**Assiut University Journal of Chemistry (AUJC) 45(2016) 58-75**

Journal homepage: www.aujc.org

(ISSN 1678-4919) (Print) ( ISSN 2357-0415) (Online)

Vol(45) No(2) 2016

Full Paper

# Synthesis and complexation of some sugarhydrazone derived from isatin

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Article history : Received: 9/3/2016; Revised : 30/4/2016; Accepted : 31/5/2016; Available Online :13/12/2016;

**Abstract**

Sugar hydrazones **4-7** were prepared through condensation of the respective sugars (D-glucose, D-mannose, D-galactose, and D-arabinose) with (3-hydrazono-2-oxo-2,3-dihydroindol-1-yl)acetic acid hydrazide **3** which was prepared from the reaction between hydrazine hydrate and (2,3-dioxo-2,3-dihydro-indol-1-yl)acetic acid ethyl ester **2**. Acetylation of **4-7** afforded the per-O-acetylsugar-N-acetylhydrazones **8-11**. Cu(II), Zn(II), Mn(II) and Fe(III) complexes of the glucose derivative **4** [HL] were prepared and characterized by elemental analysis, conductivity measurements, IR, UV-Vis. and magnetic moment measurements. TGA and DTA confirm the chemical formulation of the complexes and their thermal decomposition were evaluated.

**Keywords**: Isatin, sugar hydrazones, metal complexes, thermal decomposition.

## 1. Introduction

Isatin Schiff-bases are known to possess a wide range of pharmacological properties including antibacterial [1-3], anticonvulsant [4,5], anti-HIV [6-9], antifungal [10-13] and antiviral activity [14]. Isatin bis-Schiff bases are characterized by their capacity to co-ordinate to metal ions forming chelate rings [15], act as inhibitors of human α-thrombin [16] and its copper(II) complex catalyzed the oxidation of carbohydrates [17]. Recently it has been reported that isatin bis-imine has antimicrobial properties [18] and affects cell viability [19]. Schiff-base derivatives based on carbohydrates have functional similarities with amino alcohols and hydrazones, which can exhibit remarkable anti-TB activity [20-26]. In carbohydrate chemistry, a large number of imines have been reported, both by reaction of sugar aldehydes with amines and by reaction of amino sugars with aldehydes [27-30]. In addition, the bis(thiosemicarbazones) and their Copper (II) complexes of

D-arabinose and D-glucose and their in vivo antitumor activity in murine L-1210 were studied [31]. A series of Schiff base derivatives of D-mannitol have been synthesized and evaluated for their in vitro antibacterial activity against Mycobacterium tuberculosis H37Rv [32]. In continuation with our interest in Schiff-bases of isatin [33], we report the synthesis and characterization of new Schiff-bases of isatin with each of: D-glucose, D-mannose, D-galactose and D-arabinose. Also, Cu(II), Zn(II), Mn(II) and Fe(III) complexes of the glucose Schiff-base [HL] were prepared and characterized.

## 2.Experimental

### *2.1.General*

All the reagents, solvents and metal salts used were of analytical grade. Elemental analyses were carried out using a Heraus CHN-rapid analyzer. Infrared spectra were recorded (KBr disc) in the 400-4000 cm-1 range on Bruker Vector22 spectrometer. 1H-NMR measurements were carried out on a Bruker ARX 1H-NMR: 300.13 MHz, using DMSO as solvent unless otherwise stated, the chemical shifts (δ-ppm) are given downfield relative to tetramethylsilane (TMS), as internal standard. Mass spectral data given in m/z (relative %), are measured on Varian MAT-711 mass spectrometer. Ionization is initiated by electron impact (EI) with 70 ev of energy. The electronic absorption spectra were obtained using $10^{-3}$M DMF solutions in 1cm quartz cell using *UV-1601PC Shimadzu spectrophotometer*. Magnetic susceptibility measurements were carried out using the modified Gouy method [34] on *MSB-MK1 balance* at room temperature. TGA, DTG and DTA were recorded on Shimadzu 60 thermal analyzer under a dynamic flow of nitrogen (30ml/min.) and heating rate 10˚C/min. from ambient temperature to 750˚C. Electrical conductivity measurements were carried out at room temperature on freshly prepared $10^{-3}$M DMF solutions using WTW conductivity meter fitted with L100 conductivity cell. Thin layer chromatograph (TLC) was carried out on aluminum sheets recoated with silica gel mesh 60 F254, 0.2 mm thick.

### *Synthesis of (2,3-Dioxo-2,3-dihydro-indol-1-yl)acetic acid ethyl ester (2)*

To a stirred solution of isatin (1.5 gm, 10.18 mmol) in acetone (35 ml) $K_2CO_3$ (1.4 gm, 10.18 mmol) was added. The resulting reaction mixture was stirred for 1 h. Then a solution of ethyl chloro acetate (1 ml, 10.18 mmol) in acetone (15 ml) was added dropwise with stirring. The reaction mixture was stirred for 5h at room temperature then it was filtered. The obtained filtrate was concentrated under reduced pressure, the resulting precipitate was collected and crystallized from acetone-hexane mixture to give **2** (1.1 gm, 69.6% yield) as white crystals m.p 139-140°C. IR ν($cm^{-1}$):1696, 1675, 1653 (C=O); MS: 233[$(M)^+$, 0.08]; 205 (24); 172 (6), 162 (53); 160 (36); 148 (49.9); 120 (54); 119 (100); 91 (20); Calcd. (%) for $C_{12}H_{11}NO_4$ (233): C, 61.80; H, 4.75; N, 6.01; Found (%) : C, 61.79; H, 4.77; N, 5.87.

