Schiff Base Complexes: Synthesis, Characterization and Study of Bioactive Such As Antibacterial and Antifungal

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Abstract

The complexes of Schiff base (6-[Hydroxy - benzylidene)-amino]-pyrimidine-2,4-diol) (L) with Mn(II), Fe(II), Co(II) and Ni(II) were prepared. The Schiff base and complexes have been characterized by FT-IR, ^{1}H-NMR, UV-Vis, LC-mass spectra, magnetic moment, elemental microanalyses (C.H.N.), chloride containing, atomic absorption and molar conductance.

The Schiff base, metal salts and complexes were also screened for their bioactivity such as antibacterial and antifungal.

Keyword: Schiff base complexes, antibacterial and antifungal, bioactive studies.

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Introduction

Schiff bases are organic compounds which contain the (C=N) azomethine group [1]. The azomethine group plays an essential role for showing excellent bio active and any groups another of Schiff base and Schiff base coordination with metal ions does the same including (antifungal, antibacterial, anticancer, anti diabetic and anti inflammatory [2-6]. The interaction of these metal ions and donor Schiff base ligands give different geometries complexes and these complexes are bio active [7], heterocyclic 4-amino-2,6-dihydroxypyrimidine compound containing these (O-H) and (NH_2) groups is very bio active [8]. In this work, a new efficient route for the synthesis of Schiff base ligand and their metal complexes has been studied. The biological activity of these ligands, metal salts and their complexes is evaluated

Experimental

Materials and Methods

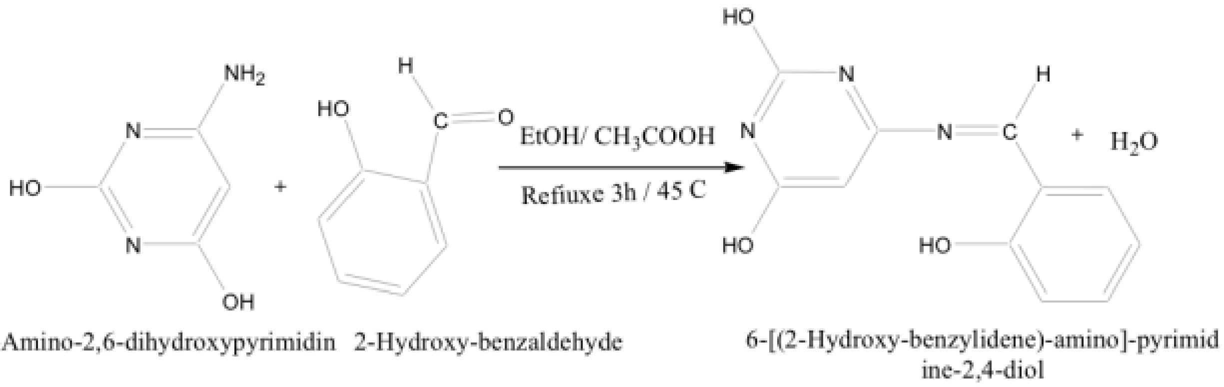
The following chemicals were commercially available and were used without further purification: 4-Amino-2,6-dihydroxypyrimidin and 4-Di methyl amino benzaldehyde DMSO, pure ethanol, methanol from Fluka, acetic acid glacial from Riedel, $FeCl_2.H_2O$, Aldrich) (diethyl ether, $CaCl_2$, $NiCl_2.6H_2O$, $MnCl_2.4H_2O$ and $CoCl_2.6H_2O$, Reedel).

Instrumentation

FT-IR spectra were recorded in the range (4000-400) cm^{-1} on a Shimadzu 3800, spectrometer as KBr disc. Electronic absorption spectra were recorded in the range (200-900) nm for solution in DMSO (1×10^{-3}) on a Shimadzu 160 Spectrophotometer. Elemental (C.H.N) analyses were carried out on a Perkin-Elmer automatic equipment model 240.B. Mass spectra were obtained by using LC-Mass 100P Shimadzu. Melting points were obtained on a Buchi SMP-20 capillary melting point apparatus and are uncorrected. Metal ratios were identified using a Shimadzu (A.A) 680G atomic absorption Spectrometer. Conductivity measurements were measured for solution in DMSO (1×10^{-3}) using a Jenway 4071 digital conductivity meter at room temperature. Magnetic properties were measured using (Magnetic susceptibility balance model MSR-MKi).

Synthesis of Schiff base Ligand: 6-[Hydroxy - benzylidene)-amino]-pyrimidine-2,4-diol (L):

A solution of 4-amino-2,6-dihydroxypyrimidine (1 g, 7.867 mmol) in ethanol (30 ml) was mixed with a solution of 2-Hydroxy-benzaldehyde (0.960 g, 7.867 mmol). The reaction mixture was stirred and heated at (40-50)°C for 3hrs. A dark yellow precipitated was formed, which was washed with diethyl ether and recrystallized from methanol: water (1:1) mixture. The product was dried via anhydrous $CaCl_2$ in vacuum as shown in Scheme (1), and shown the HOMO & LUMO for ligand theoretical Figure (1). The yield is 93.66%, mp.196°C.
^1H-NMR (DMSO-d_6, ppm):4.493, 3.426 and 3.024 (s, 3H, O-H phenol), 7.008- 8.084 (m, 5H, arom-CH), 9.197(s, 1H, N=C-H azomethine).



Scheme (1): Preparation of the ligand (L)

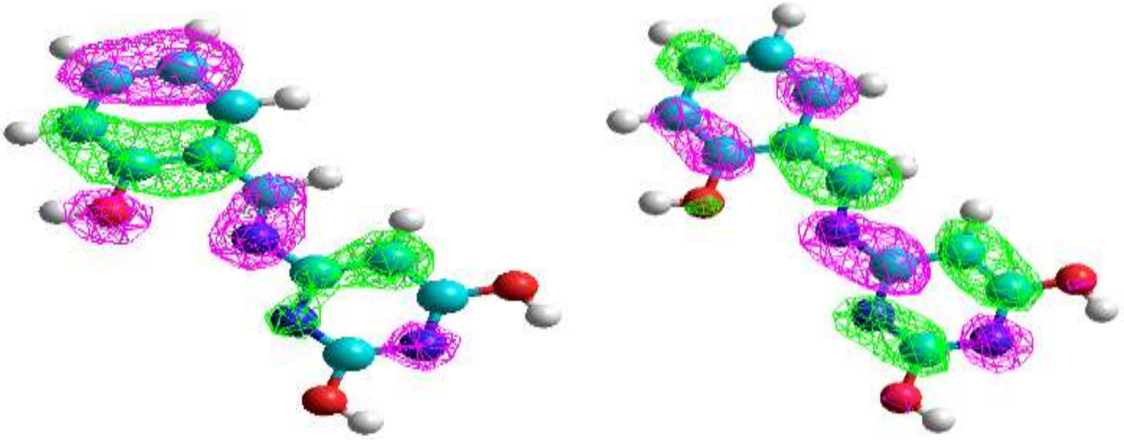
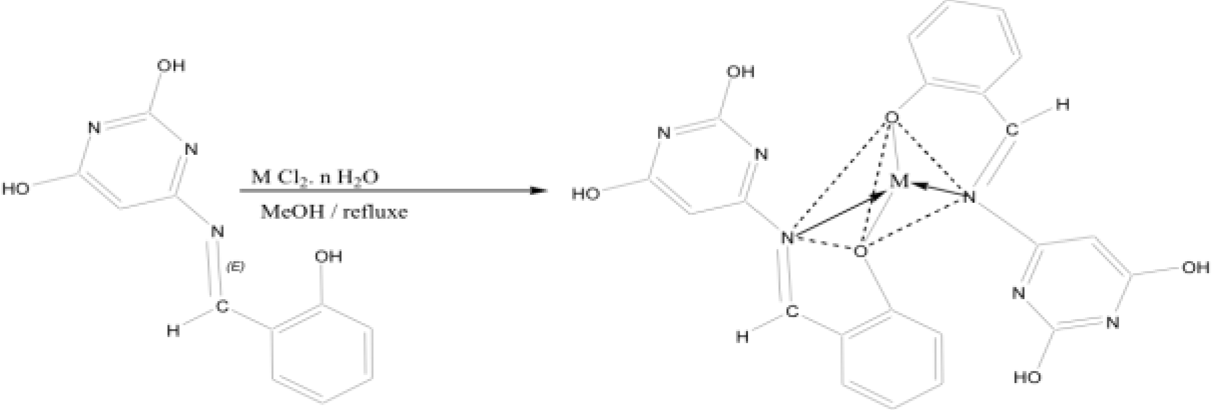


Figure (1): HOMO & LUMO for ligand

Synthesis of Schiff Base Complexes

A solution of Schiff base (6-[Hydroxy - benzylidene)-amino]-pyrimidine-2,4-diol) (1 g, 4.326 mmole) in methanol was added gradually with stirring to 0.851g, 0.622g, 1.0249g and 1.024g respectively, of $MnCl_2.4H_2O$, $FeCl_2.H_2O$, $CoCl_2.6H_2O$, and $NiCl_2.6H_2O$, respectively. The reaction mixture was allowed to reflux and the solid was collected by filtration and recrystallized from ethanol and dried at room temperature, showed in Scheme (2), Figure (2) shows: 3D structure of Co(II) complex. Physical properties and elemental microanalysis for the complexes are given in Table (1).



