Complexes with Nalidixic acid Hydrazones

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**ABSTRACT**

A series of nalidixic acid-based hydrazones and their Au III, PtIV metal complexes have been synthesized and evaluated for their in vitro antimicrobial activity based on dimension of the diameter of inhibition zone formed round the well against a panel of reference strains of microorganisms, including Gram-positive bacteria, Gram-negative bacteria, and fungi *Candida albicans* and *Candida tropicalis.* Nalidixic acid hydrazone derivatives were obtained by condensation reaction of nalidixic acid hydrazide with substituted aromatic aldehydes and acetophenone. The complexes of Au III, Pt IV metals with nalidixic acid hydrazone derivatives were synthesized. All compounds have been characterized by elemental analysis, FT-IR, $^{1}$H NMR and $^{13}$C NMR spectra. The antimicrobial activity indicated that all ligands and metal complexes showed significant activity of anti-bacterial, antifungal activity comparable to that of parent and standard.

**Keywords:** Nalidixic acid, Hydrazones, Metal complexes, Inhibition zone, Antimicrobial activity.

## INTRODUCTION

Quinolones constitute a large class of antibacterial agents that are highly effective in treatment of many types of infectious diseases particularly caused by bacteria [1], Nalidixic acid was the first clinically useful quinolone antibacterial agent. It acts against bacteria by selectively inhibiting the type II topo isomerase DNA gyrase and topo isomerase IV, enzymes that play a critical role in bacterial cell growth and division [2]

It has been suggested that transition metals like copper, nickel and others can form DNA interchelating complexes with quinolones inhibiting metalloenzymes, causing cytotoxicity[3,4]and enhance the activity of drugs[5,6].

Hydrazone ligands and their complexes with different transition metal ions have been thoroughly studied due to their biological activity. [7- 9]

Hydrazone ligands, a class of Schiff base, derived from the condensation of acid hydrazides (R–CO–NH–NH2) with aromatic 2-hydroxy carbonyl compounds are important tridentate O, N, O-donor ligands. Coordination chemistry and biochemistry of aroyl hydrazones, R–CO–NH–N=CH–R, have attracted increasing interest due to their chelating ability and their pharmacological applications [10].

Hydrazone ligands create environment similar to biological systems by usually making coordination through oxygen and nitrogen atoms.[11]

The chemistry of metal-drug coordination compounds ismore popular now than before in importance particularly in the design of more biologically active drugs [12]. Metal ions are known to affect the action of many drugs. The efficacies of the drugs on coordination with a metal have been enhanced in many cases. [13]

In this current research, we design, synthesized, and evaluated in vitro the antimicrobial activity of new nalidixic acid-based hydrazone ligands and their complexes with Au III, PtIV metals.

## MATERIALS AND METHODS

Reagents were purchased from Fluka and BDH Chemical Company.Melting points of all the compounds were taken on Electro thermal melting point apparatus and open capillary tubes were used to determine the melting points and are uncorrected. Infrared (IR)spectra were recorded as KBr disc by using shimadzu FT- IR spectrophotometer 8400s. $^{1}$H&$^{13}$C NMR were recorded on Bruker 500 MHz-Avanc III spectrometer in CDCl3 and chemical shifts were given in ppmdownfield from tetramethylsilane (TMS) the internal standard. Elemental analysis (C, H, N) of the synthesized ligands and complexes were carried out on Elemental analyzer Euro-Vector EA3000A. Absorbance λmax was taken on U.V-160 AVISIBLE spectrophotometer.

The molar conductivity of the complexes was measured with a HACH-sens ion 5 conductivity meter using $10^{-3}$ M solutions in DMSO.

### Methodology

#### *Synthesis of Nalidixic Acid Ester*

Pure nalidixic acid (1 gm) was accurately weighed into a250 ml dry, clean, round bottom flask and 2 ml of thionylchloride was added and closed in fuming cupboard chamber.The flask was kept aside for 15 min. Later 2 ml of methanolwas added to the solution in the round bottom flask drop bydrop and mixed thoroughly after each addition. The reaction should be carried out


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carefully in fuming cupboard chamber. The Nalidixoyl chloride formed, in situ, by the addition of Thionyl chloride to nalidixic acid reacted with methanol and was kept for refluxing. Time taken for complete conversion was 1 hour. This formed nalidixic acid ester.

**Formation of Nalidixic acid Hydrazide**

Nalidixic acid hydrazide was synthesized following the methods reported earlier[14-17]Hydrazine hydrate (2 ml ) was added drop wise carefully To the above formed methyl ester in solution through the side of the round bottom flask kept closed in fuming cupboard chamber. Evolution of heat took place with a violent reaction. The above mixture was then kept for refluxing for 4 hours. The contents of the flask were poured into a beaker containing ice cold water. A yellowish-orange coloured nalidixic acid hydrazide precipitated immediately.