### *Synthesis of (3-Hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-aceticacid hydrazide (3)*

Hydrazine hydrate [4 ml (80%), 80 mmol] was added to a solution of 2 (1 gm, 4.3 mmol) in $C_2H_5OH$ (15 ml), the

mixture was stirred for 4h at room temperature, concentrated under reduced pressure. The resulting solid was filtered off, crystallized from ethyl acetate to give 3, (0.7g, 70 % yield) as white crystals m.p. 183-186˚C. IR ν($cm^{-1}$): 3525(OH), 3433, 3337(NH), 1669(C=O), 1612(C=N); MS: 202 (M-$NHNH_2$, 9.16); 201 (72); 170 (100); 140 (20); 101 (38.5); 1H-NMR ($CDCl_3$) δ (ppm): 8.02 (d, 1H, H-7), 7.88 (d, 1H, H6), 7.6 (m, 1H, H5), 7.5 (m, 1H, H8), 3.54 (s, 5H, $2NH_2$, NH), 2.6 (s, 2H, $CH_2$); Calcd.(%) for $C_{10}H_{11}N_5O_2$ (233): C, 51.50; H, 4.75; N, 30.03; Found (%) : C, 51.48; H, 4.81; N, 29.98.

***Synthesis of Sugar-(3-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-aceticacid hydrazones (4-7)***

**General method:**

To a solution of **3** ( 2.3 g, 10.0 mmol) in EtOH (15 ml), the respective sugar (10.0 mmol) and few drops of $CH_3COOH$ were added. The reaction mixture was heated under reflux on a water bath for 4h, concentrated and left to cool. The resulting precipitate was filtered, washed with EtOH and crystallized from ethanol to give the following compounds.

***Synthesis of D(+)Glucose-(3-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid hydrazone (4)***

Yield 91% ; m.p 118-120˚C; IR ν($cm^{-1}$): 3504(OH), 3352, 3242(NH), 1656(C=O), 1594, 1561(C=N); $^1$H-NMR δ (ppm): 11.71 (s, 1H, NH), 8.07 (d, 1H, H4), 7.98 (d, 1H, H7), 7.75 (t, 1H, H5), 7.57 (t, 1H, H6), 7.43 (s, 2H, $NH_2$), 6.0 (d, 1H, CH=N), 5.09-4.9 (3d, 3H, OH), 4.2 (m, 1H, OH), 4.0(m, 1H, OH), 3.7-3.2 (m, protons of the alditol congregated with the solvent absorption), 2.6 (s, 2H, $CH_2$); Calcd. (%) for $C_{16}H_{21}N_5O_7$ (395.38):C, 48.61; H, 5.35; N, 17.71; Found (%) C, 48.59; H, 5.11; N, 17.67.

***Synthesis of D(+)Mannose-(3-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid hydrazone (5)***

Yield 85% ; m.p 165-167˚C; IR ν($cm^{-1}$): 3378 (OH), 1653(C=O), 1598(C=N) ; $^1$H-NMR δ (ppm): 11.83 (s, 1H, NH), 8.03-7.53 (m, 4H, Ar-H), 7.34 (s, 2H, $NH_2$), 6.6 (d, 1H, CH=N), 5.3-4.2 (m, 5H, 5OH), 3.7-3.2 (m, protons of the alditol congregated with the solvent absorption), 2.67 (s, 2H, $CH_2$); Calcd. (%) for $C_{16}H_{21}N_5O_7$ (395.38): C, 48.61; H, 5.35; N, 17.71; Found (%) C, 48.33; H, 5.09; N, 17.59

***Synthesis of D(+)Galactose-(3-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid hydrazone (6)***

Yield 89% ; m.p 138-140˚C; IR ν($cm^{-1}$): 3485 (OH), 3337, 3210 (NH), 1634(C=O), 1598(C=N); Calcd. (%) for $C_{16}H_{21}N_5O_7$ (395.38): C, 48.61; H, 5.35; N, 17.71; Found (%) C, 48.77; H, 4.99; N, 17.45.

***D(+)Arabinose-(3-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid hydrazine (7)***

Yield 45%; m.p 162-163˚C; IR ν($cm^{-1}$): 3493(OH), 3383, 3288(NH), 1639(C=O), 1595(C=N)**;** Calcd. (%) for $C_{15}H_{19}N_5O_6$ (365): C, 49.31; H, 5.24; N, 19.17; Found (%) C, 49.43; H, 4.99; N, 19.09.

***Synthesis of Per-O-acetyl-sugar [3-(acetyl-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid N-acetyl-hydrazones (8-11)***

**General method**

A cold solution of the sugar hydrazone (0.5 gm, 2.0 mmol) in dry pyridine (5.0 ml) was added to $(CH_3CO)_2O$ (5.0 ml). The mixture was left overnight with occasional shaking, then poured onto crushed ice, extracted by $CH_2Cl_2$ and finally precipitated by the addition of petroleum ether. The resulting precipitate was collected by filtration, dried, and crystallized from benzene / petroleum ether.

***Synthesis of Penta-O-acetyl-(D)-glucose-3-(Acetyl-hydrazono-2-oxo-2,3-dihydro-*indol*-1-yl)-acetic acid N-acetyl-hydrazone (8)***

Yield 35% ; m.p 70-72˚C; IR ν($cm^{-1}$): 3255(NH), 1752, 1686(C=O, 1597(C=N); $^1$H-NMR ($CDCl_3$) δ (ppm): 8.07-7.47 (m, 5H, Ar-H, NH), 5.54-4.09 (m, 6H, 2H-6`, H-5`, H-4`, H-3`, H-2`), 2.6 (s, 2H, $CH_2$), 2.16-1.67 (7s, 21H, $7COCH_3$); Calcd. (%) for $C_{30}H_{35}N_5O_{14}$ (689): C, 52.25; H, 5.12; N, 10.16; Found (%) C, 52.30; H, 4.98; N, 9.85.