M(II)= Mn, n= 4; Fe, n= 1 ; Co, n= 6; and Ni, n= 6.

Scheme (2): Preparation of the complexes

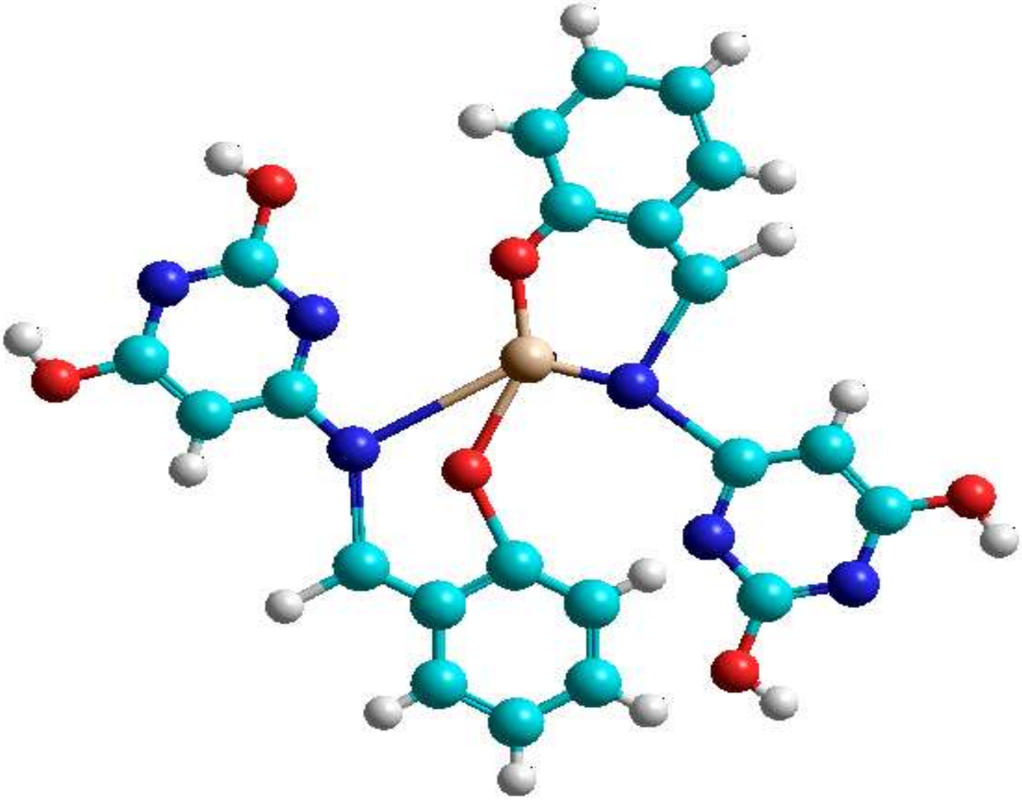


Figure (2): 3D structure of Co(II) complex

Study of Bioactivity

Schiff base, metal salts and complexes were screened against *staphylococcus aureus* (gram positive) and *Pseudomonas aeruginosa* (gram negative) bacteria as well fungi like *Penicillium expansum*, *Fusarium graminearum*, *Macrophomina phasealina*, and *Candida albicans*, by using the wall agar diffusion method. Using solvent (DMSO), the concentration of the compounds in this exposure was (1×10^{-3} M) by using disc sensitivity test. This method involves the exposure of the zone inhibition toward the diffusion of micro-organism on agar plate. The plates were incubated for (24 and 48) hrs of bacteria and fungi respectively at 37 °C.

Results and Discussion

Complexes were obtained upon reaction between metal ions and bidentate Schiff base (6-[Hydroxy - benzylidene)-amino]-pyrimidine-2,4-diol) in mole ratio (1:2) (M:L). The synthesized Schiff base and its complexes are very stable at room temperature in the solid state. The compounds are generally soluble in hot DMF and DMSO. The yields, melting/decomposition points, elemental micro analyses of Schiff base and its metals complexes are presented in Table (1). It is found that the analytical data are in a good agreement with the proposed stoichiometry of the complexes. Schiff base was melting point at temperatures 196ºC, while all complexes were decomposed at temperatures higher than (265-300) ºC. The ligand and its metal complexes have dye character due to the high molar extinction constant**.** Molar conductance values were found in the range (10-14) S. $cm^2\ mol^{-1}$ for all complexes which indicate that they are non-electrolytes [9]. These were determined in (DMSO) solution (1×10^{-3}M). Physical properties and elemental microanalysis are listed in Table (1).

Table (1): Microanalysis results and some physical properties of the ligand and its complexes

Sam	Molecular Formula =M_{Wt}	m.p. °C	Element analysis % Calc. (Found)			
			M	C	H	N
L	$C_{11}H_9N_3O_3$ 231.21	196		57.14 (57.97)	3.92 (3.01)	18.17 (20.01)
LMn	$C_{22}H_{16}N_6O_6Mn$ 515.34	300 d	10.66 (9.99)	51.27 (51.09)	3.13 (4.11)	16.31 (15.18)
LFe	$C_{22}H_{16}N_6O_6Fe$ 516.24	281 d	10.82 (9.99)	51.18 (49.79)	3.12 (4.11)	16.28 (15.18)
LCo	$C_{22}H_{16}N_6O_6Co$ 519.33	267 d	11.35 (10.99)	50.88 (49.89)	3.11 (4.11)	16.18 (15.18)
LNi	$C_{22}H_{16}N_6O_6Ni$ 519.09	265 d	11.31 (10.99)	50.90 (49.09)	3.11 (4.09)	16.19 (15.28)

d = decompose

Mass spectra for complexes

The LC-Mass spectra of complexes [L, LMn and LFe] Figure (3), Figure (4) and Figure (5) showed the parent ion peaks at (M/Z=231.4), (M/Z = 515.2) and (M/Z=516.4) corresponding to (M= $C_{11}H_9N_3O_3$), (M= $C_{22}H_{16}N_6O_6Mn$) and (M= $C_{22}H_{16}N_6O_6Fe$) respectively. The fragmentation pattern is shown in Table (2).

Table (2): The fragmentation pattern data for ligand and its metal complexes

Compounds	Peaks
L = $C_{11}H_9N_3O_3$ = 231.21	231.4, 159
LMn= [Mn $(L)_2$] $C_{22}H_{16}N_6O_6Mn$= 515.34	515.2, 282.2, 164.2
LFe = [Fe $(L)_2$] $C_{22}H_{16}N_6O_6Fe$= 516.24	516.4, 283.2, 282.2, 164.2

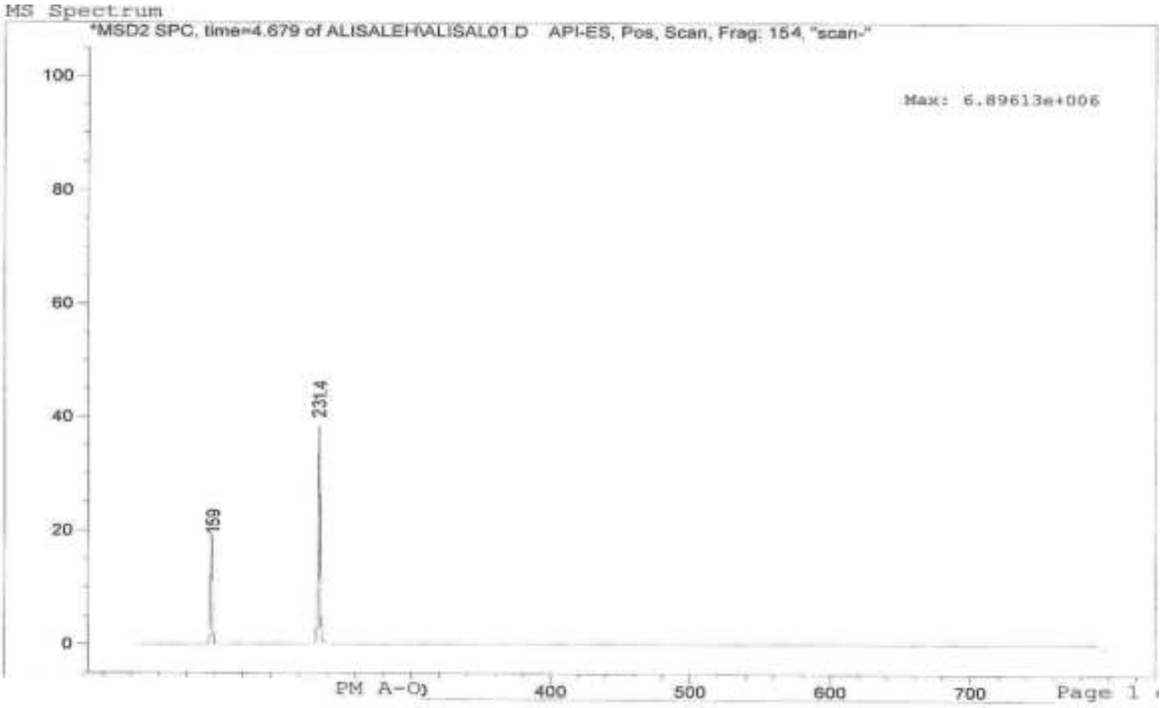


Figure (3): LC-mass spectrum of (6-[Hydroxy - benzylidene)-amino]-pyrimidine-2,4-diol)