**General Procedure for Preparation of Schiff Base ($L_{I-VIII}$)**

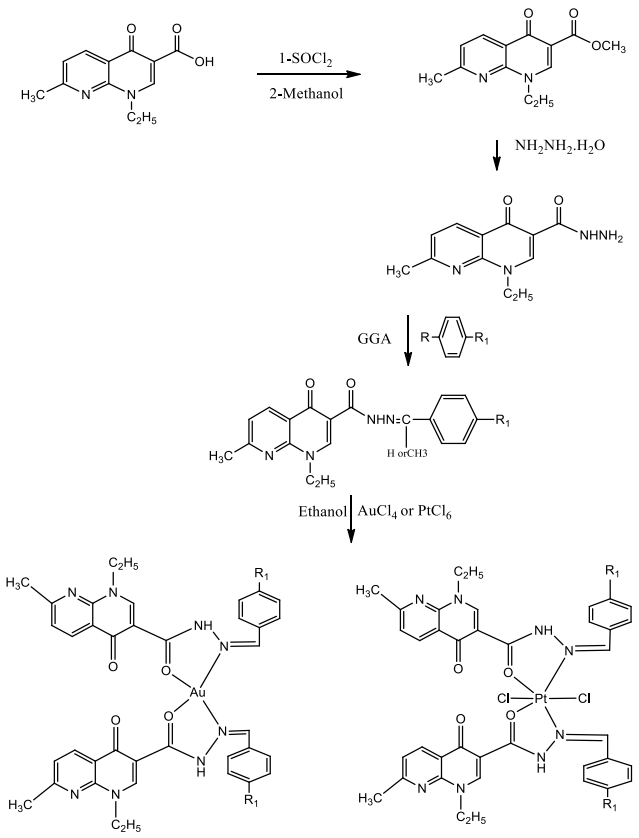
A mixture of nalidixic acid hydrazide (10.0 mmol; 2.46 g), appropriate substituted aromatic aldehydes, (11.0 mmol; 1.34 g) and ethyl alcohol (30.0 mL) were heated under reflux for a period of 0.5 h. Then (2-3) drops of glacial acetic acid was added and further refluxed for overnight. The hydrazone was formed. After completion of reaction as indicated by TLC (chloroform: methanol, 90:10), and few drops of ammonia solution .The same procedure have done with acetophenone.

**General Preparation of Complexes**

An ethanol solution of the metal ions [$H_2PtCl_6$, and $HAuCl_4.H_2O$] was added to ethanol solution of Schiff base compounds ($L_{I-VIII}$), HL in 1:2 (metal: ligand) molar ratio. Then, the mixture was heated under reflux for overnight and coloured precipitates were obtained. Later, the precipitates were filtered out, washed with distilled water and finally recrystallized from ethanol.

**Antimicrobial screening**

The antimicrobial activity of the ligands and their final complexes has been done in the Ibn Alhaitham college laboratories, Baghdad University. The antibacterial and antifungal have been done according to Well Diffusion method. All the used microbial cultures were the first sub cultured on nutrient agar or Sabouraud agar at 35°C for 18–24 h or 30°C for 24–48 h for bacteria and fungi, respectively. The antimicrobial activity has done in vitro against four tested bacteria two of them are gram-positive bacteria staphylococcus aureus , streptococcus pyogenes while the other are gram negative bacteria *Klebsiella pneumonia* , *Escherichia coli* and two fungi ,*Candida Albicans*, *Candida tropicalis* were selected. Solutions of hydrazone and metal complexes were prepared in DMSO. Nalidixic acid was used as standard and DMSO as a blank. Ciprofloxacin and nitrofurantoin (Sigma) were used as a reference antibacterial or antifungal compound, respectively. The antimicrobial action was estimated by determining the diameter of the inhibition zone (IZ) all over the place the disc in mm.




| R | CHO | CHO | CHO | CHO | C(O)$CH_3$ | CHO | CHO | CHO |
|---|---|---|---|---|---|---|---|---|
| R1 | H | 4-OH | 4-Cl | 4-$(CH_3)_2$N | H | 2-$NO_2$ | 2-Br | 4-$NO_2$ |

**Scheme 1:** Synthesis of intermediates and target compounds.

## RESULTS AND DISCUSSIONS

(LI-VIII) were synthesized by a condensation reaction of nalidixic acid hydrazide (II) with various substituted aromatic aldehydes. Using the aforementioned reactions, [18] the melting points of all synthesized compounds were found in open capillary tubes and readings were uncorrected. The structures of the synthesized compounds were supported by physical data (Table1) for ligands and Table 2 for Complexes.

