

***In vitro* Antimicrobial Activity Evaluation of Newly Synthesized Furochromone Schiff Base Complexes**

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A SERIES of VO^{II}, Ni^{II}, Cu^{II}, Co^{II}, Mn^{II}, Cd^{II} and Zn^{II} complexes of new Schiff base ligand resulting from 4-aminoantipyrine and Furobenzopyrone were prepared. The structure of newly synthesized compounds (**1-8**) was proven by studying their elemental analyses, spectral data (IR, NMR, UV-vis), molar conductivity and magnetic susceptibility. In addition the *in vitro* antimicrobial activity of all compounds was examined. The results cleared that nickel and zinc complexes exhibited promising activity compared with standard drug (chloramphenicol).

Keywords: Schiff base, Metal complexes, Antimicrobial, Furochromone.

Introduction

Furochromones (Khellin and visnagin) are one of the important heterocyclic compounds that need to be studied due to their remarkable biological activity as a potent antimicrobial agent and its derivatives showed remarkable antimicrobial activity against bacteria and Candida species,[1-3] phototherapeutic[4] potential, antispasmodic action,[5] anti-inflammatory[3] analgesic and anticonvulsant effect,[6, 7] *in vitro* cytotoxicity[8] and as antiviral.[9-11] In addition to its folk use, recently, pharmaceutical companies realized the pharmacological effect of furochromones as coronary vasodilator drug and to treat a variety of diseases as bronchial asthma, angina pectoris, and also some furochromen derivatives are component for the treatment of chronic skin or eye diseases, furochromone drugs in market are used in ophthalmic and in treatment of dermatological diseases.[12] Recently, it has been known that khellin analogs with lower toxicity and better efficacy have ability to curative vitiligo and psoriasis,[13-17] so most current researches are

focusing on their use in the treatment of vitiligo. Also, visnagin has own biological activity of reducing blood pressure by inhibiting calcium influx into the cell as a vasodilator, and neuro protective effect which are associated with its anti-inflammatory effects.[18, 19] Eventually it's announced that radio iodinated khellin is used in imaging urinary tract.[20]

In view of the above mentioned facts, and as resumption to our work on the preparation of bioactive metal complexes,[21-26] the present work is devoted to synthesize, characterize and evaluate antimicrobial activity of some furochromone Schiff base complexes.

Experimental

Chemistry

Materials

All the reagents employed for the preparation of the ligand and its complexes were synthetic grade and used without further purification. All other chemicals and reagents used in this biological study were of analytical grade and

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purchased from Sigma-Aldrich Chemical Co. (St. Louis, MO, USA). 9-dimethoxy-5-oxo-5H-furo[3,2-g]chromene-6-carbaldehyde was prepared by a published Vilsmier-Haack reaction. [27-30]

Physical Measurements

The ligand and its metal complexes were analyzed for C, H, N and S on VARIO EL III GERMANY at the Microanalytical center, Faculty of Science Cairo University. IR spectra of the ligand and its metal complexes was measured using KBr discs with a Jasco FT/IR 300E Fourier transform infrared spectrophotometer covering the range 400-4000 cm^{-1} . Electronic spectra in the 200-1100 nm regions were recorded on a on a SHMADZU 2600 spectrophotometer using 1 cm quartz cells taking DMF as solvent. The thermal analysis (TG) was carried out on an Shimadzu DT-30 thermal analyzer from room temperature to 800 °C at a heating rate of 10 °C/min. Magnetic susceptibilities were measured by the Gouy method at 25°C on a Johnson Matthey Magnetic Susceptibility Balance using mercuric tetrathiocyanatocobaltate(II) as the magnetic susceptibility standard. Diamagnetic corrections were estimated from Pascal's constant.[31] The magnetic moments were calculated from the equation: $\mu_{\text{eff}} = 2.8 \sqrt{\chi_M^{\text{corr}} \cdot T}$. Molar conductance was measured on a Tacussel type CD₆NG conductivity bridge using 10⁻³M DMF solutions. NMR spectrum was obtained on a JEOL EX-270 MHz spectrometers.

Synthesis of compounds

Synthesis of ligand: The ligand, 4-((4,9-dimethoxy-5-oxo-5H-furo[3,2-g]chromen-6-yl)-methyleneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (L) was prepared by refluxing an equimolar amounts of 4-amino-1,5-dimethyl-2-phenyl-1-H-pyrazol-3(2H)-one (203 mg, 1.0 mmol) in 20 mL hot methanol (60 °C) with (274 mg, 1.0 mmol) of 4,9-dimethoxy-5-oxo-5H-furo[3,2-g]chromene-6-carbaldehyde in 50 mL hot methanol (60 °C) in presence of 3 drops of glacial acetic acid. The mixture was refluxed while stirring for 3 h. then the solvent was evaporated to 30 mL. The solid product was filtered off, washed with cold methanol, crystallization from ethanol and dried in oven (60 °C) for 4 h. Yield (312 mg, 68%), color is dark yellow, m.p. 163, Elemental analysis for C₂₅H₂₁N₃O₆ (459.46): Found (calcd) %C 65.35 (64.80), %H 4.61 (5.00), %N 9.15 (8.70). IR (KBr, cm^{-1}), 1680, 1652 $\nu(\text{C}=\text{O})$, 1625 $\nu(\text{C}=\text{N})$. ¹H-NMR (270 MHz, DMSO-*d*₆): 8.79 (s,