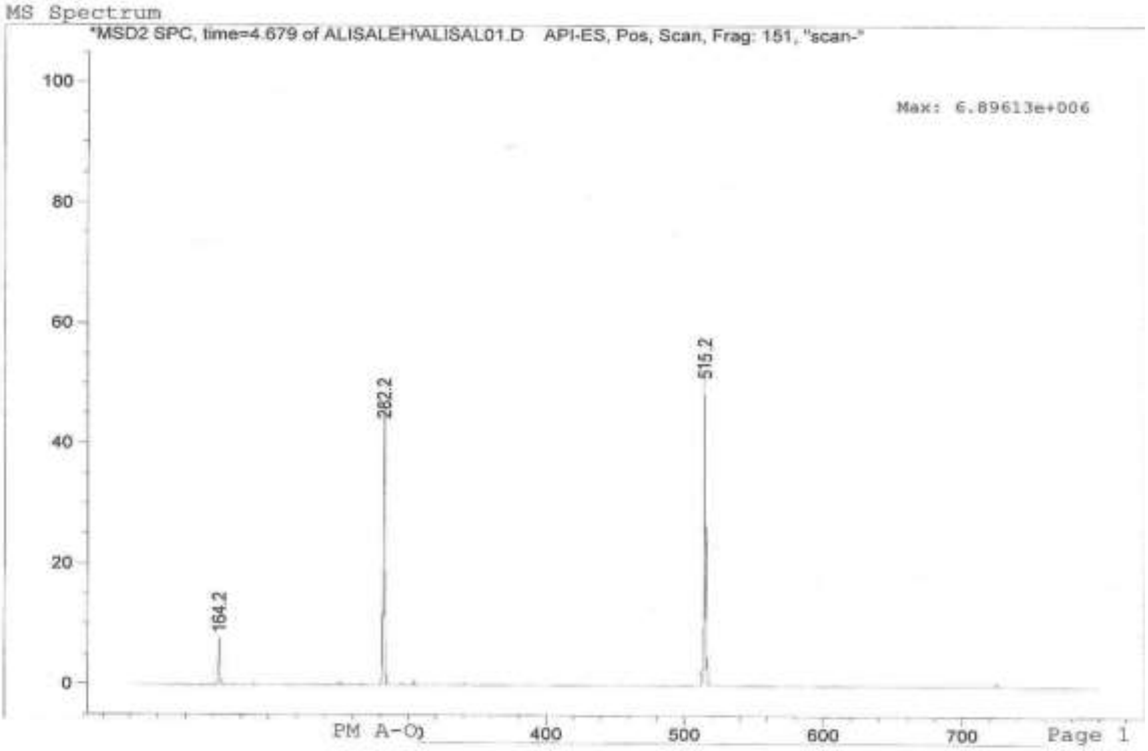


Figure (4): LC-mass spectrum of [Mn $(L)_2$]

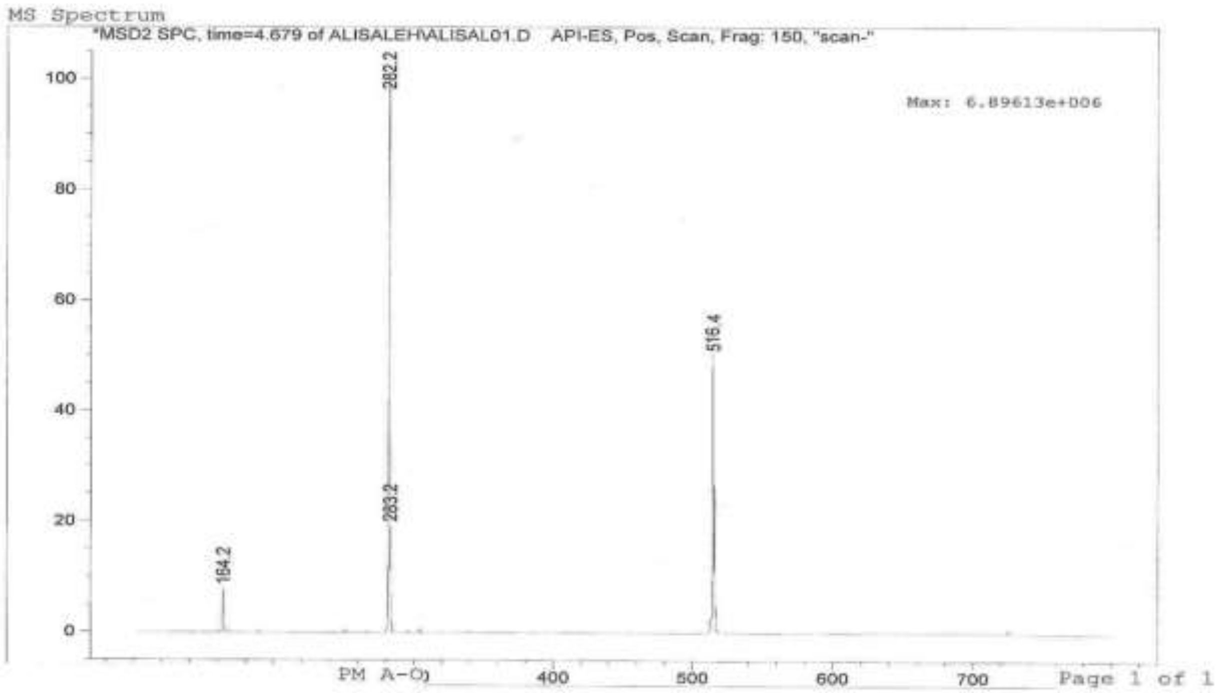


Figure (5): LC-mass spectrum of [Fe (L)2]

IR Spectra

The IR spectrum of the ligand (6-[Hydroxy- benzylidene)-amino]-pyrimidine-2,4-diol) (L) and its complexes show characteristic bands at 3066 and 3047 cm-1 due to the ν(CH) aromatic, 2988, 2994 cm-1 ν(CH) aldehyde, 3500 cm-1ν(O-H) phenol,1655, 1608 cm-1 υ(C=C) and 1713 cm-1 υ(C=N) azomethine, functional groups, respectively, for the ligand[10].

The IR spectra of the complexes exhibited ligand bands with the appropriate shifts dueto complexes formation [10,11]. This indicates that the ligand was coordinated with the metal ions through the (N) azomethine group, and (O) phenol group. At lower frequency the complexes exhibited new bands around (532-470), and (448-420) cm^{-1} assigned to the υ(M-N) and υ(M-O), respectively [12,13].

Table (2): FT-IR spectral data (wave number υ^{-}) cm^{-1} for the ligand and its complexes

Compounds	υ (O-H) phenol	υ (C-H) aromatic	υ (C-H) aldehyde	C=C	C=N	M-N	M-O
L	3500	3066 3047	2988, 2994	1655 1608	1713	-	-
LMn	3516	3047	2824	1605	1643	470 497	424
LFe	3624	3045	2889	1621 1604	1667	479 520	448 420
LCo	3634	3040 3043	2824	1655, 1601	1676	470 532	428
LNi	3516	3048	2854	1643 1605	1647	498 563	424 470