**The spectral details of the synthesized compounds**

***N'-benzylidene-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3 carbohydrazide(LI)***

IR (KBr) **ν**max :3180 (N-H),3070-3041 (C-H,Ar), 2985( CH str. of CH3), 1670(C=O str. of amidic),1620,1604(C=N), 1363 (CN); 1H NMR (DMSO-d6) δ (ppm)=1.41 (t, 3H, CH3), 2.70 (s, 3H, CH3), 4.65 (q, 2H, CH2),6.8(d,1H, naphthyridine) 7.4–7.6 (m, 1H, Ar), 7.75 (d, 1H, naphthyridine), 7.8 (d, 1H, Ar H), 8.4 (s, 1H, -N=CH),9.1(s,1H, naphthyridine),13.1 (s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24, 49, 113, 119, 128, 129,129.9,131,133,135,147(N=CH),148,148.5,163,163.5(C=O),176(C=O).


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**Table1:** The characterization and physical parameters of the ligands

| Comp. | Formula | Physical state | %Yield | mp (°C ) | $R_f$ | Conductivity µ s/cm | ƛmax |
|---|---|---|---|---|---|---|---|
| I | $C_{19}H_{18}N_4O_2$ | Yellow | 52,6 | 252-254 | 0,711 | - | 323 |
| II | $C_{19}H_{18}N_4O_3$ | Orange | 69,4 | 270-272 | 0,612 | - | 316 |
| III | $C_{19}H_{17}ClN_4O_2$ | Yellow | 60,2 | 318-320 | 0,532 | - | 332 |
| IV | $C_{21}H_{23}N_5O_2$ | Orange | 64 | 296* | 0.712 | - | 360 |
| V | $C_{20}H_{20}N_4O_2$ | Yellow | 66,4 | 284-286 | 0,632 | - | 321 |
| VI | $C_{19}H_{17}N_5O_4$ | Yellow | 50,2 | 276-278 | 0,521 | - | 337 |
| VII | $C_{19}H_{17}BrN_4O_2$ | Yellow | 56,8 | 263-265 | 0,547 | - | 326 |
| VIII | $C_{19}H_{17}N_5O_4$ | Yellow | 68,4 | Decomposed at 354* | 0,543 | - | 340 |

**Table 2:** The characterization and physical parameters of the complexes

| Comp. | Formula | Physical State | %Yield | mp (°C ) | $R_f$ | Conductivity µ s/cm | ƛmax |
|---|---|---|---|---|---|---|---|
| I a | $C_{38}H_{36}AuN_8O_4$ | Brown | 45 | 240-242 | 0,75 | 1.7 | 325 |
| I b | $C_{38}H_{36}Cl_2N_8O_4Pt$ | Brown | 50 | 236-238 | 0,78 | 4.1 | 325 |
| II a | $C_{38}H_{36}AuN_8O_6$ | Brown | 47 | 304-306 | 0,66 | 1 | 330 |
| II b | $C_{38}H_{36}Cl_2N_8O_6Pt$ | Brown | 53 | 292 | 0,67 | 1.2 | 321 |
| III a | $C_{38}H_{34}AuCl_2N_8O_4$ | Brown | 48 | 300 | 0,583 | 1.1 | 333 |
| III b | $C_{38}H_{34}Cl_4N_8O_4Pt$ | Brown | 54 | 265* | 0,578 | 1.7 | 340 |
| IV a | $C_{42}H_{46}AuN_{10}O_4$ | Brown | 52 | 298* | 0,764 | 3.3 | 365 |
| IV b | $C_{42}H_{46}C_{l2}N_{10}O_4Pt$ | Brown | 59 | 254* | 0,785 | 4.9 | 363 |
| V a | $C_{40}H_{40}AuN_8O_4$ | Brown | 51 | 296-298 | 0,664 | 0.9 | 325 |
| V b | $C_{40}H_{40}C_{l2}N_8O_4Pt$ | Brown | 56 | 274-276 | 0,671 | 1.1 | 323 |
| VI a | $C_{38}H_{34}AuN_{10}O_8$ | Brown | 43 | 298-300 | 0,574 | 1 | 338 |
| VI b | $C_{38}H_{34}C_{l2}N_{10}O_8Pt$ | Brown | 46 | 254-256 | 0,582 | 0.8 | 339 |
| VII a | $C_{38}H_{34}AuBr_2N_8O_4$ | Brown | 46 | 274-276 | 0,570 | 1.1 | 330 |
| VII b | $C_{38}H_{34}Br_2C_{l2}N_8O_4Pt$ | Brown | 51 | 238-240 | 0,562 | 1.1 | 328 |
| VIII a | $C_{38}H_{34}AuN_{10}O_8$ | Brown | 50 | 360* | 0,589 | 1 | 346 |
| VIII b | $C_{38}H_{34}C_{l2}N_{10}O_8Pt$ | Brown | 56 | 309* | 0,578 | 1 | 345 |

** indicate decomposition melting point*

Analysis for C19H18N4O2,(334) Calculated: C: 68.67 %, H: 5.56%, N: 16.76%;Found: C: 67.76%, H: 5.38%, N: 16.13%.