1H, ¹C-H), 7.85 (s, 1H, ²²C-H), 7.50 (d, 1H, ¹⁵C-H), 7.07 (d, 1H, ¹⁴C-H), 7.47 (m, 2H, ^{31,33}C-H), 7.37 (d, 2H, ^{30,34}C-H), 7.30 (t, 1H, ³⁵C-H), 4.10 (s, 3H, O²⁸CH₃), 2.42 (s, 3H, N-¹⁰CH₃), 3.14 (s, 3H, C-⁷CH₃). UV. vis. 1 cm quartz cells, DMSO) 260, 290, 335, 385.

Synthesis of metal complexes: The metal complexes (**2-8**), were prepared by adding drop wisely a hot ethanolic solution (50 mL, 60 °C) of 1 mmol of the following metal salts VOSO₄·3H₂O (217 mg), Mn(CH₃COO)₂·4H₂O, Co(CH₃COO)₂·4H₂O (249 mg), Ni(CH₃COO)₂·4H₂O (249 mg), Cu(CH₃COO)₂·H₂O (199 mg), (245 mg), Zn(CH₃COO)₂·2H₂O (219 mg), and Cd(CH₃COO)₂·2H₂O (267 mg) to a hot ethanolic solution (50 mL, 60 °C) of the ligand (459 mg 1 mmol). The reaction mixtures were refluxed for 4h accompanied by stirring. The precipitates which formed were filtered off, washed with ethanol then by diethyl ether and dried in vacuum desiccators over P₄O₁₀.

Complex (2): Yield (346 mg, 54%), m.p. >300 °C; color: green; molar conductivity (Λ_m): 29.30 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$, μ_{eff} (Magnetic susceptibility value): 1.66 BM. Elemental analysis for [VO(L)(SO₄(H₂O))], C₂₅H₂₃N₃O₁₂SV, (640.47): Found (calcd.) %C 45.90(46.88), %H 3.50(3.62), %N 6.70(6.56), %S 4.23(5.01). IR (KBr, cm^{-1}), 3426, $\nu(\text{H}_2\text{O})$, 1667, 1629 $\nu(\text{C}=\text{O})$, 1570 $\nu(\text{C}=\text{N})$, 549 $\nu(\text{V} \leftarrow \text{O})$, 476 $\nu(\text{V} \leftarrow \text{N})$, 954 $\nu(\text{V}=\text{O})$, 1141, 1063, 710 $\nu(\text{SO}_4^{2-})$. UV. vis. (1 cm quartz cells, DMF) 260, 295, 340, 395, 425, 510, 590, 870 nm.

Complex (3): Yield (453 mg, 64.3%), m.p. >300 °C; color: brown; molar conductivity (Λ_m): 8.99 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$, $\mu_{\text{eff}} = 6.05$ BM. Elemental analysis for [Mn(L)(CH₃COO)₂(H₂O)]·3H₂O, C₂₉H₃₅N₃O₁₄Mn, (704.54): Found (calcd) %C 49.56(49.44), %H 4.04(4.32), %N 6.31(5.96). IR (KBr, cm^{-1}), 3412, $\nu(\text{H}_2\text{O})$, 1665, 1617 $\nu(\text{C}=\text{O})$, 1594 $\nu(\text{C}=\text{N})$, 589 $\nu(\text{Mn} \leftarrow \text{O})$, 511 $\nu(\text{Mn} \leftarrow \text{N})$, $\nu_{\text{s}} \text{CH}_3\text{COO}$, $\nu_{\text{as}} \text{CH}_3\text{COO}$ 1571, 1370 ($\Delta = 201 \text{ cm}^{-1}$), UV. vis. (1 cm quartz cells, DMF) 255, 290, 350, 395, 415, 465, 510, 605 nm.

Complex (4): Yield (400 mg, 54.9%), m.p. >300 °C; color: Reddish brown, molar conductivity (Λ_m): 13.98 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ $\mu_{\text{eff}} = 4.33$ BM. Elemental analysis for [Co(L)(CH₃COO)₂(H₂O)]·4H₂O, C₂₉H₃₇N₃O₁₅Co, (726.55): Found (calcd) %C 47.39(47.94), %H 4.50(5.13), %N 6.51(5.78). IR (KBr, cm^{-1}), 3423, $\nu(\text{H}_2\text{O})$, 1660, 1627 $\nu(\text{C}=\text{O})$, 1612 $\nu(\text{C}=\text{N})$, 587 $\nu(\text{CoO})$, 465 $\nu(\text{CoN})$, $\nu_{\text{s}} \text{CH}_3\text{COO}$, $\nu_{\text{as}} \text{CH}_3\text{COO}$ 1579, 1349 ($\Delta = 230 \text{ cm}^{-1}$).