***Synthesis of Penta-O-acetyl-(D)-mannose-3-(Acetyl-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid N-acetyl-hydrazone (9)***

Yield 30% ; m.p 54-56˚C; IR ν($cm^{-1}$): 3204(NH), 1750, 1665(C=O), 1597(C=N); $^1$H-NMR ($CDCl_3$) δ (ppm): 8.1-7.05 (m, 5H, Ar-H, NH), 5.61-4.0 (m, 6H, 2H-6`, H-5`, H-4`, H-3`, H-2`), 2.7 (s, 2H, $CH_2$), 2.15-1.79 (7s, 21H, $7COCH_3$); Calcd. (%) for $C_{30}H_{35}N_5O_{14}$ (689): C, 52.25; H, 5.12; N, 10.16; Found (%) C, 52.11; H, 5.33; N, 10.40.

***Synthesis of Penta-O-acetyl-(D)-galactose-3-(Acetyl-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid N-acetyl-hydrazone (10)***

Yield 25% ; m.p 60-62˚C; IR ν($cm^{-1}$): 3279(NH), 1750, 1701 (C=O), 1597(C=N); Calcd. (%) for $C_{30}H_{35}N_5O_{14}$ (689): C, 52.25; H, 5.12; N, 10.16; Found (%) C, 52.42; H, 5.26; N, 10.31.

***Synthesis of Tetra-O-acetyl-(D)-arabinose[3-(Acetyl-hydrazono-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid N-acetyl-hydrazone (11)***

Yield 30% ; m.p 59-61˚C; IR ν($cm^{-1}$): 3200(NH), 1745(OAc), 1682(NAc), 1595(C=N) ; $^1$H-NMR δ (ppm): 7.64-7.41 (m, 5H, 4Ar-H, NH), 5.14-4.07 (m, 5H, 2H-5`, H-4`, H-3`, H-2`), 2.6 (s, 2H, $CH_2$), 1.89-2.03 (6s, 18 H, 6 $COCH_3$); Calcd. (%) for $C_{27}H_{31}N_5O_{12}$ (617): C, 52.51; H, 5.06; N, 11.34; Found (%) C, 52.66; H, 5.11; N, 11.55.

***2.2.Synthesis of the metal complexes***

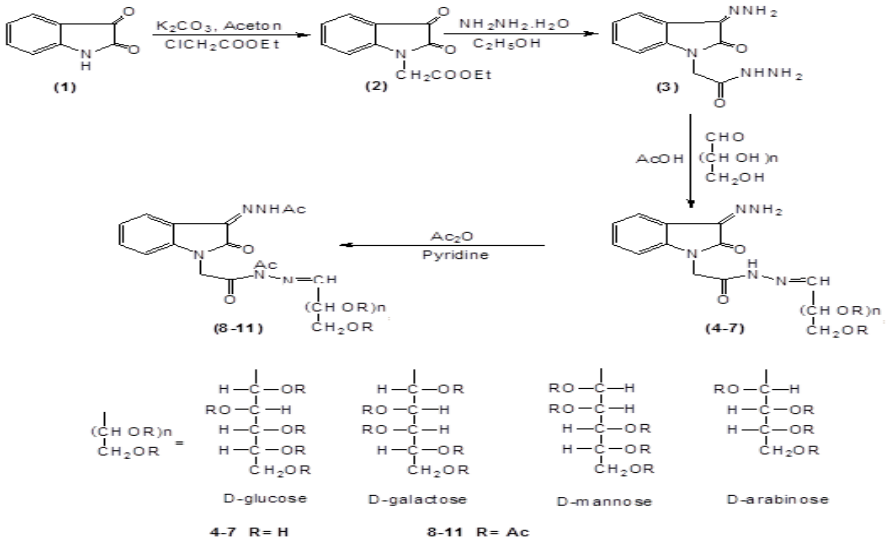
To a solution of the prepared Schiff-base (**4**) (2 mmol) in ethanol (10 ml), a solution of the metal salt (1 mmol) in ethanol (10 ml) was added dropwise with stirring. The pH of the mixture was increased to 7–7.5 by addition of dilute KOH solution. The reaction mixture was refluxed with stirring for 2 hours. The formed precipitate was filtered, washed with hot ethanol and dried under vacuum over anhydrous $CaCl_2$. Since the complexes were insoluble and non-crystallizable in common organic solvents, they were purified by washing thoroughly with hot ethanol to remove unreacted materials.