**N'-(4-hydroxybenzylidene-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3 carbohydrazide(LII)**

IR (KBr) **ν**max :3286 (Ph-OH) 3184 (N-H),3072-3041 (C-H, Ar), 2983( CH str. of CH3), 1660(C=O str. of amidic),1602 (C=N), 1365 (CN); 1H NMR (DMSO-d6) δ (ppm)=1.40 (t, 3H, CH3), 2.50 (s, 3H, CH3), 4.65 (q, 2H, CH2), 6.8 (d, 1H, naphthyridine), 7.5 (d, 1H, Ar), 7. 76(d, 1H, naphthyridine), 7.78, (d, 1H, Ar), 8.3 (s, 1H, -N=CH), 9.1(s, 1H, naphthyridine), 9.9 (s, C-OH), 12.9, (s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24, 49, 111, 115, 1118, 125.24, 128.9,130,135.9, 146(N=CH), 148.13, 148.36,160(C-OH), 163,163.43(C=O), 175 (C=O).
Analysis for, C19H18N4O3 (350) Calculated: C: 65.14 %, H: 5.14%, N: 16.0 %; Found: C: 64.70%, H: 5.9%, N: 16.35%.

**N'-(4-chlorobenzylidene-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3 carbohydrazide (LIII)**

IR (KBr) **ν** max : 3240 (N-H), 3047 (C-H, Ar), 2983( CH str. of CH3), 1678(C=O str. of amidic),1608(C=N), 1363 (CN);1087 (C-Cl); 1H NMR (DMSO-d6) δ (ppm)=1.40 (t, 3H, CH3), 2.7 (s, 3H, CH3), 4.65 (q, 2H, CH2), 6.8 (d, 1H, naphthyridine), 7.75 (d, 1H, Ar), 7.4-7.6 (d, 1H, naphthyridine), 7.8,(d,1H,Ar) ,8.4 (s, 1H, -N=CH),


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9.1(s,1H, naphthyridine), 13.1 (s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24, 49, 113, 119, 128.8,129.9,131, ,132, 135,135.9, 147(N=CH),148, 148.6, 163, 163.52(C=O), 175 (C=O).
Analysis for, $C_{19}H_{17}ClN_4O_2$ (368) Calculated: C: 68.67 %, H: 5.65 %, N: 16.76 %; Found: C: 67.76 %, H: 5.38 %, N: 16.13%.

**N'-(4-dimethylaminobenzylidene-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3 carbohydrazide (LIV).**

IR (KBr) **ν** max : 3194 (N-H),3142- 3041 (C-H, Ar), 2987-2945( CH str. of CH3), 1670 (C=O str. of amidic),1610(C=N), 1365 (C-N);1329 (N-$(CH_3)_2$ str.; 1H NMR (DMSO-d6) δ (ppm)=1.40 (t, 3H, CH3), 2.7 (s, 3H, CH3), 3.0 (s,6H-N$(CH_3)_2$) ,4.6 (q, 2H, CH2), 6.7 (d, 1H, Ar), 6.8 (d, 1H, naphthyridine), 7.5 (d, 1H,Ar), 7.7 8, (d,1H, naphthyridine), 8.3 (s, 1H, -N=CH), 9.1(s,1H, naphthyridine), 12.7 (s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24,41(N-$(CH_3)_2$ ), 49, 111, 113,118, 121, 128.6, 129, ,137, 146(N=CH), 148.13, 148.9, 153, 160, 163.43(C=O), 175 (C=O).
Analysis for, $C_{21}H_{23}N_5O_2$ (377) Calculated: C: 66.8 %, H: 6.1 %, N: 18.5 %; Found: C: 66.2%, H: 6.42 %, N: 18.29%.

**N'-(1-phenylethylidene)-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3 carbohydrazide (LV).**

IR (KBr) **ν** max : 3112 (N-H), 3041 (C-H, Ar), 2986-2931( CH str. of CH3), 1670 (C=O str. of amidic),1612(C=N), 1367 (CN); 1H NMR (DMSO-d6) δ (ppm)=1.4 (t, 3H, CH3),2.4(s,3H,N=C-$CH_3$ ) 2.7 (s, 3H, CH3), ,4.65 (q, 2H, CH2), 6.8 (d, 1H, naphthyridine), 7.4-7.6 (d, 1H,Ar),7.7-7.9(d, 1H,Ar),8.6 (d, 1H, naphthyridine), 9.1(s,1H, naphthyridine), 13.1 (s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24, 40 (N=C-$CH_3$), 46, 113, 121, 128, 128.3, 129.2, 131, 135 ,136, 148 (N=CH), 148.5 , 150, 163, 163.43(C=O), 175(C=O).Analysis for, $C_{20}H_{20}N_4O_2$ (348) Calculated: C: 68.9 %, H: 5.74 %, N: 16.09%; Found: C: 69.10%, H: 5.47 %, N: 16.87%.