¹), UV. vis. (1 cm quartz cells, DMF) 260, 295, 365, 420, 510, 615, 925 nm.

Complex (5): Yield (395 mg, 55.8%), m.p. >300°C; color: green; molar conductivity (κ_m): 9.78 ohm⁻¹cm²mol⁻¹, $\mu_{\text{eff}} = 3.05$ BM. Elemental analysis for [Ni(L)(CH₃COO)₂(H₂O)].3H₂O, C₂₉H₃₅N₃O₁₄Ni, (708.29): Found (calcd.) %C 49.56(49.18), %H 4.56(4.98), %N 6.70(5.93). IR (KBr, cm⁻¹), 3416, ν (H₂O), 1658, 1627 ν (C=O), 1580 ν (C=N), 584 ν (NiO), 483 ν (NiN), ν_s CH₃COO, ν_{as} CH₃COO 1563, 1344 ($\Delta = 219$ cm⁻¹), UV-vis. (1 cm quartz cells, DMF) 265, 280, 350, 415, 455, 495, 635, 905 nm.

Complex (6): Yield (412 mg, 57.8%), m.p. >300 °C; color: olive; molar conductivity (κ_m): 11.34 ohm⁻¹cm²mol⁻¹, $\mu_{\text{eff}} = 1.79$ BM. Elemental analysis for [Cu(L)(CH₃COO)₂(H₂O)].3H₂O, C₂₉H₃₅N₃O₁₄Cu, (713.15): Found (calcd) %C 48.73(48.84), %H 4.39(4.95), %N 6.53(5.89). IR (KBr, cm⁻¹), 3421, ν (H₂O), 1655, 1629 ν (C=O), 1606 ν (C=N), 583 ν (CuO), 496 ν (CuN), ν_s CH₃COO, ν_{as} CH₃COO 1579, 1353 ($\Delta = 226$ cm⁻¹), UV-vis. (1 cm quartz cells, DMF) 255, 285, 340, 405, 440, 705 nm.

Complex (7): Yield (412 mg, 57.8%), m.p. >300 °C; color: Yellow; molar conductivity (κ_m): 5.78 ohm⁻¹cm²mol⁻¹, Elemental analysis for [Zn(L)(CH₃COO)₂], C₂₉H₂₇N₃O₁₀Zn, (642.92): Found (calcd) %C 48.73 (46.88), %H 4.39 (3.62), %N 6.53 (6.56). IR (KBr, cm⁻¹), 3421, ν (H₂O), 1655, 1629 ν (C=O), 1606 ν (C=N), 583 ν (Cu←O), 496 ν (Cu←N), ν_s CH₃COO, ν_{as} CH₃COO 1579, 1353 ($D=226$ cm⁻¹), UV. vis. (1 cm quartz cells, DMF) 270, 285, 355, 410, 445 nm.

Complex (8): Yield (412 mg, 57.8%), m.p. >300 °C; color: Dark Yellow; molar conductivity (κ_m): 18.67 ohm⁻¹cm²mol⁻¹, Elemental analysis for [Cd(L)(CH₃COO)₂(H₂O)].3H₂O, C₂₉H₃₅N₃O₁₄Cd, (762.01): Found (calcd) %C 48.73 (46.88), %H 4.39 (3.62), %N 6.53 (6.56). IR (KBr, cm⁻¹), 3421, ν (H₂O), 1655, 1629 ν (C=O), 1606 ν (C=N), 583 ν (Cd←O), 496 ν (Cd←N), ν_s CH₃COO, ν_{as} CH₃COO 1579, 1353 ($D=226$ cm⁻¹), UV- vis. (1 cm quartz cells, DMF) 275, 295, 365, 435, 470 nm.

Biological activity

Antimicrobial activity

Antimicrobial activities of the synthesized compounds (**1-8**) were evaluated against a panel of microorganisms in comparison with control drug chloramphenicol and metal salt solution.

Microorganisms used were Gram positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*), Gram-negative bacteria (*Escherichia coli* and *Alcaligenes faecalis*) and fungi (*Candida albicans* and *Aspergillus niger*). All microorganisms used were obtained from the culture collection of the Department of Chemistry of Natural and Microbial Products, National Research Center, Cairo, Egypt. The microorganisms were passaged at least twice to ensure purity and viability. The compounds were mounted on a concentration of 100 µg/disc. The bacteria were maintained on nutrient agar medium while yeast and fungi were maintained on potato dextrose agar medium. DMSO showed no inhibition zone was used as a negative control. The agar media were incubated with different microorganism cultures tested. After 24 h of incubation at 30 °C for bacteria and yeast and 72 h of incubation at 28 °C for fungi, the diameter of inhibition zone in mm was measured. Chloramphenicol was used as a positive control for antimicrobial activity at concentration of 100 µg/disc.