**3. Results and discussion**

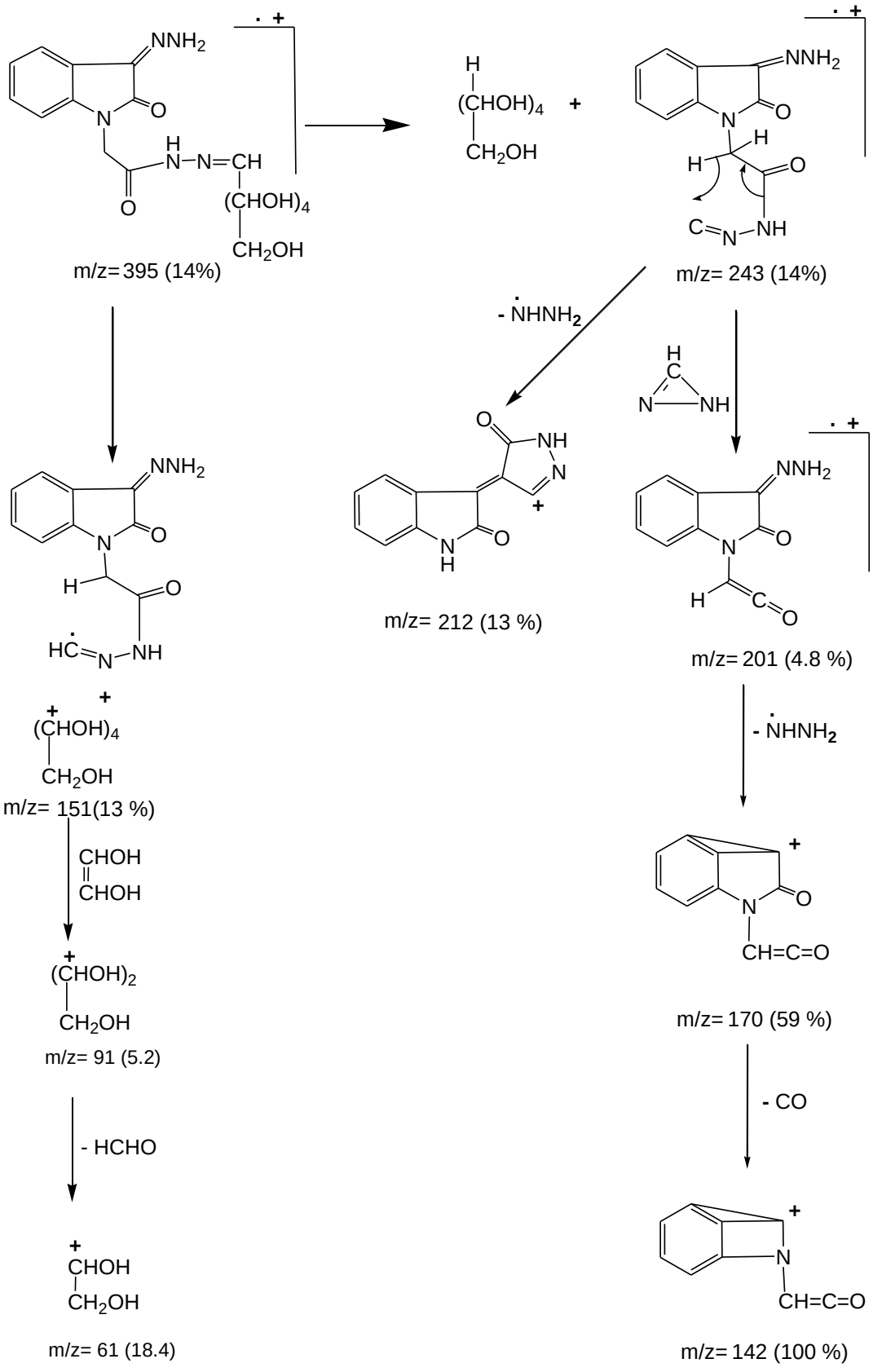
Reaction of isatin 1 with ethyl chloroacetate afforded (2,3-dioxo-2,3-dihydroindol-1-yl) acetic acid ethyl ester 2 which upon reaction with hydrazine hydrate in presence of few drops of acetic acid gave 3-hydrazono-2-oxo-2,3-dihydro-indole-1-yl)acetic acid hydrazide 3. Heating of 3 with the respective sugar, D-glucose, D-mannose, D-galactose and D-arabinose in ethanol under reflux yields a series of hydrazones. This reaction was catalyzed with a few drops of acetic acid to give the corresponding hydrazones 4-7 Acetylation of the resulting hydrazones 4-7 with acetic acid anhydride in dry pyridine gave the respective per-O-acetyl-N-acetyl derivatives 8-11 (Scheme 1).

IR spectrum of **2** showed three absorption bands at 1696, 1675 and 1653 $cm^{-1}$ for the three carbonyl groups together with a medium absorption band at 3184 $cm^{-1}$ for the enol form. On the other hand, **3** showed three absorption bands for the hydrazide and hydrazone groups at 3525, 3433 and 3337 $cm^{-1}$ respectively. The structure was also confirmed by $^1H$ NMR spectrum which showed the presence of a broad singlet at δ 3.54 ppm assigned for the hydrazide and hydrazone groups together with two douplets and three triplets for the four aromatic protons beside a singlet at δ 2.6 ppm for the methylene protons. Mass spectra of compound **2** showed the expected m/z at 233 which losses the ethyl radical to give the cation m/z at 205. Compound **3** losses a hydrazine molecule to give the ketene radical cation m/z at 201. IR spectra of the hydrazones **4-7** showed the OH peaks in the 3504-3378 $cm^{-1}$ range, the NH at 3383-3210 $cm^{-1}$, the C=O at 1653-1634 and the new absorption peak at 1598-1561 $cm^{-1}$ for the C=N. $^1H$ NMR showed in addition to the aromatic and the NH signals the sugar hydroxyl signals at the δ 4.0-5.2 ppm range, the anomeric proton signal at δ 6.0-6.6 ppm and a singlet at δ 2.6 ppm for the $CH_2$ group. IR spectra of compounds **8-11** showed a new absorption peaks in the 1745-1752 $cm^{-1}$ range for the acetyl groups. $^1$HNMR showed the disappearance of the OH signals and appearance of the expected O-acetyl and N-acetyl signals.

Mass spectrum of **4** was outlined in (Scheme 2).




**Scheme 1**


m/z= 395 (14%)
m/z= 243 (14%)
- ·NHNH2
m/z= 212 (13 %)
m/z= 201 (4.8 %)
- ·NHNH2
m/z= 151(13 %)
m/z= 91 (5.2)
- HCHO
m/z= 61 (18.4)
m/z= 170 (59 %)
- CO
m/z= 142 (100 %)

**Scheme 2**

### *3.1.Complexes of the HL Schiff-base (4)*

Cu(II), Zn(II), Mn(II) and Fe(III) complexes of the glucose derivative (**4)** [HL] were prepared and characterized. All the complexes are insoluble in common organic solvents (ethanol, methanol, chloroform, benzene, acetone and diethylether) but partially soluble in DMF and DMSO. The complexes decompose without melting when heated above 380˚C. Elemental analysis show 2:1 (metal: ligand) stoichiometry for the complexes. The analytical data along with some physical properties of the complexes are summarized in (Table 1). The complexes can be represented by the formulae:

$[M_2HL(NO_3)_x(H_2O)_y].zNO_3.nH_2O$ where M=Cu(II), Fe(III), Zn(III) and Mn(II); x=2, 5, 0; y=2, 4; z=1, 0, 3 and n=3, respectively. The molar conductance values for $10^{-3}$M DMF solution of the complexes are non-electrolyte (Fe complex), 1:1 (Cu complex) and 1:3 electrolytes (Zn and Mn complexes) [35].