**N'-(2-nitrobenzylidene-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3 carbohydrazide (LVI).**

IR (KBr) **ν** max : 3111 (N-H), 3040 (C-H, Ar), 2980-2939( CH str. of CH3), 1683 (C=O str. of amidic),1608(C=N), 1343(C-N);1524 ($NO_2$ str. vibration); 1H NMR (DMSO-d6) δ (ppm)=1.4 (t, 3H, CH3),2.7(s,3H, $CH_3$) ; 4.65 (q, 2H, CH2), 6.8 (d, 1H, naphthyridine), 7.75 (d, 1H, , naphthyridine); 7.6-7.8 (m, 1H,Ar),7.8-8 (m, 1H,Ar),8.2(d,1H,Ar); 8.12 (N=CH); 9.1(s,1H, naphthyridine), 13.1 (s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24, 49, , 113, 118,124,128,129, 130,131 ,134,135, 143(N=CH),147,148,148.8,163,163.43(C=O), 175(C=O).
Analysis for, C19H17N5O4 (379) Calculated: C: 60.15 %, H: 4.48 %, N: 18.46%; Found: C: 59.24%, H: 4.44 %, N: 18.87%.

**N'-(2-bromobenzylidene-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3 carbohydrazide (LVII).**

IR (KBr) **ν** max : 3145 (N-H), 3053 (C-H, Ar), 2985-2933 (CH str. of CH3), 1678 (C=O str. of amidic), 1610(C=N), 1363 (C-N); 1022 (C-Br. str. vibration); 1H NMR (DMSO-d6) δ (ppm) =1.4 (t, 3H, CH3),2.7(s,3H, $CH_3$) ; 4.65 (q, 2H, CH2), 6.8 (d, 1H, naphthyridine), 7.4 (m, 1H, Ar); 7.5 (m, 1H,Ar),7.6 (s, 1H, Ar), 7.75(d, 1H, naphthyridine); 8.4 (N=CH); 9.1 (s, 1H, naphthyridine), 13.1 (s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24, 46, 113, 118, 121, 127.1, 127.6, 128.5, 130.5, 133, 135, 135, 143 (N=CH), 146, 158, 167, 168, 177(C=O).
Analysis for, $C_{19}H_{17}BrN_4O_2$ (413) Calculated: C: 55.2 %, H: 4.11 %, N: 13.55%; Found: C: 54.7 %, H: 4.9 %, N: 12.7%.

**N'-(4-nitrobenzylidene-1-ethyl-1, 4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3 carbohydrazide (LVIII).**

IR (KBr) **ν** max : 3182 (N-H), 3101 (C-H, Ar),3060-3024(C-H, Ar), 2980-2928( CH str. of CH3), 1680 (C=O str. of amidic),1618(C=N), 1343(C-N);1527 ($NO_2$ str. vibration); 1H NMR (DMSO-d6) δ (ppm)=1.4 (t, 3H, CH3),2.7(s,3H, $CH_3$) ; 4.65 (q, 2H, CH2), 6.8 (d, 1H, naphthyridine), 7.9 (d, 1H, , naphthyridine); 8.12 (m, 1H,Ar),8.35 (d, 1H,Ar),8.2(d,1H,Ar); 8.45 (N=CH); 9.1(s,1H, naphthyridine), 12.7(s, 1H, CO-NH) ; $^{13}$C NMR (DMSO) δ (ppm)= 15, 24, 49, , 113, 118, 127, 128, 135, 139, 146(N=CH), 147, 148.6, 150, 160, 163.5(C=O),175 (C=O).
Analysis for, $C_{19}H_{17}N_5O_4$ (379) Calculated: C: 60.1 %, H: 4.4 %, N: 18.64%; Found: C: 58.9%, H: 4.7 %, N: 18.27%.

The elemental analysis showed a stoichiometry of 1:2 (metal: ligand) for the complexes, and they were in agreement with the predicted formula for complexes. The low values of the molar conductivity supported a non-electrolyte nature for the metal complexes.

The amide band, ν(C=O), for the Au III & Pt VI complexes was present at 1670-1650 $cm^{-1}$, these findings support involvement of C=O in coordination. The absorption of the ν(C=N) azomethine group1620-1602 $cm^{-1}$ for all the complexes was situated at lower wave numbers than the value for the free ligand, consequently confirming the coordination of the azomethine nitrogen atom. The band for C=N, C-N almost constant in ligand and complexes, which indicates that the naphthyridine nitrogens did not involve in complex formation. The appearance of new non ligand bands between 470-430 and 330-320 due to the (M–O) and (M–N) vibrations in all complexes these bands are in the expected order of increasing energy: (M–N)<(M–O) [19], as expected due to the greater dipole moment change in the

M–O vibration, greater electro negativity of the O atom N atom, and shorter M–O bond length than the M–N bond length [20].

**Antimicrobial Activity**

The new synthesis compounds were screened for its antimicrobial activity [21] and most of these compounds


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show good antimicrobial activity comparable with parent compounds (nalidixic acid), standers and control.