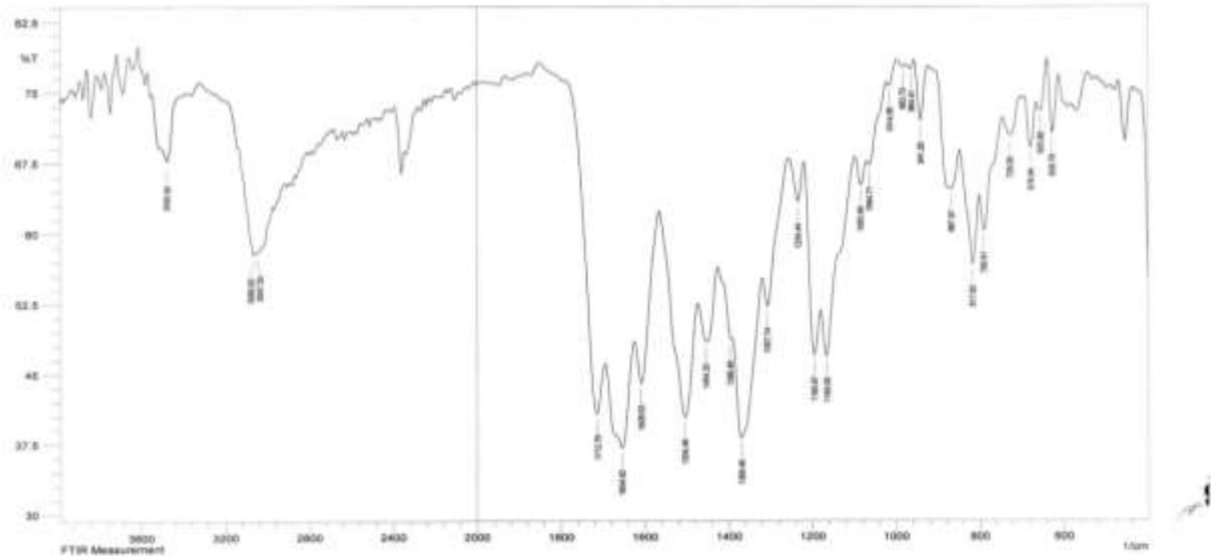


Figure (6): FT-IR spectrum of (6-[Hydroxy - benzylidene)-amino]-pyrimidine-2,4-diol)

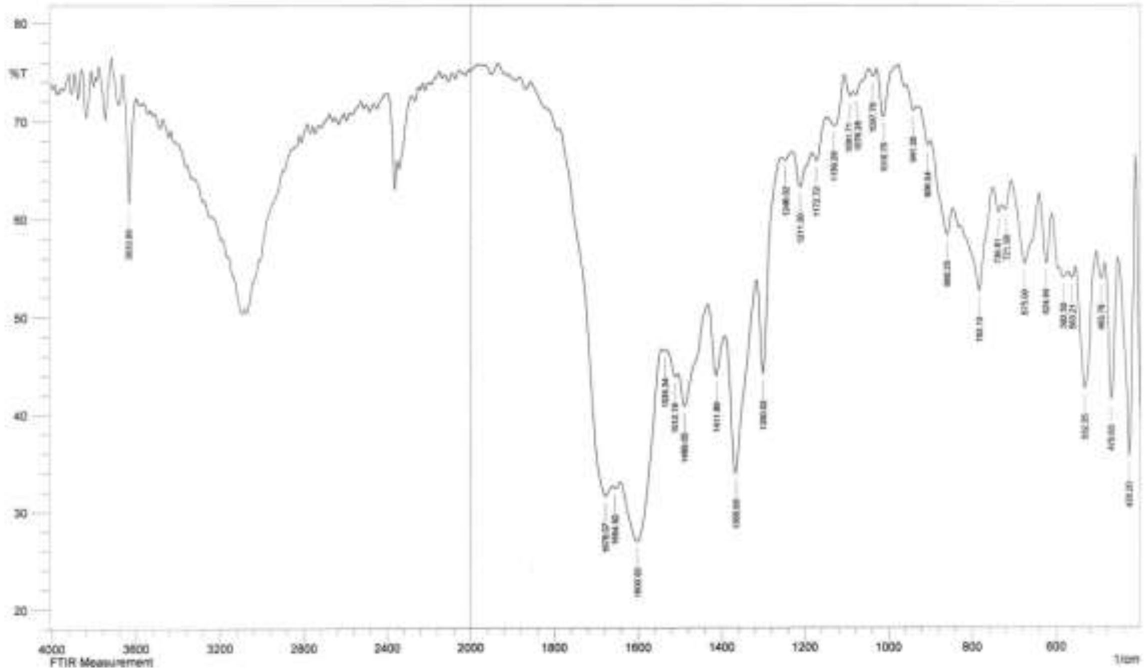


Figure (7): FT-IR spectrum of [Co (L)$_2$]

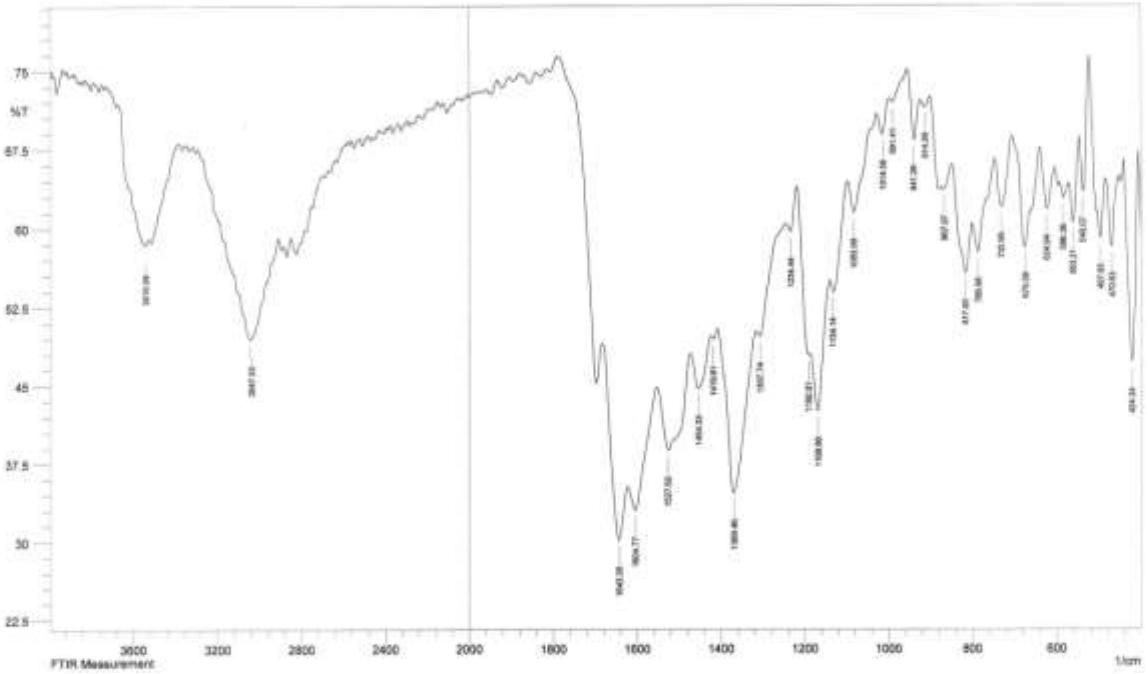


Figure (8): FT-IR spectrum of [Ni (L)$_2$]

Electronic Spectral

The electronic spectrum of the ligand exhibits intense absorption at 465,336 and 268 nm attributed to n→ π* and π→π* respectively, Figure (9). The electronic spectrum of Co$^{(II)}$ complex showed three broad peaks at 663,341and 271 nm assigned to $^4A_2$→$^4T_1$(p), n→π*and π →π* respectively, suggesting a tetrahedral geometry Figure (10). The electronic spectrum of Ni$^{(II)}$ complex showed five broad peaks at 615, 490 attributed to $^4A_2$→$^4T_1$(p) and 407, 322 nm and 268 nm assigned to n→π* and π →π* respectively, suggesting a tetrahedral geometry [14,15]. Mn$^{(II)}$ Complex showed strong bands at 271nm and 341nm, whic attributed to (π→π*) and (n →π*), respectively, while the peak at 485nm attributed to charge transfer (C.T) The shoulder at 666 nm due to $^6A_1$→$^4E_{(D)}$, finally the band at 508 nm belong to $^6A_1$→$^4T_{2(D)}$, these values are accepted for tetrahedral complex. The dark-green complex of Fe$^{(II)}$ showed band at 275 and 351nm related to π→π* and charge transfer, respectively. The peak at 663 nm caused by the electronic transition $^5E_{(D)}$→$^5T_{2(D)}$suggesting an tetrahedral geometry [14, 16].

Magnetic Moments

In this case the magnetic moment for Mn$^{(II)}$, Fe$^{(II)}$, Co$^{(II)}$ and Ni $^{(II)}$ complexes are 4.656, 4.7, 3.88 and 2.93 B.M respectively which confirmed the tetrahedral geometry for complexes [16]. All the absorption bands were fully assigned in Table (3).