### *3.2.Infrared spectra*

Infrared spectrum of the Schiff-base exhibit a medium sharp band at 3504$cm^{-1}$ which can be attributed to υ(OH) [36]. Another medium intensity splitted band at 3242 and 3159 $cm^{-1}$ can be assigned to the stretching vibration of $\upsilon(NH_2)$ which also shows a strong intensity band at 750 $cm^{-1}$ due to wagging vibration. Strong sharp band at 1656 $cm^{-1}$ is due to υ(C=O) of isatin [37]. Vibrations of the ketimine and aldimine groups were observed at 1594 and 1561 $cm^{-1}$.

Infrared spectral data of the complexes are presented in (Table 2) along with their tentative assignments. It shows the absence of $\upsilon(NH_2)$ band which could be due to overlapping with coordinated water molecules while the band due to wagging vibration is shifted to lower frequency indicating coordination through the amino nitrogen atom. The band corresponding to υ(C=O) shifts either to lower frequency by about 12-20 $cm^{-1}$ or to higher frequency by about 18-24 $cm^{-1}$ in the spectrum of the metal complexes indicating coordination by the carbonyl oxygen. The azomethine group υ(C=N) of the Schiff-base is shifted to lower frequency by about 27-40 $cm^{-1}$ in the complexes, which is a clear evidence for the involvement of this group in chelation with metals. However, the vibrational characteristic of the ketimine υ(C=N) at 1594 $cm^{-1}$ remain almost unaffected, indicating non-involvement in coordination. In the Cu(II) complex the presence of the coordinated nitrates is indicated by two medium intensity bands at 1463 and 1297 due to $\upsilon_4$ and $\upsilon_1$ vibrations of the nitrate ion of $C_{2v}$ symmetry [38]. Since $(\upsilon_4–\upsilon_1)$ = 114 $cm^{-1}$, the nitrate ions are coordinated as unidentate group while the Fe(III) complex exhibits bands due to unidentate (1420 and 1305 $cm^{-1}$) and bidentate (1500 and 1295 $cm^{-1}$) groups. This is emphasized by the molar conductance of the complex which has a value equal to 23 $ohm^{-1}.cm^2.mol^{-1}$ of $10^{-3}$ M solution, indicating its non-electrolytic nature and hence the nitrate ions are coordinated to the ligand as mentioned above. The Cu(II), Zn(II) and Mn(II) show strong bands at 1391, 1384 and a medium intensity bands at 823, 822 and 882$cm^{-1}$, respectively, due to the $\upsilon_3$ and $\upsilon_2$ vibrations, of the uncoordinated nitrate ion ($D_{3h}$) of the complexes [39]. All complexes show a broad bands at 3420, 3394, 3456 and 3387 $cm^{-1}$ which could be attributed to $\upsilon(H_2O)$ for Cu(II), Fe(III), Zn(II) and Mn(II), respectively. The υ(M–O) and υ(M–N) stretching vibrations are observed in the 521-595 and 425-508 $cm^{-1}$ range in the spectra of the complexes [40] .

**Table 1.** Analytical data, conductivity measurements and magnetic moments of the HL Schiff-base and its complexes

| Compound | M. wt. | Color | M.p. (°C ) | Yield % | Elemental analysis Found Calcd. % | | | | $^{*}\Lambda_M$ DMF | $^{**}\mu_{eff}$/M |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | N | M | | |
| HL | 394.39 | white | 120 | 91 | 48.61<br>48.67 | 5.11<br>5.31 | 17.67<br>17.74 | --- | --- | --- |
| $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ | 796.37 | green | >380 | 63 | 23.98<br>24.10 | 3.93<br>3.89 | 14.11<br>14.06 | 16.41<br>15.95 | 93 | 0.72 |
| $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ | 904.92 | black | >380 | 67 | 21.38<br>21.23 | 3.11<br>3.42 | 15.53<br>15.47 | 12.31<br>12.34 | 23 | 2.11 |
| $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 837.08 | brown | >380 | 51 | 22.81<br>22.93 | 4.22<br>4.17 | 13.11<br>13.37 | 15.54<br>15.62 | 210 | dia |
| $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 815.17 | brown | >380 | 53 | 23.73<br>23.55 | 4.11<br>4.29 | 13.53<br>13.73 | 13.30<br>13.47 | 205 | 1.85 |

* Conductance of $10^{-3}$M ($ohm^{-1}.cm2.mol^{-1}$)

** $\mu_{eff}$ at T=298°K B.M.

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**Table 2.** IR spectral data of the HL Schiff-base and its complexes ($cm^{-1}$)

| Complexes | ν $H_2O$<br>ν OH<br>ν $NH_2$ | ν(C=O) | ν(C=N) | ν($NO_3$) | ν(M-O) | ν(M-N) |
|---|---|---|---|---|---|---|
| HL | ----<br>3504 br.<br>3242 }s.<br>3159 } | 1657s. | 1594s.<br>1561s. | ---- | ---- | ---- |
| $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ | 3420 br. | 1644m. | 1596s.<br>1537s. | 1463m.<br>1297m.<br>1391s.<br>823m. | 595m. | 508m. |
| $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ | 3394 br. | 1676m. | 1590m.<br>1534m. | 1500m.<br>1420m.<br>1305s.<br>1295m. | 521m. | 431m. |
| $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 3456 br. | 1674m. | 1596m.<br>1522m. | 1384s.<br>822m. | 577m. | 425br. |
| $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 3387 br. | 1636m. | 1593m.<br>1521m. | 1384s.<br>882m. | 570m. | 436m. |

s.= strong, m.= medium, br.= broad.

### *3.3.Magnetic moment and electronic absorption spectra*

Magnetic moments and visible spectra of the various complexes were used to study the geometrical configuration of the metal complexes. The magnetic moment value for the Zinc(II) complex is zero consistent with its $d^{10}$ configuration.