The assessment of antibacterial was based on dimension of the diameter of inhibition zone formed round the well, and display that the zone of inhibition increased with the increasing of conc. of the tested compounds. All ligands and metal complexes shown good activity against gram positive bacteria and gram negative bacteria in compared with parent drug except LI at Conc.( 125,62.5) µg/ml and its metal complexes did not give any inhibition with all concentrations. LVII only its pt complex give activity against Escherichia coli at Conc.(500, 250) µg/ml.

In general, all tested compounds showed an interesting activity in comparison with parent against Gram-positive *staphylococcus aureus, streptococcus pyogenes* also the activity against *klebsiella pneumonia* was more than activity against *Escherichia coli.*

Most the ligand and metal complexes showed good activity against *Candida Albicans* and *Candida Tropicalis* .in compared with parent most tested compounds give activity more against *Candida Albicans* at conc. 500 µg/ml LVII Au complex .while in compared with parent most tested compounds give activity against *Candida Tropicalis* but less than *Candida Albicans* . LIV Au complex at conc. 500 µg/ml give more activity against *Candida Tropicalis.* In compared with nitrofurantoin as reference, tested compounds exert more activity against *Candida Albicans* than *Candida Tropicalis*.

The significantly high antimicrobial properties of hydrazone derivatives were due to an electronwithdrawing nitro group and an electron-releasing group at *para* position. The increase of activity was observed when a hydroxyl group and N-dimethyl groups was placed at *para* position in aromatic ring. Also aromatic compounds with halogen substituents at *para* position were more active as compared to other substituents. [22, 23]The results were tabulated in table 3 and 4.

**Table 3:** Antimicrobial activity of the ligands (LI-VIII) and their complexes against tested bacteria

| Comp. No. | R | Conc. µg/ml | Inhibition Zone (mm) | | | |
|---|---|---|---|---|---|---|
| | | | *Staphylococcus aureus* | *Streptococcus pyogenes* | *Klebsiella pneumonia* | *Escherichia coli* |
| **LI** | H | 500 | 41 | 42 | 39 | 38 |
| | | 250 | 31 | 35 | 27 | 28 |
| | | 125 | - | - | - | - |
| | | 62,5 | - | - | - | - |
| **LI- Pt complex** | = | 500 | - | - | - | - |
| | | 250 | - | - | - | - |
| | | 125 | - | - | - | - |
| | | 62,5 | - | - | - | - |
| **LI-Au complex** | = | 500 | - | - | - | - |
| | | 250 | - | - | - | - |
| | | 125 | - | - | - | - |
| | | 62,5 | - | - | - | - |
| **LII** | OH | 500 | 44 | 40 | 31 | 41 |
| | | 250 | 43 | 37 | 26 | 36 |
| | | 125 | 34 | 39 | 32 | 33 |
| | | 62,5 | 34 | 40 | 32 | 33 |
| **LII -Pt complex** | = | 500 | 42 | 46 | 43 | 40 |
| | | 250 | 29 | 33 | 32 | 30 |
| | | 125 | 39 | 44 | 34 | 41 |
| | | 62,5 | 31 | 33 | 28 | 32 |
| **LII- Au complex** | = | 500 | 45 | 34 | 40 | 42 |
| | | 250 | 31 | 11 | 36 | 33 |
| | | 125 | 29 | 35 | 36 | 25 |
| | | 62,5 | 23 | 25 | 35 | 26 |
| **LIII** | Cl | 500 | 45 | 27 | 34 | 41 |
| | | 250 | 29 | 30 | 29 | 29 |
| | | 125 | 32 | 34 | 30 | 34 |
| | | 62,5 | 28 | 29 | 29 | 27 |
| **LIII -Pt complex** | = | 500 | 40 | 34 | 42 | 41 |
| | | 250 | 40 | 43 | 39 | 43 |