Preparation of the discs

Compounds (**1-8**) together with the positive control (Chloramphenicol) were mounted on a paper disc prepared from blotting paper (5 mm diameter) with the help of a micropipette in a concentration of 100 µg/disc. The discs were applied on the microorganism-grown agar plates.

Preparation of agar plates

Minimal agar was used for the growth of specific microbial species. The preparation of agar plates for *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* (bacteria) utilized nutrient agar (2.30 g/ 100 ml distilled water; obtained from Panreac Quimica SA, Spain), and potato dextrose agar medium (3.9 g/100 ml distilled water; obtained from Merck) for *Candida albicans* and *Aspergillus niger* (fungi). This was allowed to soak for 15 min and then boiled on a water bath until the agar was completely dissolved. The mixture was autoclaved for 15 min at 120 °C and then poured into previously sterilized Petri dishes and stored at 30 °C for inoculation.

Inoculation procedure: Spore suspension was prepared with the help of a platinum wire loop to reach a microbial concentration equivalent 0.5 Mac-Farland.

Application of the discs: Sterilized forceps were used for the application of the paper disc on

previously inoculated agar plates. When the discs were applied, they were incubated at 37 °C for 24 h for bacteria and yeast, and at 28 °C for 48 h for fungi. The zone of inhibition around the disc was then measured in millimeters.

Results and Discussion

Chemistry

A new Schiff base ligand was prepared from condensation of 4-aminoantipyrine and Furobenzopyrone. The furochromone Schiff base forms 1:1 complexes with VO^{II} , Ni^{II} , Cu^{II} , Co^{II} , Mn^{II} , Cd^{II} and Zn^{II} salts. The elemental analysis and spectroscopic studies of the newly synthesized compounds (**1-8**) are consistent with the proposed structures (Fig.1-3). All the obtained metal complexes are colored, non-hygroscopic, air-stable and insoluble in water, but they demonstrated a good solubility character in DMF and DMSO.

Infrared spectra

IR spectral data of the prepared compounds (**1-8**) are given in experimental part. The ligand IR spectrum showed peaks at 1680, 1652 and 1625 cm^{-1} , that due to the two carbonyl groups of antipyrine moiety, Furobenzopyrone moiety and azomethine group respectively.[23, 32, 33] The comparison of the IR spectra of the ligand and its complexes showed that, the ligand works

as a neutral tridentate ligand coordinating to the metal ions through the carbonyl oxygen atoms of furobezopyrone, antipyrine moieties and azomethine nitrogen atom. This coordination can be demonstrated through the following observations i) the lower frequency shift in bands characteristic to the two carbonyl and azomethine groups of ligand.[32] ii) The existence of new bands in the 565-594 and 465-511 cm^{-1} ranges could be due to the $\nu(\text{M}\leftarrow\text{O})$, and $\nu(\text{M}\leftarrow\text{N})$ respectively. [32] iii) the appearance of two characteristic peaks in the 1555-1579 cm^{-1} and 1344-1370 cm^{-1} ranges were attributed to $\nu_{\text{as}}(\text{COO}^-)$ and $\nu_{\text{s}}(\text{COO}^-)$, respectively, indicating the involvement of the carboxylate oxygen in the chelation as monodentate ligand.[33] iv) the presence of new bands appeared at 1141, 1063, 710 cm^{-1} in the IR spectrum of complex (**2**). These bands indicate that the sulphate group is coordinated to the VO^{II} ion as chelating unidentate fashion. Also, it exhibits a peak at 954 cm^{-1} that, could be imputed to $\nu(\text{V}=\text{O})$ [34]

Nuclear magnetic resonance spectrum

The ligand $^1\text{H-NMR}$ spectrum in DMSO-d_6 is in agreement with the proposing structure (Fig. 1). The singlet at 8.79 ppm was ascribed to the azomethine proton (s, 1H, $\text{N}=\text{CH}$).[35] Whereas the chemical shifts observed as singlet at 7.85 (s, 1H, ^{22}CH) as well as the doublet at 7.50 (d, 1H,

