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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITIES OF SOME 5-BROMOURACIL–METAL ION COMPLEXES

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ABSTRACT. Six new complexes, $[\text{Mn}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2]\cdot 4\text{H}_2\text{O}$ (**1**), $[\text{Cd}(\text{Br}-\text{U})_2]\cdot 2\text{H}_2\text{O}$ (**2**), $[\text{Cu}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2]\cdot 2\text{H}_2\text{O}$ (**3**), $[\text{Co}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2]\cdot 4\text{H}_2\text{O}$ (**4**), $[\text{Ni}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2]\cdot 4\text{H}_2\text{O}$ (**5**) and $[\text{Ag}(\text{Br}-\text{U})(\text{Br}-\text{U}-\text{H})]\cdot 2(\text{H}_2\text{O})$ (**6**) were prepared by the reaction of 5-bromouracil with $\text{MnCl}_2\cdot 4\text{H}_2\text{O}$, $\text{CdCl}_2\cdot 2.5\text{H}_2\text{O}$, $\text{CuSO}_4\cdot 5\text{H}_2\text{O}$, $(\text{CH}_3\text{COO})_2\text{Co}\cdot 4\text{H}_2\text{O}$, $(\text{CH}_3\text{COO})_2\text{Ni}\cdot 4\text{H}_2\text{O}$ and AgNO_3 respectively. The complexes were characterized by melting point, elemental microanalyses, IR and ¹H NMR spectroscopy. The obtained data indicated that the ligand interacted with the metal ions in its mononegatively charged enol form in a bidentate fashion. Thermogravimetric analyses (TGA and DTG) were also carried out. The data obtained agreed well the proposed structures and showed that the complexes were finally decomposed to the corresponding metal or metal oxide. The ligand and its metal-ion complexes were tested for their antimicrobial activities against four bacterial strains (*B. subtilis*, *S. aureus*, *E. coli* and *P. aeruginosa*) by the agar-well diffusion technique using DMSO as a solvent. The obtained data showed that the complexes were more potent antimicrobial agents than the parent ligand.

KEY WORDS: 5-Bromouracil–M²⁺ complexes, IR, Thermal analyses, ¹H NMR, Antimicrobial activity

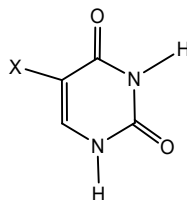
INTRODUCTION

Uracil is a naturally occurring nucleic acid [1] and is the most important pyrimidine base that represents remarkable roles in the structures and functions of enzymes and drugs [2]. In recent years, uracil and its derivatives and complexes have been used in the synthesis of antibacterial, antiviral and anti-tumour agents [3–5]. Intensive investigations have shed light on the natures of the interactions between metal ions and nucleic acid bases, including their abilities to form complexes [2] which have wide-ranging biological activities, such as antimalarial, antitumoural, antibacterial, and antiviral activities [6, 7].

5-Bromouracil (Br–U–H), (5-bromopyrimidine-2,4(1H,3H)-dione) (Scheme 1), is a halogenated derivative of uracil which has the ability to terminate DNA replication in viruses and other cell culture systems [8–11]. This termination of DNA replication occurs via the replacement of a thymine base in the genetic code with 5-bromouracil, resulting in an unusual code that stops the replication process [12, 13]. On the other hand, the thymine replacement by 5-bromouracil in the DNA genetic sequence has a significant influence on cancer therapy, leading to higher sensitivity to ionizing radiation [14, 15] without influencing the un-irradiated cells. Moreover, 5-bromouracil has a great influence on the growth of viruses, bacteria and other microorganisms [8–11]. Heterocyclic molecules have tautomeric forms at equilibrium in solutions, where hydrogen atoms can move to various locations within the molecules. In this respect, 5-bromouracil isomers exist in enol and keto tautomeric forms [13], Scheme 2.

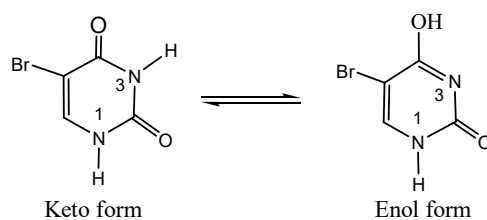
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where X = H (uracil) X = Br (5-bromouracil)

Scheme 1. Molecular structure of uracil and 5-bromouracil.



Scheme 2. Tautomeric forms of bromouracil.

At alkaline pH values, the hydrogen atom bonded to the N(3) atom in the keto form of 5-bromouracil is removed, indicating that the N(3) hydrogen atom is acidic ($pK_a = 8$); however, the N(1) atom is basic [13, 16]. 5-Bromouracil is a nucleotide base that can bind to metals or bind to tissues via metals [17–19]. Additionally, its complexes or compounds have been identified as biologically active materials acting as antibacterial and anti-tumour agents [18, 20].