The magnetic moments of the Cu(II), Fe(III) and Mn(II) complexes calculated from the corrected magnetic susceptibility determined at room temperature are given in (Table 1). The data show that the magnetic moments reported for the complexes are lower than the spin only values. The subnormal magnetic moments observed for the complexes may be accounted for by the following:

a- Antiferromagnetic exchange interaction between the metal ions, suggesting the possibility of spin-spin coupling [41,42].

b- The possibility that the reduced moment represent a solid state intermolecular interaction rather than an intramolecular coupling.

These considerations confirm the bi-structure of the complexes. Such lowering of the magnetic moment has been observed with other polynuclear complexes [43]. Electronic spectra of the Schiff-base and its complexes in DMF are presented in (Table 3). The electronic spectra of the complexes show three bands in the 268-319 regions. The ligand bands at 278, 305and 318 nm show no shift on complexation. The spectra of the Fe(III) complex exhibit a band at 520 nm corresponding to $^6A_{1g} \rightarrow {}^4T_{1g}$ transition consistent with octahedral Fe(III) complexes [45,46].

The electronic spectrum of the low-spin manganese complex is dominated by strong charge-transfer bands. Any d-d band occurring in the visible region is masked by strong charge-transfer bands. Tetracoordinated Mn(II) and Zn(II) complexes may have tetragonal stereochemistry [45].

**Table 3.** Electronic spectra (nm) of the HL Schiff-base and its complexes in DMF

| Compound | Inter ligand and CT bands | d-d bands |
|---|---|---|
| HL | 278, 305, 318 | …… |
| $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ | 268, 305, 319 | 702 br. |
| $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ | 276, 305, 318 | 520 |
| $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 275, 306, 319 | ……. |
| $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 284, 307, 319 | ……. |

### *3.4.Thermal analysis*

Thermal behavior of the synthesized complexes has been studied using TGA, DTG and DTA. Typical calorigrams are presented in Fig. 1. The decomposition stages, temperature ranges, decomposition products as well as the found and calculated weight loss of the complexes are given in (Tables 4, 5). Dehydration process in the studied complexes with evaporation of three water molecules takes place in the 32-106, 29-78, 15-130 and 30-102˚C range with DTG maxima at 68, 58, 78 and 60˚C, respectively. This process is associated with weight loss of 7.25, 5.56, 6.36 and 6.66% (calcd. 6.93, 5.96, 6.45 and 6.62%). DTA calorigrams confirm the dehydration process by endothermic changes in the 32-119, 39-82, 32-130 and 40-120˚C range with maxima at 71, 62, 73 and 69˚C, respectively. In the second decomposition step $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ and $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ complexes show decomposition of the ionization sphere and evaporation of two molecules of nitrate ions as nitric acid while in $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ complex the coordinated water together with a nitrate ion are eliminated. It takes place in the 144-214, 135-192 and 147-247 ˚C range with DTG maxima at 183, 173 and 199˚C associated with weight loss of 12.22, 14.93 and 15.71% (calcd. 12.42, 15.04 and 15.44%). Exothermic DTA peaks in the 156-206, 147-205 and 140-226 ˚C range with maxima at 181, 175 and 185˚C confirm this step in the complexes. On the other hand, $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ undergoes the second decomposition step in the 145-188˚C range with maximum at 173˚C. This step shows loss of two molecules of coordinated nitrate ions with mass loss of 14.35% (calcd. 13.91%) and is confirmed with exothermic DTA peak at 177˚C. Evolution of three molecules of the coordinated nitrate as well as the coordinated water is taken place in the third decomposition step. This process is shown in the 237-304˚C range with DTG maximum at 304˚C and mass loss of 24.77% (calcd. 24.85%), accompanied with exothermic change in the 263-285˚C range with DTA maximum at 309˚C. The third step in $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ complex correlated with loss of two molecules of coordinated nitrate ions as well as decomposition of 0.16 of the

ligand. It takes place in 244-292˚C range and show DTG maximum at 276˚C and mass loss of 23.4% (calcd. 23.73%). This step is associated with DTA maximum at 378˚C. The $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ and $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ complexes show loss of a nitrate ion together with four coordinated water molecules in the third step in the 193-275 and 248-345˚C range with DTG maximum at 241 and 288˚C and mass loss of 16.44 and 16.32% (calcd. 16.12 and 16.55%). DTA confirms this step by exothermic changes at 239 and 293˚C. The partial decomposition of the Schiff-base starts at the fourth decomposition step except for the Cu(II) complex where it is started at the third decomposition step and continue until the formation of CuO, $Fe_3O_4$ and ZnO as a final products. $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ has no plateau at 700˚C which indicate that it is not completely decomposed. Decomposition of the ligand is indicated by DTA variation in the 432-553, 567-712, 455-608, 613-638, 317-390, 487-572, 573-640 and 381-472˚C range with exothermic peaks at 483, 613, 554, 628, 350, 535 and 622˚C, respectively, and endothermic peak at 374˚C. Accordingly, the dehydration step of the complexes has the following order $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ < $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ < $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ < $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ which may be proportional to the number of 3d electrons in each element. Based on the above analytical data and physicochemical properties, the following structures are proposed in which the metal ion is coordinated through the $NH_2$, the carbonyl groups C=O of isatin, C=O or the enolized carbonyl group C–OH of the amide, azomethine nitrogen C=N of the aldeimine moiety, the coordinated water and the coordinated nitrate (Scheme 3).