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| | | | | | | |
|---|---|---|---|---|---|---|
| | | 125 | 31 | 43 | 34 | 32 |
| | | 62,5 | 43 | 35 | 32 | 33 |
| **LIII -Au complex** | = | 500 | 42 | 43 | 38 | 37 |
| | | 250 | 30 | 31 | 36 | 31 |
| | | 125 | 33 | 39 | 39 | 32 |
| | | 62,5 | 32 | 38 | 32 | 26 |
| **LIV** | dimethyl | 500 | 40 | 37 | 40 | 30 |
| | | 250 | 37 | 30 | 30 | 27 |
| | | 125 | 29 | 20 | 25 | 31 |
| | | 62,5 | 25 | 31 | 32 | 22 |
| **LIV-Pt complex** | = | 500 | 40 | 42 | 43 | 35 |
| | | 250 | 41 | 43 | 42 | 34 |
| | | 125 | 31 | 27 | 27 | 20 |
| | | 62,5 | 25 | 20 | 25 | 15 |
| **LIV-Au complex** | = | 500 | 45 | 41 | 29 | 39 |
| | | 250 | 37 | 40 | 28 | 34 |
| | | 125 | 43 | 36 | 25 | 31 |
| | | 62,5 | 40 | 41 | 26 | 27 |
| **LV** | - | 500 | 30 | 40 | 35 | 38 |
| | | 250 | 32 | 41 | 36 | 35 |
| | | 125 | 19 | 23 | 22 | 27 |
| | | 62,5 | 23 | 20 | 20 | 21 |
| **LV- Pt complex** | = | 500 | 35 | 30 | 33 | 34 |
| | | 250 | 36 | 33 | 32 | 32 |
| | | 125 | 32 | 38 | 24 | 22 |
| | | 62,5 | 29 | 34 | 19 | 23 |
| **LV- Au complex** | = | 500 | 29 | 34 | 29 | 32 |
| | | 250 | 30 | 32 | 21 | 27 |
| | | 125 | 31 | 27 | 20 | 27 |
| | | 62,5 | 29 | 24 | 20 | 21 |
| **LVI** | 2-$NO_2$ | 500 | 35 | 41 | 34 | 37 |
| | | 250 | 34 | 42 | 38 | 35 |
| | | 125 | 20 | 24 | 25 | 24 |
| | | 62,5 | 18 | 30 | 25 | 25 |
| **LVI- Pt complex** | = | 500 | 35 | 36 | 34 | 36 |
| | | 250 | 37 | 33 | 30 | 34 |
| | | 125 | 32 | 37 | 30 | 20 |
| | | 62,5 | 34 | 32 | 27 | 27 |
| **LVI -Au complex** | = | 500 | 30 | 32 | 39 | 37 |
| | | 250 | 33 | 20 | 43 | 40 |
| | | 125 | 32 | 29 | 32 | 25 |
| | | 62,5 | 30 | 27 | 31 | 34 |
| **LVII** | Br | 500 | - | - | - | - |
| | | 250 | - | - | - | - |
| | | 125 | - | - | - | - |
| | | 62,5 | - | - | - | 24 |
| **LVII -Pt complex** | = | 500 | - | - | - | 28 |
| | | 250 | - | - | - | 27 |
| | | 125 | - | - | - | - |
| | | 62,5 | - | - | - | - |
| **LVII -Au complex** | = | 500 | - | - | - | - |
| | | 250 | - | - | - | - |
| | | 125 | - | - | - | - |
| | | 62,5 | - | - | - | - |
| **LVIII** | 4-$NO_2$ | 500 | 35 | 40 | 40 | 40 |


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| | | | | | | |
|---|---|---|---|---|---|---|
| | | 250 | 28 | 29 | 28 | 27 |
| | | 125 | 40 | 36 | 33 | 35 |
| | | 62,5 | 32 | 30 | 27 | 40 |
| **LVIII -Pt complex** | = | 500 | 45 | 32 | 35 | 37 |
| | | 250 | 43 | 30 | 28 | 30 |
| | | 125 | 32 | 29 | 27 | 25 |
| | | 62,5 | 26 | 22 | 25 | 27 |
| **LVIII -Au complex** | = | 500 | 38 | 40 | 40 | 40 |
| | | 250 | 32 | 31 | 31 | 27 |
| | | 125 | 31 | 27 | 30 | 26 |
| | | 62,5 | 21 | 20 | 22 | 21 |
| **Nalidixic acid** | Stander 1 | 500 | - | - | - | - |
| | | 250 | - | - | - | - |
| | | 125 | 21 | 19 | - | 27 |
| | | 62,5 | - | 21 | - | 25 |
| **Ciprofloxacin** | Stander 2 | 500 | 25 | 29 | 32 | 32 |
| | | 250 | 25 | 28 | 34 | 30 |
| | | 125 | 25 | 20 | 30 | 30 |
| | | 62,5 | 25 | 15 | 29 | 28 |
| **DMSO** | | pure | - | - | - | - |

Key to symbols: (-) = no inhibition

**Table 4:** Antimicrobial activity of the ligands (LI-VIII) and their complexes against tested fungus

| Comp. No. | R | Conc. (µg/ml) | Inhibition Zone (mm) | |
|---|---|---|---|---|
| | | | *Candida Albicans* | *Candida tropicalis* |
| **LI** | H | 500 | 14 | 19 |
| | | 250 | 14 | - |
| | | 125 | 14 | - |
| | | 62,5 | 10 | 18 |
| **LI- Pt complex** | = | 500 | 15 | 19 |
| | | 250 | 13 | 19 |
| | | 125 | - | - |
| | | 62,5 | 13 | 14 |
| **LI- Au complex** | = | 500 | 14 | 19 |
| | | 250 | 13 | 18 |
| | | 125 | 13 | - |
| | | 62,5 | - | 14 |
| **LII** | OH | 500 | 13 | 14 |
| | | 250 | 13 | 12 |
| | | 125 | 11 | - |
| | | 62,5 | 11 | 11 |
| **LII -Pt complex** | = | 500 | 12 | 16 |
| | | 250 | 12 | 15 |
| | | 125 | 11 | - |
| | | 62,5 | 11 | 10 |
| **LII - Au complex** | = | 500 | 14 | 17 |
| | | 250 | 14 | 17 |
| | | 125 | 13 | - |
| | | 62,5 | 10 | 14 |
| **LIII** | 4-Choro | 500 | 18 | 17 |
| | | 250 | 14 | 16 |
| | | 125 | 11 | - |