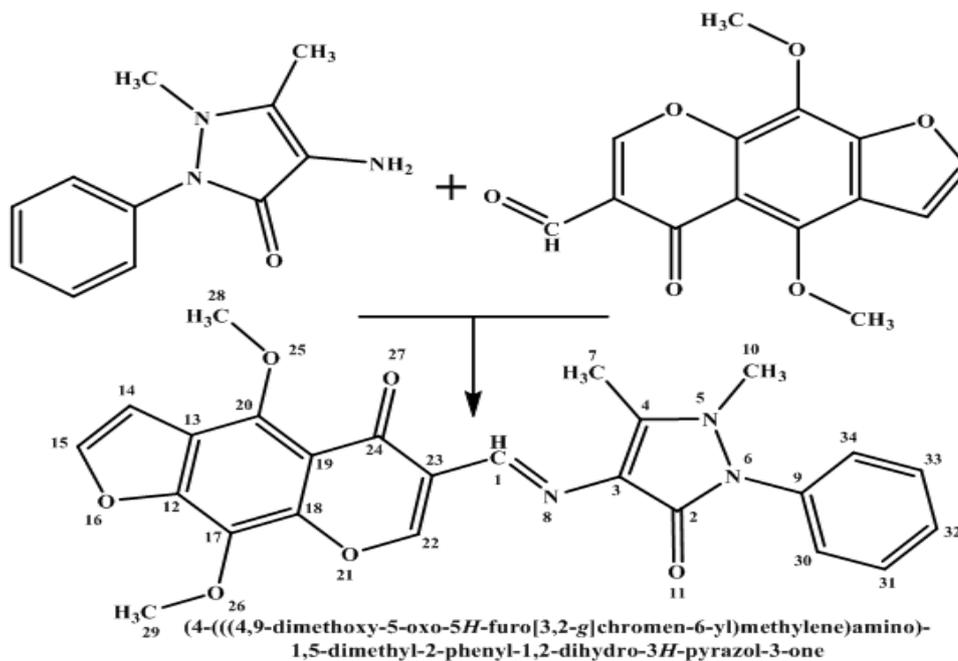


Fig.1: Synthesis of furochromone Schiff base ligand.

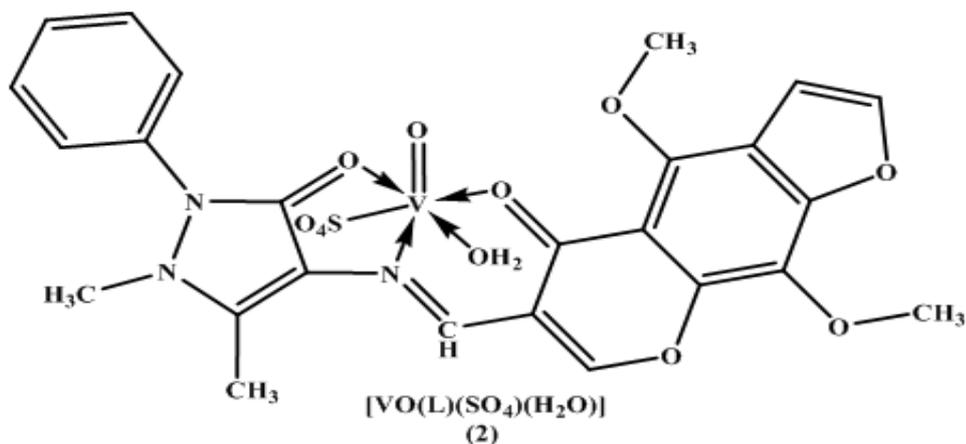


Fig. 2: Proposed structure for vanadyl complex (2).

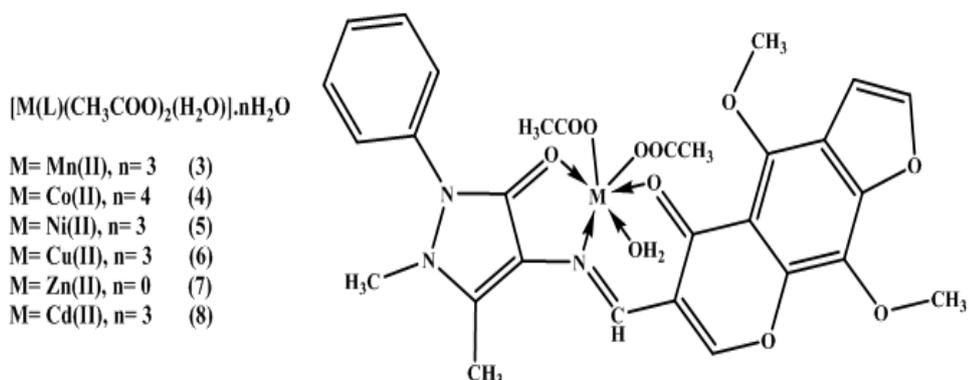


Fig. 3: Proposed structure for metal complexes (3-8).

^{15}CH) and 7.07 (d, 1H, ^{14}CH) could be ascribed to the protons of khellin moiety.[3] The protons of the methoxy groups of khellin moiety were observed as singlet at 4.10 and 3.97 ppm.[3] The aromatic protons of antipyryne moiety appeared in the 7.30-7.47 ppm.[23-26] While the singlet appeared at 2.42 ppm (s, 3H, N- $^{10}CH_3$) and 3.14 ppm (s, 3H, C- 7CH_3) attributed to the protons of antipyryne moiety methyl groups.[23-26]

Molar-conductance measurements

The molar conductivity measurements for the complexes (2-8) are carried out in DMF at concentration 10^{-3} M and given in experimental part. The molar conductivity values fall in the range 5.78-29.30 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ which is confirmed that complexes (2-8) are nonelectrolytes.[36] These values also support the participation of the acetate and sulfate groups in coordination.