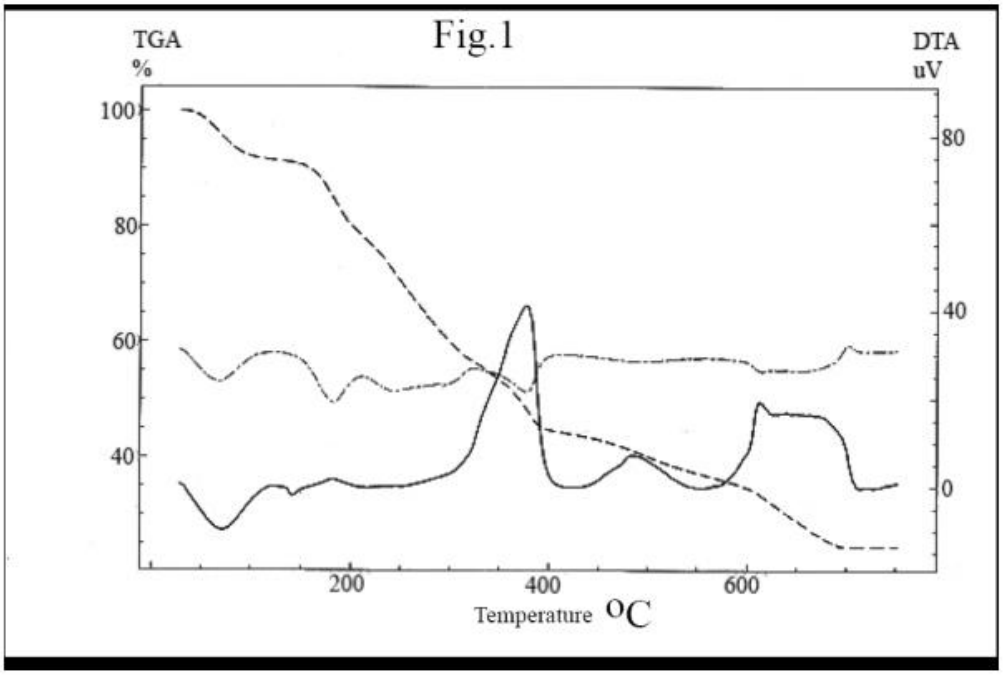


**Fig.1.** TGA, DTG and DTA of the $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ complex.

**Table 4.** TGA and DTG data of the complexes of HL Schiff-base

| Complexes | Temp. range °C | DTG °C | Mass loss% Found | Calcd. | Process | Residue% and type Found(Calcd.) | |
|---|---|---|---|---|---|---|---|
| $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3$ .$3H_2O$ | 32-106 | 68 | 7.25 | 6.93 | Dehydration | $3H_2O$ | 23.62 (19.97) |
| | 144-214 | 183 | 12.22 | 12.42 | Ionization sphere + coordinated water | $HNO_3 + 2H_2O$ | CuO |
| | | 276 | | | | $2HNO_3$+ 0.16L | |
| | 244-292 | 378 | 23.40 | 23.73 | Coordination sphere | 0.27 L | |
| | 344-406 | 488 | 13.35 | 13.61 | Ligand decomposition | 0.13 L | |
| | 432-558 | 649 | 6.30 | 6.58 | Ligand decomposition | 0.28 L | |
| | 597-703 | | 13.52 | 13.68 | Final decomposition | | |
| $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ | 29-78 | 58 | 5.56 | 5.96 | Dehydration | 3 $H_2O$ | 17.65 (17.74) |
| | 145-188 | 173 | 14.35 | 13.91 | Coordination sphere | 2 $HNO_3$ | $Fe_3O_4$ |
| | 237-304 | 304 | 24.77 | 24.85 | Coordination sphere. | 3 $HNO_3 + 2H_2O$ | |
| | 478-603 | 553 | 34.98 | 34.86 | Final decomposition | 0.8 L | |
| | 624-638 | 627 | 2.65 | 3.05 | Solid state reaction | 0.07 L | |
| $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 15-130 | 78 | 6.36 | 6.45 | Dehydration | 3 $H_2O$ | 19.5(19.44) |
| | 135-192 | 173 | 14.93 | 15.04 | Ionization sphere | 2 $HNO_3$ | ZnO |
| | 193-275 | 241 | 16.44 | 16.12 | Ionization sphere + | $HNO_3$ +4 $H_2O$ | |
| | 317-382 | 344 | 19.12 | 19.31 | coordinated water | 0.41 L | |
| | | | 14.98 | | Partial decomposition. | 0.33 L | |
| | 497-575 | 534 | 9.50 | 15.07 | Decomposition | 0.21 L | |
| | 587-647 | 620 | | 9.42 | Final decomposition | | |
| $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 30-102 | 60 | 6.66 | 6.62 | Dehydration | 3 $H_2O$ | Not complete |
| | 147-247 | 199 | 15.71 | 15.44 | Ionization sphere | 2 $HNO_3$ | |
| | 248-345 | 288 | 16.32 | 16.55 | Ionization sphere + | $HNO_3$ + 4 $H_2O$ | |
| | | | | | coordinated water | 0.34 L | |
| | 346-425 | 377 | 16.18 | 16.44 | Decomposition | | |

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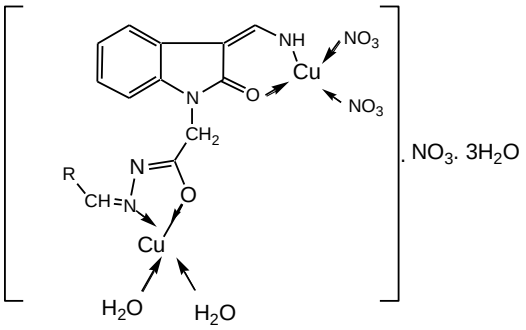
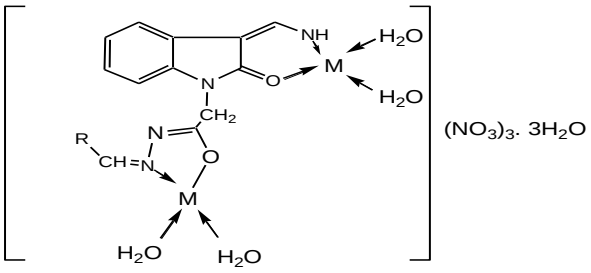
**Table 5.** DTA data of the complexes of HL Schiff-base