Table (3): Electronic data magnetic moment and molar conductivity for ligand and its complexes

compounds	λ_{max} nm	ύ cm^{-1}	Assignment	μ_{eff} M.B.
L	465 336 268	21505.37 29761.90 37313.43	$n\rightarrow\pi^*$ $n\rightarrow\pi^*$ $\pi\rightarrow\pi^*$	-
LMn	666 508 485 341 271	15015.01 19685.04 20618.55 29325.51 36900.36	$^6A_1\rightarrow{}^4E_{(D)}$ $^6A_1\rightarrow{}^4T_{2\,(D)}$ C.T $n\rightarrow\pi^*$ $\pi\rightarrow\pi^*$	4.656
LFe	663 351 275	15082.95 28490.03 36363.6	$^5E_{(D)}\rightarrow{}^5T_{2(D)}$ C.T $\pi\rightarrow\pi^*$	4.7
LCo	663 341 271	15082.95 29325.51 36900.36	$^4A_2\rightarrow{}^4T_1(p)$ $n\rightarrow\pi^*$ $\pi\rightarrow\pi^*$	3.88
LNi	615 490 407 322 268	16260.16 20408.16 24570.02 3105590 37313.43	$^3T_1\rightarrow{}^3T_1(p)$ $n\rightarrow\pi^*$ $n\rightarrow\pi^*$ $\pi\rightarrow\pi^*$	2.93

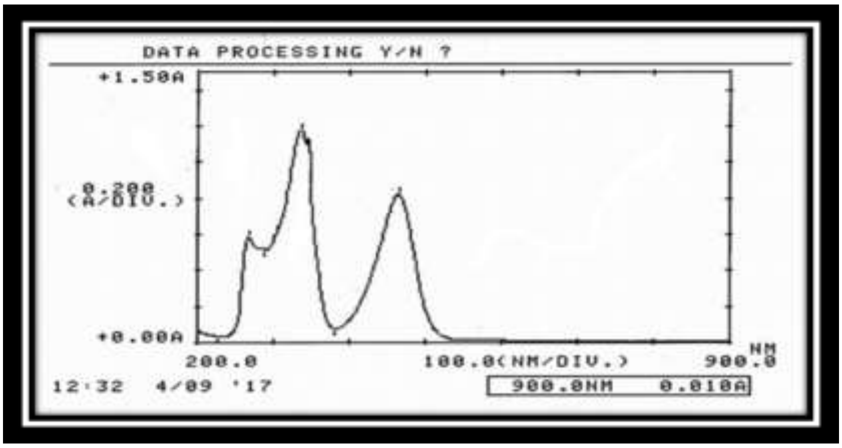


Figure (9): UV-Vis Spectrum of Ligand L

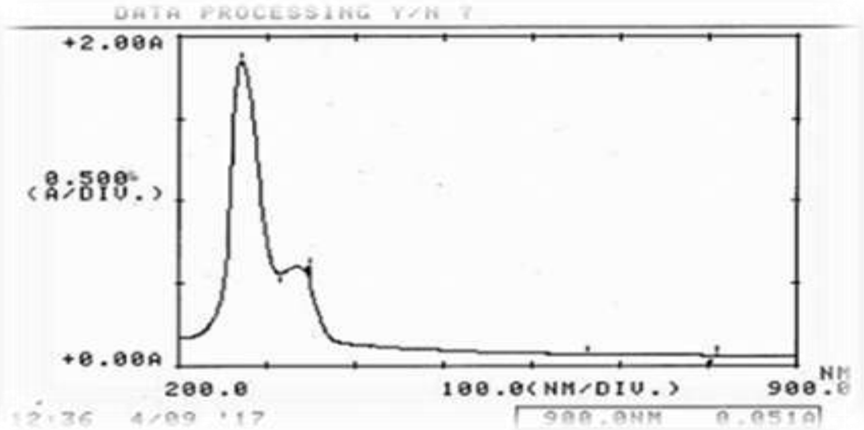


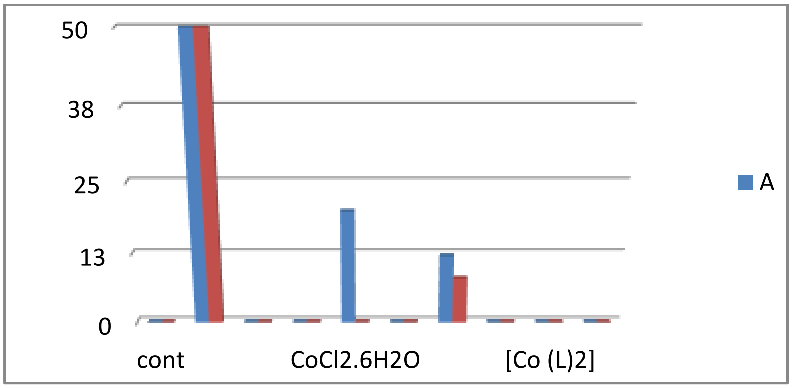
Figure (10): (UV-Vis) Spectrum of complex CoL

Antimicrobial activity of ligand, metal salts and all complexes

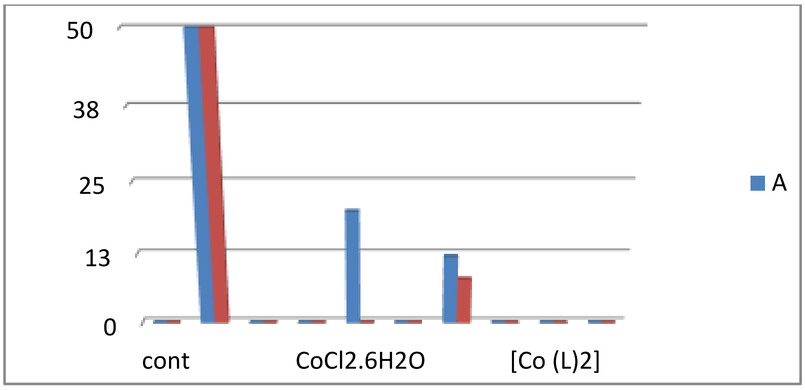
Schiff base, metal salts and their complexes of transition metals were screened for antibacterial and antifungal activity. The entire tested compound exhibited variable antibacterial and antifungal activity as shown in Figures (11) and (12).
Ligand exhibited activity antibacterial against S. aureus and P.aeruginosa,It's known that the activity is higher in complexes and metal salts than that in ligand. While the ligand and some salts metals exhibiting antifungal strong activity against P.expansum and C. albicans, by not exhibited antifungal activity against F.graminearum and M. phaseolina as compared with the antimicrobial activity with some metal complexes which exhibited antifungal activity top than ligand, exhibited some complexes. Prepared antifungal activity strong against F.graminearum and M.phaseolina as compared with the ligand which did not exhibite antimicrobial activity, from the data shown in Table (4) and Figures (13-18) a lot of compounds exhibited bio activity against 2 kinds of bacteria and 4 kinds of fungal.

Table (4): Antibacterial and antifungal activities for ligand, metal salts and its metal complexes

Comp.	***Staphylococcus aureus*** **gram(+)**		***Pseudomonas aeruginosa*** **gram (-)**		***Penicillium expansum***		***Fusarium expansum***		***Macropho- -mina phaseolino***		***Candida albicans***	
	A	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**
L	**35**	**32**	**35**	**32**	**46**	**36**	**-**	**-**	**-**	**-**	*******	*******
$MnCl_2.4H_2O$	**40**	**18**	**20**	**14**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
$FeCl_2. H_2O$	**30**	**12**	**15**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
$CoCl_2.6H_2O$	**40**	**25**	**23**	**18**	**30**	**18**	**26**	**15**	**-**	**-**	**20**	**10-**
$NiCl_2.6H_2O$	**15**	**12**	**16**	**15**	**38**	**28**	**38**	**33**	**-**	**-**	**-**	**-**
$[Mn (L)_2]$	**24**	**-**	**20**	**15**	**12**	**-**	**12**	**-**	**24**	**20**	**12**	**8**
$[Fe (L)_2]$	**24**	**-**	**14**	**10**	**-**	**-**	**-**	**-**	**20**	**15**	**-**	**-**
$[Co (L)_2]$	**20**	**12**	**14**	**12**	**-**	**-**	**-**	**-**	**25**	**14**	**-**	**-**
$[Ni (L)_2]$	**18**	**-**	**20**	**18**	**23**	**20**	**-**	**-**	**25**	**15**	**-**	**-**
Con	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
*****= highly active; A= Conc. ; B= dilu.**												