Electronic absorption spectra and magnetic susceptibility measurements

The electronic spectral data of the compounds in DMSO as well as magnetic moment data for

solid complexes are illustrated in experimental part. The ligand spectrum displayed four peaks at 255, 295, 330 and 385 nm, the first two peaks ascribed to the $\pi \rightarrow p^*$ transition within the benzoniod and Furobenzopyrone moieties.[37] Whereas the other two peaks imputed to $n \rightarrow p^*$ of the imine and carbonyl groups.[38] The last two peaks showed a bathochromic shift denoting that the imine nitrogen and carbonyl oxygen atoms are involved in coordination to the metal ion.[39] The VO^{2+} complex (2) exhibited magnetic moment value equal 1.66 BM and three absorption bands at 870, 590, 510 nm, for $\{^2B_2(d_{xy}) \rightarrow E_1(d_{xz}, d_{yz})(v_1), ^2B_2(d_{xy}) \rightarrow ^2B_1(d_{x^2-y^2})(v_2), ^2B_2(d_{xy}) \rightarrow ^2A_1(d_{z^2})(v_3)\}$ transitions respectively.[26] These results correspond to distorted octahedral geometry.[40, 41] The Mn^{2+} complex (3) electronic absorption spectrum displayed weak absorption peaks at 605, 510, 465 nm assignable to $\{^6A_{1g} \rightarrow ^4T_{1g}(4G)(v_1), ^6A_{1g} \rightarrow ^4E_g(4G)(v_2), ^6A_{1g} \rightarrow ^4E_g(4D)(v_3)\}$ transitions respectively, which are well-matched with the octahedral geometry.[40, 42] The magnetic moment value of this complex equals 6.05 BM,

inductive to five unpaired electrons system and close to high spin Mn^{2+} (d^5). Co^{2+} complex (**4**) spectrum showed peaks at 925, 615 and 510 for $\{^4T_{1g}(F) \rightarrow ^4T_{2g}(F)(v_1), ^4T_{1g}(F) \rightarrow ^4A_{2g}(F)(v_2), ^4T_{1g}(F) \rightarrow ^4T_{2g}(P)(v_3)\}$ transitions respectively, which referring that the ligands arranged around the cobalt(II) in an octahedral geometry.[40, 43] The magnetic moment value of cobalt complex is 3.88 BM, which Inductive to three unpaired electrons and close to a high spin Co^{2+} (d^7). The Ni^{2+} complex (**5**) displayed a magnetic moment value at 3.05 BM and three absorption peaks at 905, 605 and 495 nm inductive to $\{^3A_{2g}(F) \rightarrow ^3T_{2g}(F)(v_1), ^3A_{2g}(F) \rightarrow ^3T_{1g}(F)(v_2), ^3A_{2g}(F) \rightarrow ^3T_{1g}(P)(v_3)\}$ transitions respectively.[40, 43] These data supported the distorted octahedral geometry for Ni^{2+} complex.[43] The Cu^{2+} complex (**6**) showed magnetic moment value at 1.79 BM and only one broad band at 705 nm, which could be imputed to superimposed transitions $\{^2B_{1g}(d_{x^2-y^2}) \rightarrow ^2A_{1g}(d_{z^2}(v_1)), ^2B_{1g}(d_{x^2-y^2}) \rightarrow ^2B_{2g}(d_{xy})(v_2), ^2B_{1g}(d_{x^2-y^2}) \rightarrow ^2E_g(d_{yz}, d_{xz})(v_3)\}$. These data referring that this Cu^{2+} complex (**6**) has a distorted octahedral molecular geometry. [25, 40] The diamagnetic Zn^{2+} and Cd^{2+} complexes (**7**) and (**8**) have d^{10} system, so it does not show d-d transitions. The peaks which observed could be owing to intra-ligand transitions.[44]

Thermal analysis of complexes

The water molecules nature in the complexes (**2-8**) was elucidated by measuring the TG analysis in the 20-800 °C range. The thermal manner of complexes (**2-8**) displayed that the calculated weight loss is agreeable with the found calculated weight loss. The TG data (Table 1) displayed that, the complexes (**3-6**) and (**8**) decomposed in four successive steps. The first step carried out in the 60-110 °C range with found weight loss ranged between 6.77 and 9.12 % (calcd. 7.09-9.92%) owing to the departure of water molecules of hydration. The second step procured between 110-190 °C with found weight loss 2.32 - 2.66 % (calcd. 2.36-2.56%) due to departure of coordination water molecules. The third step occurred in the 180-260 °C range with found weight loss ranged between 14.87 and 16.50 % (calcd. 15.60-16.87%) which imputed to the acetate ions removal ($2CH_3COOH$). The last step which represent the whole degeneration was occurred in the range 390-600 °C with found weight lack ranged between 55.87-60.57 % (calcd. 58.09-62.83 %) ending with formation of metal oxides MnO , CoO , NiO , CuO and CdO consecutively. Complexes (**2**) and (**7**) degraded in three successive stages. The first stage take place