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| | | | | |
|---|---|---|---|---|
| | | 62,5 | - | 15 |
| **LIII -Pt complex** | = | 500 | 16 | 19 |
| | | 250 | 15 | 16 |
| | | 125 | 12 | - |
| | | 62,5 | - | 14 |
| **LIII - Au complex** | = | 500 | 18 | 18 |
| | | 250 | 15 | 17 |
| | | 125 | 13 | - |
| | | 62,5 | - | 15 |
| **LIV** | dimethyl | 500 | 18 | 15 |
| | | 250 | 16 | - |
| | | 125 | 12 | 13 |
| | | 62,5 | 11 | 10 |
| **LIV - Pt complex** | = | 500 | 18 | 18 |
| | | 250 | 16 | - |
| | | 125 | 14 | - |
| | | 62,5 | 10 | 15 |
| **LIV -Au complex** | = | 500 | 19 | 20 |
| | | 250 | 15 | 14 |
| | | 125 | 13 | - |
| | | 62,5 | 10 | 12 |
| **LV** | - | 500 | 17 | 18 |
| | | 250 | 11 | 13 |
| | | 125 | - | 13 |
| | | 62,5 | 11 | 10 |
| **LV -Pt Complex** | - | 500 | 15 | 17 |
| | | 250 | 13 | 15 |
| | | 125 | - | - |
| | | 62,5 | 12 | 12 |
| **LV- Au complex** | - | 500 | 19 | 16 |
| | | 250 | 19 | 15 |
| | | 125 | - | - |
| | | 62,5 | 12 | 15 |
| **LVI** | o-nitro | 500 | 18 | 18 |
| | | 250 | 14 | 16 |
| | | 125 | 13 | - |
| | | 62,5 | 10 | 13 |
| **LVI-Pt complex** | = | 500 | 16 | 17 |
| | | 250 | 14 | 15 |
| | | 125 | 13 | - |
| | | 62,5 | 12 | 14 |
| **LVI-Au complex** | = | 500 | 15 | 17 |
| | | 250 | 13 | 14 |
| | | 125 | 13 | - |
| | | 62,5 | - | 14 |
| **LVII** | Br | 500 | 20 | 13 |
| | | 250 | 13 | - |
| | | 125 | 13 | - |
| | | 62,5 | - | 10 |
| **LVII - Pt complex** | = | 500 | 22 | 18 |
| | | 250 | 14 | 17 |
| | | 125 | 14 | - |
| | | 62,5 | - | 15 |


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| | | | | |
|---|---|---|---|---|
| **LVII -Au complex** | = | 500 | 23 | 19 |
| | | 250 | 17 | 16 |
| | | 125 | 15 | - |
| | | 62,5 | 12 | 11 |
| **LVIII** | 4-Nitro | 500 | 14 | 15 |
| | | 250 | 14 | 15 |
| | | 125 | 13 | - |
| | | 62,5 | 13 | 12 |
| **LVIII- Pt complex** | = | 500 | 14 | 17 |
| | | 250 | 13 | 17 |
| | | 125 | 13 | - |
| | | 62,5 | 12 | 14 |
| **LVIII-Au complex** | = | 500 | 15 | 18 |
| | | 250 | 13 | 13 |
| | | 125 | 13 | - |
| | | 62,5 | 13 | 12 |
| **Stander1 Nalidixic acid** | | 500 | 11 | - |
| | | 250 | - | - |
| | | 125 | 10 | - |
| | | 62,5 | 10 | - |
| **Stander2 nitrofurantoin** | = | 500 | 13 | 14 |
| | | 250 | 12 | 14 |
| | | 125 | 11 | 14 |
| | | 62,5 | 11 | 14 |
| **DMSO** | | pure | - | - |

## CONCLUSION

The synthesis of the designed compounds has been successfully achieved, in the present investigation, the coordination features of novel hydrazone were studied by using equilibrium methods. The solid metal complexes of the candidate compounds involvingAu (III) and Pt(IV) complexes were synthesized and characterized by various spectral analytical techniques viz., FT-IR, UV-Vis, TGA, and NMR studies. Ligands and their complexes were assayed for their antimicrobial activity, which showed that Au (III) and Pt(IV)complexeshad the best profile property displaying prominent activity against gram positive and gram negative bacteria especially *streptococcus pyogenes, Staphylococcus aureus, klebsiella pneumonia* and *Escherichia coli.* The compounds could be further modified to enhance their antibacterial and antifungal activity.

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