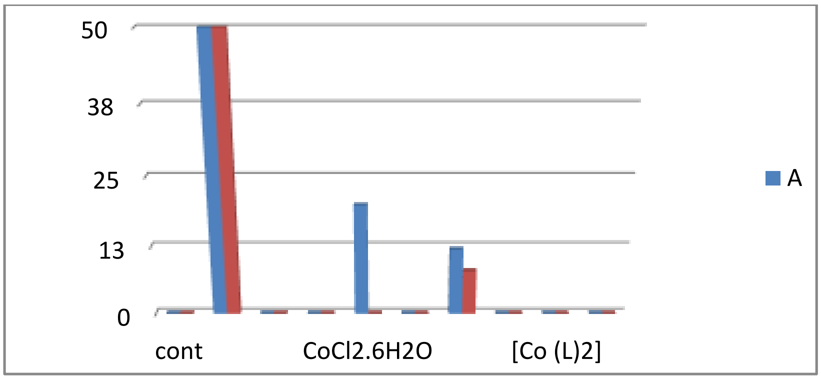


Staphylococcus aureus **gram(+), with A= Conc. ; B= dilu**

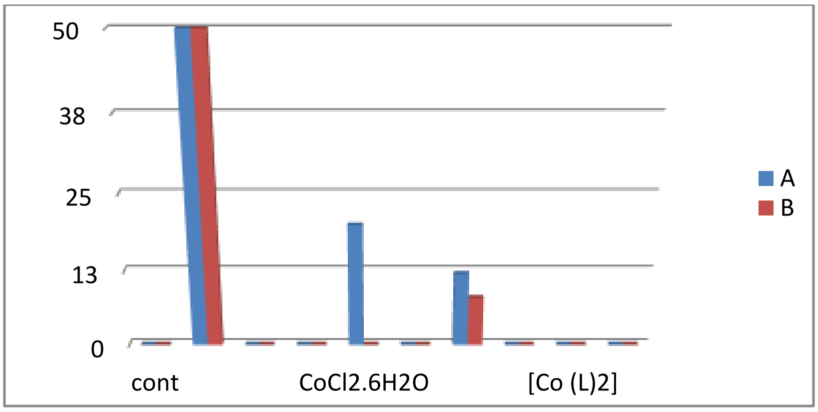


Pseudomonas aeruginosa **gram (-), with A= Conc. ; B= dilu**

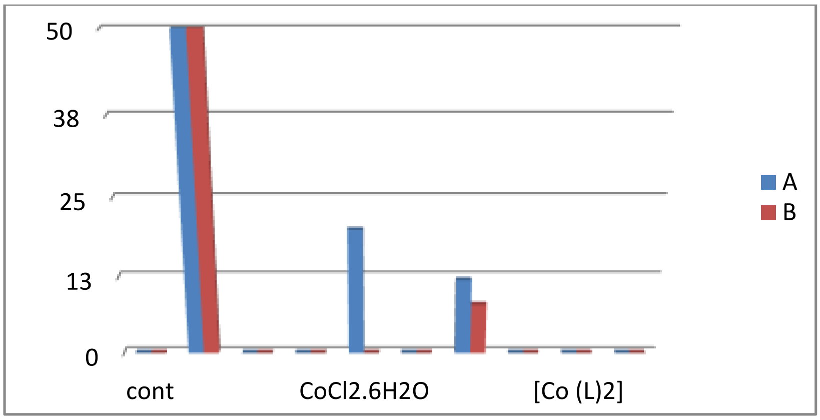
Figure (11): The antibacterial activity of compounds against *S. aureus* and *P. aeruginosa*



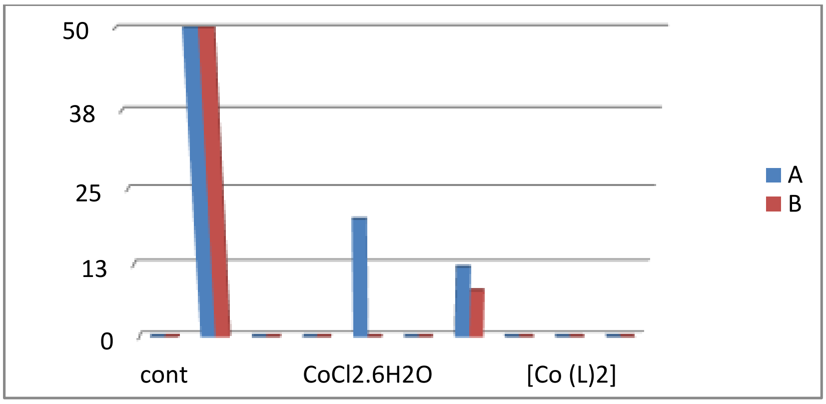
***Penicillium expansum*, with A= Conc. ; B= dilu**



***Fusarium expansum*, with A= Conc. ; B= dilu**



***Macropho--mina phaseolino*, with A= Conc. ; B= dilu**



Candida albicans, with A= Conc. ; B= dilu

Figure (12): The antibacterial activity of compounds against *P.expansum*, *F.graminearum*, *Macropho--mina phaseolino* and *Candida albicans*