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in the 125-175 °C with 2.55, 2.58 % weight loss (calcd. 2.81 and 2.80 %) due to departure of the coordination water molecules. The next step in the 135-190 °C with 14.33 and 17.66 % weight loss (calcd. 15.00, 18.49 %) which imputed to the removal the sulfate and acetate ions ($2CH_3COOH$) for two complexes consecutively. The last step which represents the whole degeneration occurred in the 390-545 °C with found weight loss equal to 65.66 and 65.28 % (calcd. 68.79 and 66.05 %) ending with formation of metal oxides V_2O_5 and ZnO consecutively.

Biological activity study

All compounds (**1-8**) were subjected to antibacterial and antifungal screening tests against panel of microorganisms as *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Alcaligenes faecalis*, *Candida albicans*, *Aspergillus niger*. The screening data in Table 2 revealed that; the ligand (**1**) exhibits weak antifungal activity and does not show antibacterial activity while metal salts solution exhibits week antifungal and antibacterial activities. The Metal complexes (**2-8**) exhibit antimicrobial activity ranged from moderate to strong compared with positive control (chloramphenicol). Among the tested compounds, complexes (**6-7**) reveal potent antimicrobial activity towards the tested species {gram positive bacteria, gram negative bacteria, fungi}. Whereas complexes (**2-3, 8**) show moderate antimicrobial activity, while complexes (**4-5**) display moderate antifungal activity with weak antibacterial activity (only against the *G* +ve bacterium *A. Faecalis*). The antifungal and antibacterial activities of the ligand (**1**) can be enhanced through coordination with metal ions.^[45] Where the chelation reduces the polarity of metal ions and increases their lipophilic nature, thus the penetration of these metal ions through the cell membrane of microorganism can be increased. [46] So that the chelating increase the bactericidal properties of the ligand, thus inhibiting the growth of microorganism.[46-49] Besides, the significant biological activity of complexes (**2-8**) may also due to the change in their dipole moment, solubility and conductivity.

Conclusion

In this study a new furochromone Schiff base was prepared from condensation of 4-aminoantipyrine and 4,9-dimethoxy furochromene-6-carbaldehyde. The furochromone Schiff base forms 1:1 complexes with VO^{II} , Ni^{II} , Cu^{II} , Co^{II} , Mn^{II} , Cd^{II} and Zn^{II} salts. The elemental

TABLE 1. Thermal analyses for metal (II) complexes (2-8)

| No. | Temp. range °C | Loss in weight | | Assignment | Composition of the residue |
|-----|----------------|----------------|----------|---|--|
| | | Found | (calcd.) | | |
| (2) | 130-160 | 2.55 | (2.81) | Removal of coordinated water molecule (H ₂ O) | [VO(L)SO ₄] |
| | 160-190 | 14.33 | (15.00) | Removal of sulphate group (SO ₄) | [VO(L)] |
| | 390-525 | 65.66 | (68.79) | Complex decomposition forming V ₂ O ₅ | [(V ₂ O ₅)] |
| (3) | 65-95 | 7.78 | (7.67) | Dehydration process (3H ₂ O) | [Mn(L)(CH ₃ COO) ₂ (H ₂ O)] |
| | 110-180 | 2.32 | (2.56) | Removal of coordinated water molecule (H ₂ O) | [Mn(L)(CH ₃ COO) ₂] |
| | 205-265 | 16.50 | (16.87) | Removal of two acetate ions (2CH ₃ COOH) | [Mn(L)] |
| | 400-535 | 60.28 | (62.83) | Complex decomposition forming MnO | MnO |
| (4) | 75-110 | 9.12 | (9.92) | Dehydration process (4H ₂ O) | [Co(L)(CH ₃ COO) ₂ (H ₂ O)] |
| | 120-175 | 2.59 | (2.48) | Removal of coordinated water molecule (H ₂ O) | [Co(L)(CH ₃ COO) ₂] |
| | 195-235 | 15.55 | (16.36) | Removal of two acetate ions (2CH ₃ COOH) | [Co(L)] |
| | 450-600 | 56.88 | (60.93) | Complex decomposition forming CoO | CoO |
| (5) | 70-100 | 7.50 | (7.63) | Dehydration process (3H ₂ O) | [Ni(L)(CH ₃ COO) ₂ (H ₂ O)] |
| | 110-155 | 2.33 | (2.54) | Removal of coordinated water molecule (H ₂ O) | [Ni(L)(CH ₃ COO) ₂] |
| | 200-240 | 16.22 | (16.78) | Loss of two acetate ions (2CH ₃ COOH) | [Ni(L)] |
| | 430-520 | 60.57 | (62.50) | Complex decomposition forming NiO | NiO |
| (6) | 65-105 | 7.77 | (7.58) | Dehydration process (3H ₂ O) | [Cu(L)(CH ₃ COO) ₂ (H ₂ O)] |
| | 115-165 | 2.49 | (2.53) | Removal of coordinated water molecule (H ₂ O) | [Cu(L)(CH ₃ COO) ₂] |
| | 180-245 | 16.07 | (16.67) | Removal of two acetate ions (2CH ₃ COOH) | [Cu(L)] |
| | 400-555 | 59.33 | (62.07) | Complex decomposition forming CuO | CuO |
| (7) | 125-175 | 2.58 | (2.80) | Removal of coordinated water molecule (H ₂ O) | [Zn(L)(CH ₃ COO) ₂] |
| | 195-235 | 17.66 | (18.49) | Removal of two acetate ion (2CH ₃ COOH) | [Zn(L)] |
| | 390-545 | 65.28 | (66.05) | Complex decomposition forming ZnO | ZnO |
| (8) | 60-95 | 6.77 | (7.09) | Dehydration process (3H ₂ O) | [Cd(L)(CH ₃ COO) ₂ (H ₂ O)] |
| | 135-190 | 2.66 | (2.36) | Removal of coordinated water molecule (H ₂ O) | [Cd(L)(CH ₃ COO) ₂] |
| | 205-260 | 14.87 | (15.60) | Removal of two acetate ions (2CH ₃ COOH) | [Cd(L)] |
| | 450-585 | 55.67 | (58.09) | Complex decomposition forming CdO | CdO |