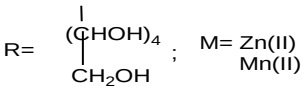
| Complexes | Temp. rang. °C | DTA peak °C | | ΔH J/g | Process |
|---|---|---|---|---|---|
| $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ | 32-119 | 71 | endo. | 345 | Dehydration |
| | 156-206 | 181 | exo. | -33 | Ionization sphere + coordinated water |
| | 249-411 | 378 | exo. | -1570 | Coordination sphere |
| | 432-553 | 483 | exo. | -99 | Decomposition |
| | 567-712 | 613 | exo. | -1270 | Final decomposition |
| $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ | 39-82 | 62 | endo. | 46 | Dehydration |
| | 143-203 | 177 | exo. | -169 | Coordination sphere |
| | 263-285 | 309 | exo. | -1360 | Coordination sphere |
| | 455-608 | 554 | exo. | -5810 | Final decomposition |
| | 613-638 | 628 | exo. | -105 | Solid state reaction |
| $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 32-130 | 73 | endo. | 13 | Dehydration |
| | 147-205 | 175 | exo. | - 181 | Ionization sphere |
| | 207-260 | 239 | exo. | - 226 | Ionization sphere + coordinated water |
| | 317-390 | 350 | exo. | - 444 | Partial decomposition. |
| | 487-572 | 535 | exo. | - 1110 | Decomposition |
| | 573-640 | 622 | exo. | - 1590 | Final decomposition |
| $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | 40-120 | 69 | endo. | 134 | Dehydration |
| | 140-226 | 185 | exo. | - 155 | Ionization sphere |
| | 255-365 | 293 | exo. | - 145 | Ionization sphere + coordinated water |
| | 381-472 | 374 | endo. | 174 | Decomposition |



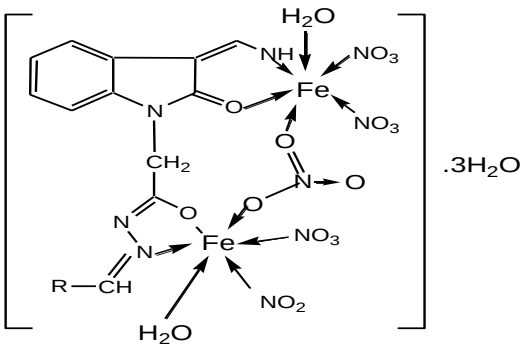


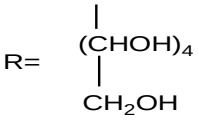
**$[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$**




**$[M_2HL(H_2O)_4].(NO_3)_3.3H_2O$**




**$[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$**

**Scheme 3: Structure of the metal complexes.**

***4.Antibacterial activity***

Antibacterial activity of the synthesized compounds has been screened using different strains of bacteria [*Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli, Proteus vulgaris*]. The desk diffusion method has been adapted for antibacterial activity [47]. The diameter of cleaning area around wells and desks (in mm) has been taken as indication to the antibacterial activity.

***4.1.Growth media***

Nutrient agar medium of the following composition (g/l) has been used for growing test organisms: peptone 5.0g, beef extract 3.0g, NaCl 5.0g, agar 18.0g and 1000 ml water. Spore suspensions from actively growing cultures were prepared using sterile distilled water. The media was prepared, poured into 9 cm diameter plates, allowed to solidify, and then one ml/plate of spore suspension was transferred especially to these plates and incubated at 37˚C for appropriate growth periods (1-3 d.).

100 ppm of the tested compound was dissolved in DMF, while DMF itself was used as control for comparison. The diameters of cleaning zones (in mm) have been used as a parameter to express antibacterial activity of each compound.

Accordingly, the resulting effects have been tentatively classified as follows: (+) small clearing zone (1-10 mm zone of inhibition), slightly active; (++) medium clearing zone (11-20 mm zone of inhibition), moderately active; (+++) large clearing zone, highly active; (over +++) very large zone, very highly active and (–) no clearing zone, inactive. The obtained results are shown in Table (6). As expected, no growth inhibition was observed for DMF, it seems that all the synthesized compounds are devoted of activity against Protus vulgaries while all the compounds are slightly active against Klebsiella pneumoniae and Escherichia coli. It is also obvious that the free sugar compounds 4-7 were more active than the acetylated compounds 8-11 against Staphylococcus aureus. The antibacterial activity of compound 4 and its complexes with Cu(II), Zn(II), Mn(II), and Fe(III) are shown in table (6) it shows that the complexation of the studied ligand with Cu(II), Zn(II), Mn(II), and Fe(III) has no effect on the activity of the ligand against the studied bacteria.

**Table 6.** The antibacterial activity of the synthesized compounds

| Compound | Gram positive | Gram negative | | |
|---|---|---|---|---|
| | Staphylococcus aureus | Klebsiella pneumoniae | Escherichia coli | Proteus vulgaris |
| DMF(Control) | - | - | - | - |
| **2** | ++ | + | + | - |
| **3** | ++ | + | + | - |
| **4** (HL) | ++ | + | + | - |
| $[Cu_2HL(NO_3)_2(H_2O)_2].NO_3.3H_2O$ | ++ | + | + | - |
| $[Fe_2HL(NO_3)_5(H_2O)_2].3H_2O$ | ++ | + | + | - |
| $[Zn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | ++ | + | + | - |
| $[Mn_2HL(H_2O)_4].(NO_3)_3.3H_2O$ | ++ | + | + | - |
| **5** | ++ | + | + | - |
| **6** | ++ | + | + | - |
| **7** | ++ | + | + | - |
| **8** | + | + | + | - |
| **9** | + | + | + | - |
| **10** | + | + | + | - |
| **11** | + | + | + | - |

- No zone of inhibition, + 1-10 mm zone of inhibition, ++ 11-20 mm zone of inhibition

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