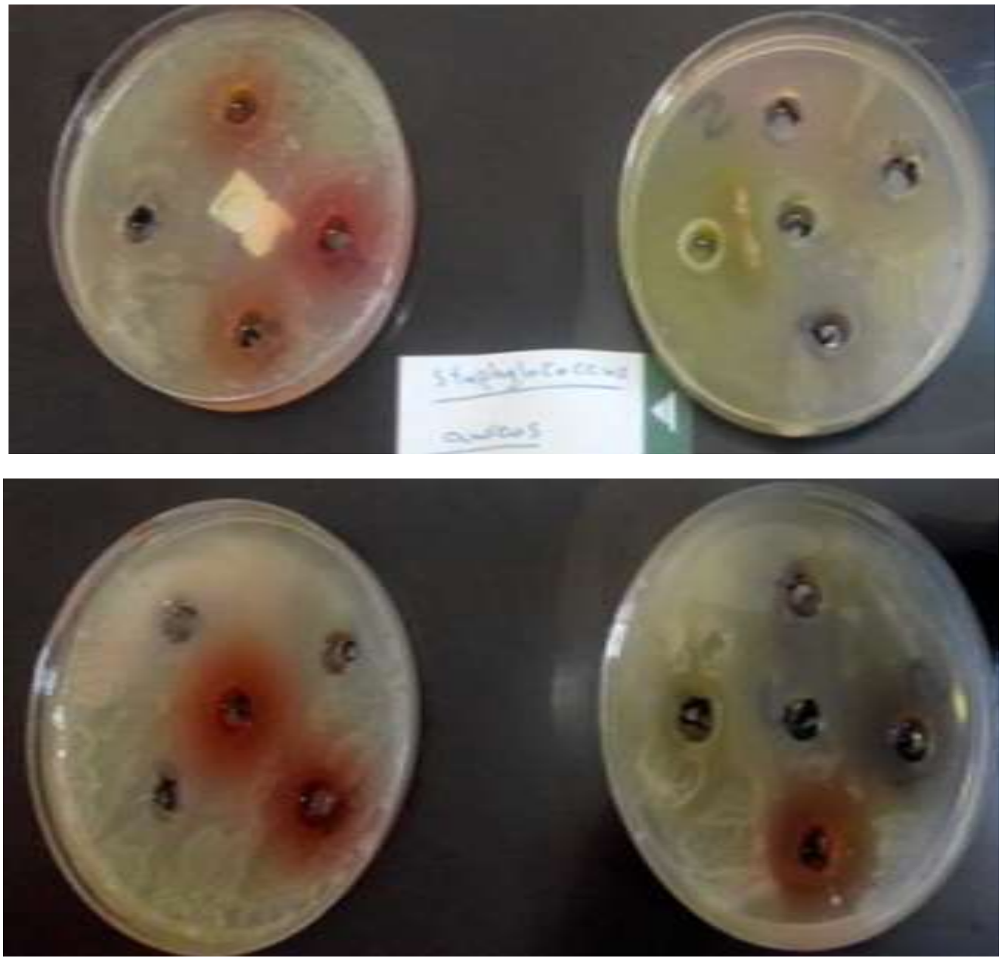


Figure (13): *Staphylococcus aureus* gram (+) for compounds

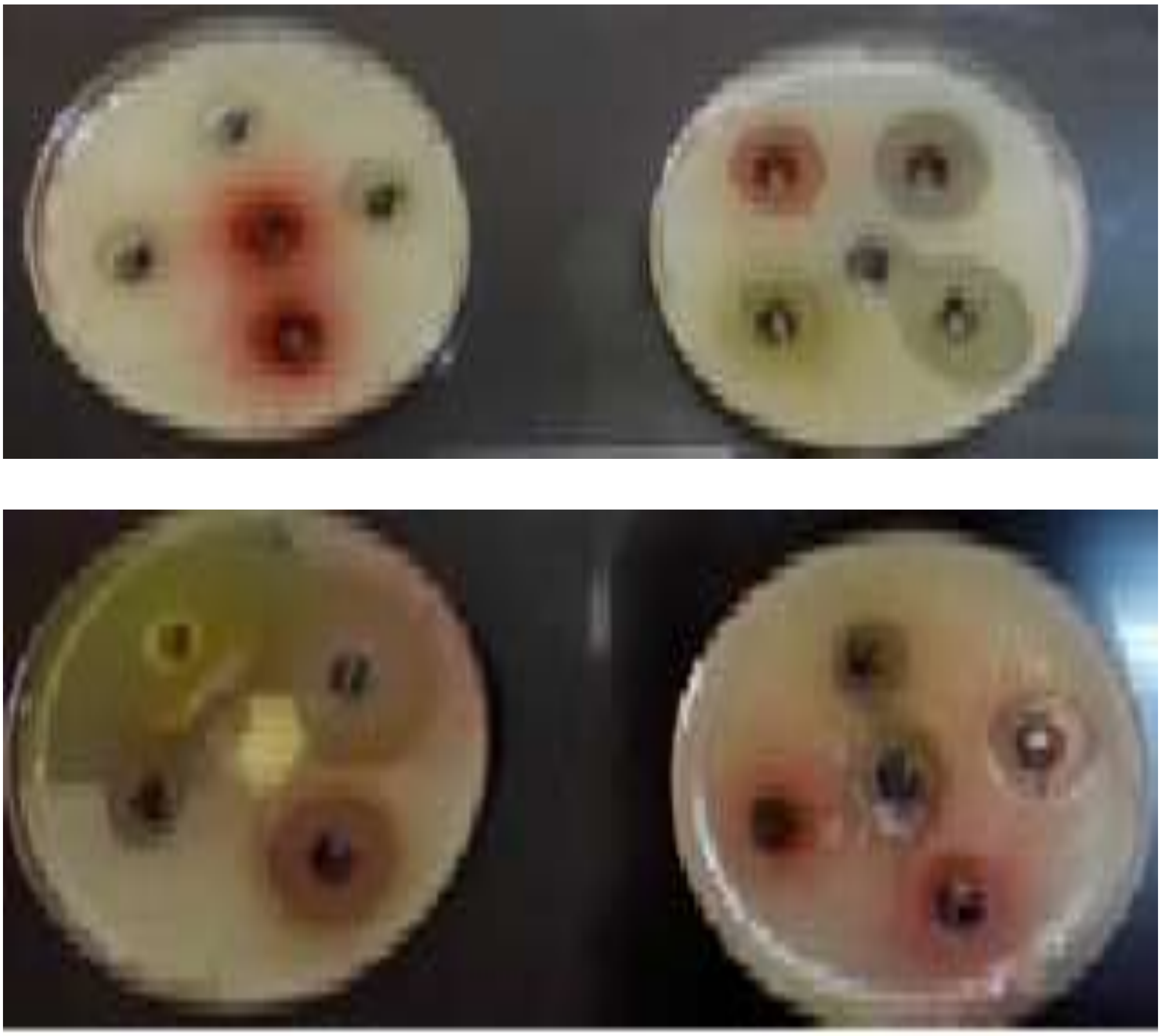


Figure (14): *Pseudomonas aeruginosa* gram (-) for compounds

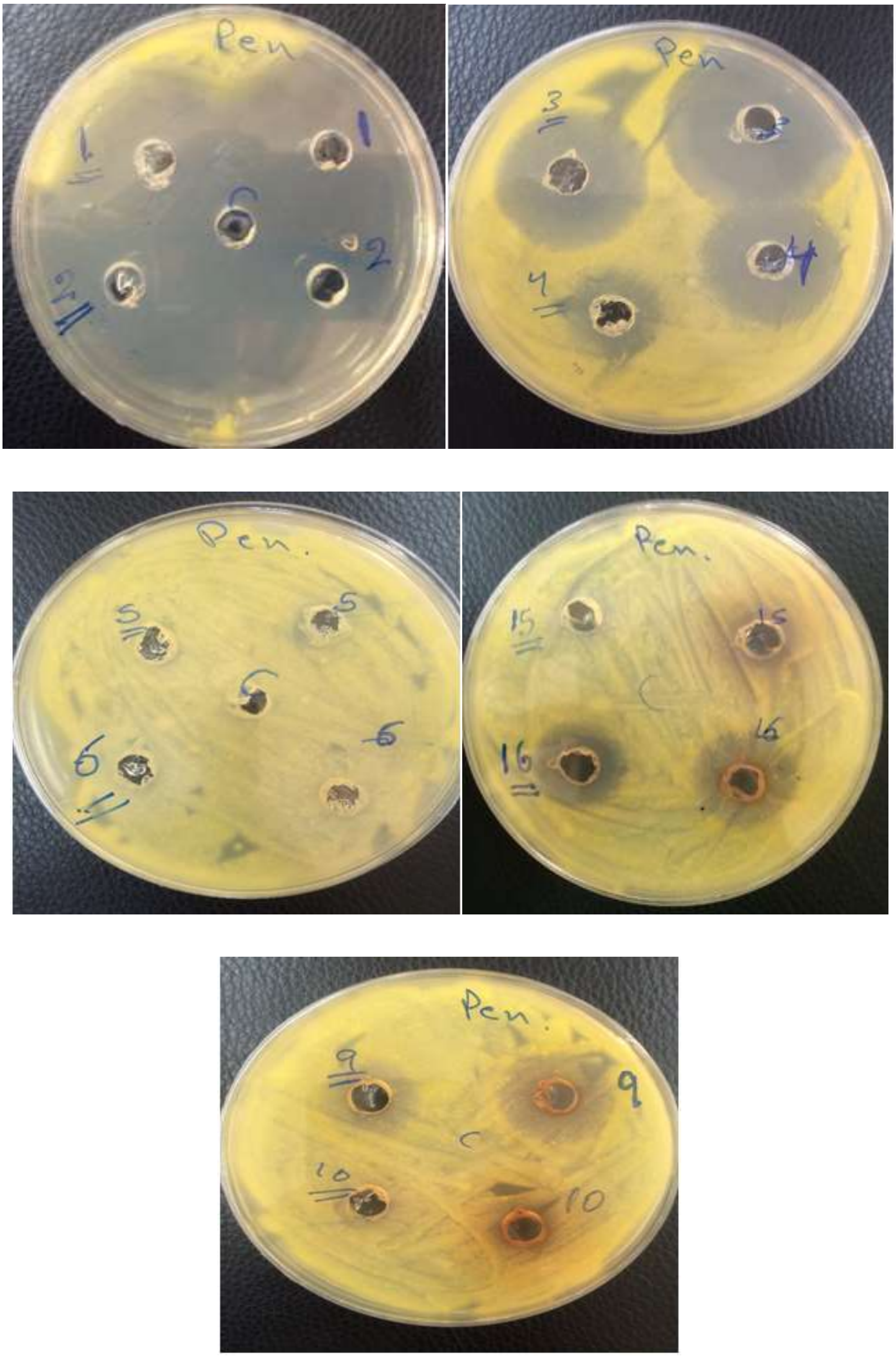


Figure (15): ***Penicillium expansum*** **for compounds**

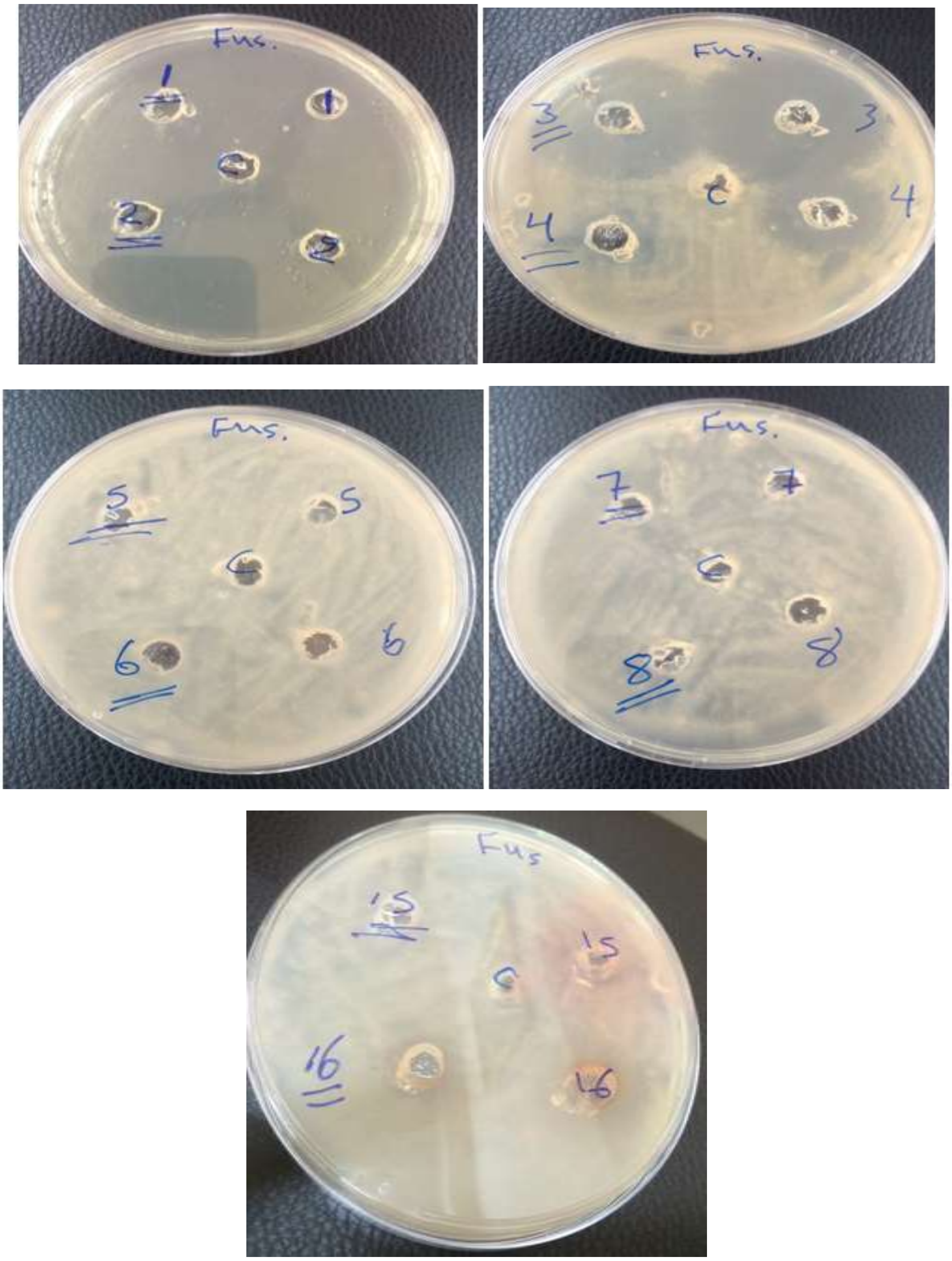