TABLE 2. Antimicrobial activity of furochromone Schiff base compounds (1-8).

| No. | Organisms | Gram positive bacteria | | Gram negative bacteria | | Fungi | |
|-----|--------------------------|------------------------|-------------|------------------------|-------------|-------------|----------|
| | | E. coli | A. faecalis | S. aureus | B. subtilis | C. albicans | A. niger |
| 1 | Ligand (L) | - | - | + | - | ++ | + |
| 2 | VO ^{II} complex | | | | | | |
| 3 | Mn ^{II} complex | ++ | + | +++ | + | +++ | +++ |
| 4 | Co ^{II} complex | ++ | ++ | + | + | ++ | ++ |
| 5 | Ni ^{II} complex | + | + | - | + | +++ | ++ |
| 6 | Cu ^{II} complex | +++ | ++ | +++ | ++ | ++++ | ++++ |
| 7 | Zn ^{II} complex | +++ | ++++ | ++++ | ++++ | ++++ | ++++ |
| 8 | Cd ^{II} complex | | | | | | |
| (a) | Chloramphenicol | ++++ | ++++ | ++++ | ++++ | ++++ | +++ |
| (b) | DMSO | - | - | - | - | - | - |

Inhibition zone diameter (% inhibition) : +6-9 mm (33-50%); ++ 10-12 mm(55-67%); +++ 13-15 mm (72-83%); ++++ 16-18 mm (89-100%);
a:standard drug (positive control)
b:solvent (negative control)

analysis and spectroscopic studies of the newly synthesized compounds (**1-8**) showed that, the furochromone Schiff base acts as tridentate ligand. Where, it is coordinating with metal ions through the carbonyl oxygen atoms of furobezopyrone and antipyrine moieties and azomethine nitrogen atom. All prepared metal complexes showed a non-electrolytes nature. The coordination geometries around the metal centers in these complexes are distorted octahedral geometry. The antimicrobial evaluation of all compounds revealed that the ligand exhibits weak antifungal activity, whereas the metal complexes exhibit antimicrobial activity ranged from moderate to strong. Nickel and Zinc complexes exhibit potent antimicrobial activity compared with other complexes and standard drug (chloramphenicol).

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تقييم نشاط مترابطات قاعدة شيف فيروكرومونات الجديدة كمضادات ميكروبية خارج الخلية

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تم تحضير سلسلة من مترابطات أكسيد الفانديل الثنائي (الفانديوم الرباعي) والنحاس، النيكل، الكوبلت، المنجنيز، الكادميوم و الزنك الثنائية الجديدة لمترايط قاعدة شيف المحضرة من ٤-أمينوانتي بيرين وفيورونوبنزوبيرون.

وقد تم توصيف التركيب البنائي للمركبات الجديدة المحضرة (١-٨) من خلال دراسة التحليل العنصرى (كربون، هيدروجين، نيتروجين)، والتحليلات الطيفية (الأشعة تحت الحمراء، رنين النووي المغناطيسي، طيف الامتصاص الإلكتروني) والعزم المغناطيسي والتوصيل الكهربى.

و علاوة على ذلك فقد تم تقييم نشاط المركبات كمضادات للميكروبات خارج الخلية. وأوضحت الدراسات أن مترابطات النيكل والزنك أظهرت نشاطا مبشرا مقارنة بدواء (الكلورامفينيكول) المستخدم كمرجع.