Figure (16): ***Fusarium expansum*** **for compounds**

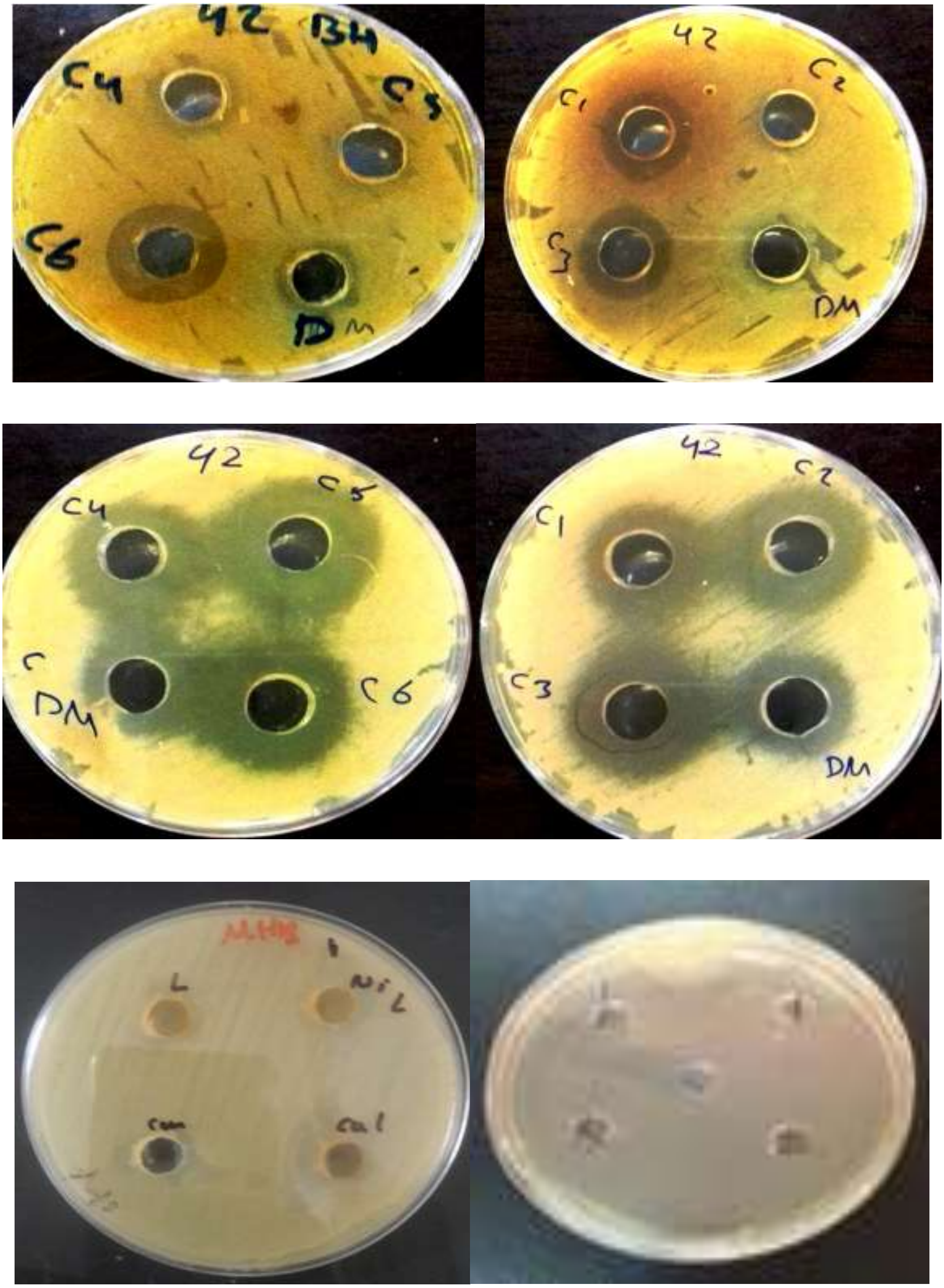


Figure (17): ***Macrophomina phaseolino*** **for compounds**

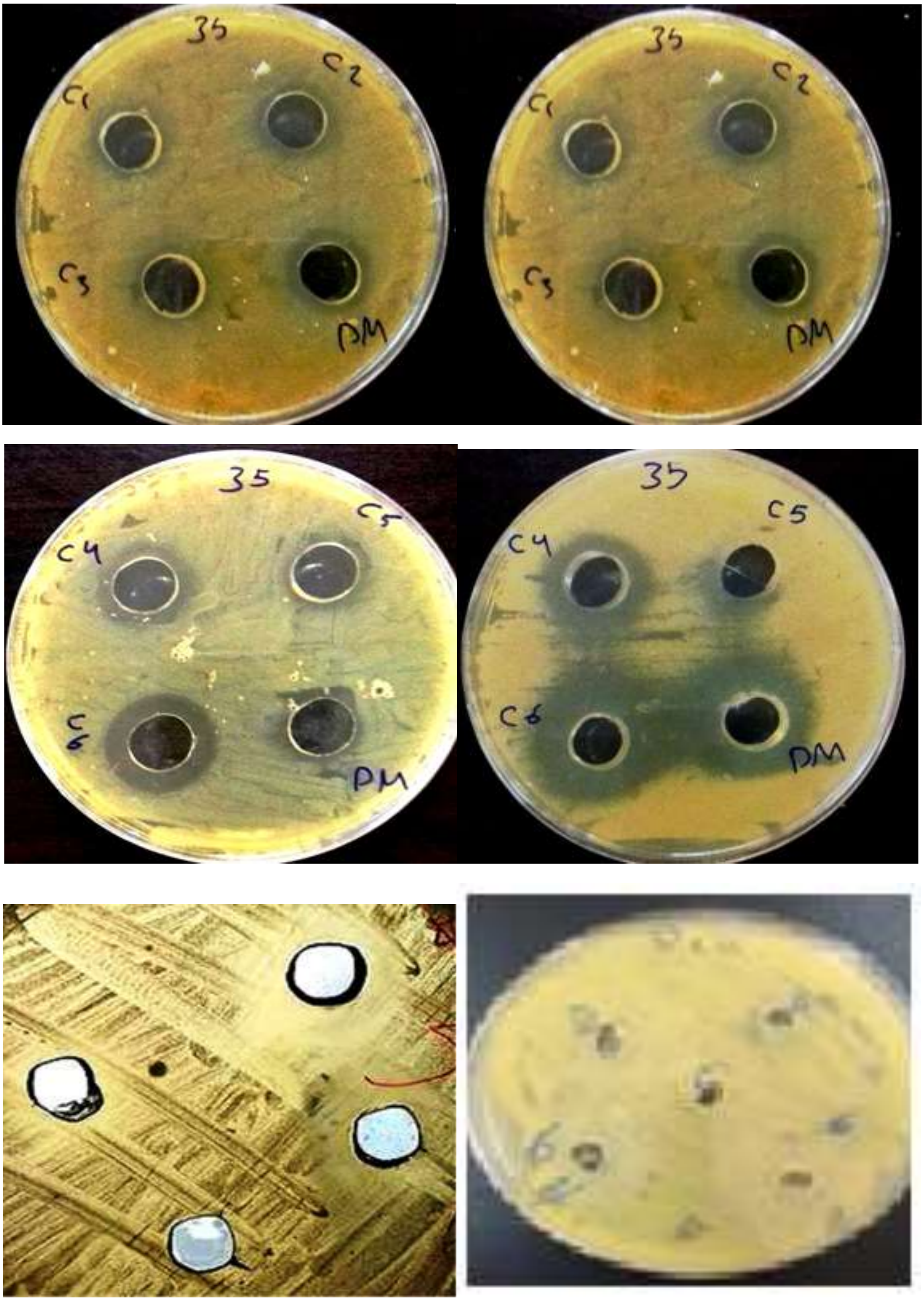


Figure (18): ***Candida albicans*** **for compounds**

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