In this article, the preparation, characterization and biological activities of Mn(II), Cd(II), Co(II), Ni(II), Cu(II) and Ag(I) complexes with 5-bromouracil has been described. The determination of the binding sites of 5-bromouracil with these metal ions can give additional value by correlating the coordination modes of 5-bromouracil with its biological activity. The obtained complexes were characterized by elemental analysis, infrared (IR) spectroscopy, ^1H nuclear magnetic resonance (NMR) spectroscopy, melting point, conductivity measurements as well as thermal analysis (thermogravimetric analysis, TGA, and differential thermogravimetric analysis, DTG).

EXPERIMENTAL

Materials and spectral measurements

Reagents

5-Bromouracil, KOH and metal salts, i.e. $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{CdCl}_2 \cdot 2.5\text{H}_2\text{O}$, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, $\text{Co}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$, $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ and AgNO_3 , used in this study were purchased in analytical grade and used without further purification.

Instruments

Elemental analysis for C, H and N was carried out in the Microanalysis Department of Cairo University, Egypt, using a VARIO EL III elemental analyzer. Infrared measurements (KBr-pellets) were carried out on a Unicam SP 1000 IR spectrophotometer (Pharmaceutical

Analytical Department, Al-Azhar University, Cairo, Egypt). ^1H NMR measurements were performed using DMSO as a solvent on a Bruker spectrometer (Zagazig University, NMR Department, Zagazig, Egypt). TGA was carried out at a heating rate of $10\text{ }^\circ\text{C}$ using a Universal TGA Q500 instrument (Science & Technology Center of Excellence, Cairo, Egypt). Molar conductivities of the complex solutions ($1 \times 10^{-3}\text{ M}$) in dimethylformamide (DMF) were measured at room temperature using a Jenway 4510 conductivity meter. The heavy metals which include manganese (Mn), cadmium (Cd), copper (Cu), cobalt (Co), nickel (Ni), and silver (Ag) are detected by ICP Spectrophotometer Thermo Jarrel Ash model POEMS 3, using 1000 mg/L (Merck) stock solution for standard preparations.

Preparation of the ligand solution

5-Bromouracil (764.0 mg, 4.0 mmol) was suspended in 30.0 mL of distilled H_2O , (pH = 4.2), and a KOH solution (1.0 M) was added dropwise until reaching pH to 10 or and complete dissolution of the ligand.

Syntheses of the metal complexes

To the prepared ligand solution, 50.0 mL of an aqueous solution (2.0 mmol) of the corresponding metal salt, i.e. $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ (395.0 mg), $\text{CdCl}_2 \cdot 2.5\text{H}_2\text{O}$ (456.0 mg), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (499.0 mg), $\text{Co}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ (498.0 mg), $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ (497.0 mg) or AgNO_3 (393.7 mg), was added. The reaction mixture was stirred for around 5 h at $65\text{ }^\circ\text{C}$. The obtained precipitate was filtered, washed several times with a few drops of distilled water, and then dried in an oven ($50\text{ }^\circ\text{C}$) for 2 h and then in a silica gel desiccator.

$[\text{Mn}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O}$ (**1**). Yield: (50.10%). M.P.: $340\text{ }^\circ\text{C}$. Colour: yellowish brown. Analysis found% (calculated % for $\text{C}_8\text{H}_{16}\text{Br}_2\text{MnN}_4\text{O}_{10}$, 542.98): C, 18.05 (17.70); H, 2.96 (2.97); Mn 10.19 (10.12); N, 10.74 (10.32).

$[\text{Cd}(\text{Br}-\text{U})_2] \cdot 2\text{H}_2\text{O}$ (**2**). Yield: (39.60%). M.P.: $>350\text{ }^\circ\text{C}$. Colour: white. Analysis found% (calculated % for $\text{C}_8\text{H}_8\text{Br}_2\text{CdN}_4\text{O}_6$, 528.39): C, 18.24 (18.18); H, 1.99 (1.53); Cd, 21.50 (21.27), N, 10.34 (10.60).

$[\text{Cu}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$ (**3**). Yield: (65.80%). M.P.: $295\text{ }^\circ\text{C}$. Colour: green. Analysis found% (calculated % for $\text{C}_8\text{H}_{12}\text{Br}_2\text{CuN}_4\text{O}_8$, 515.56): C, 18.23 (18.64); H, 2.52 (2.35); Cu, 12.48 (12.33); N, 10.54 (10.87).

$[\text{Co}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O}$ (**4**). Yield: (66.90%). M.P.: $315\text{ }^\circ\text{C}$. Colour: red. Analysis found% (Calculated% for $\text{C}_8\text{H}_{16}\text{Br}_2\text{CoN}_4\text{O}_{10}$, 546.97): C, 17.50 (17.57); H, 3.33 (2.95); Co, 10.89 (10.77); N 10.43 (10.24).

$[\text{Ni}(\text{Br}-\text{U})_2(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O}$ (**5**). Yield: (85.90%). M.P.: $318\text{ }^\circ\text{C}$. Colour: faint green. Analysis found% (calculated % for $\text{C}_8\text{H}_{16}\text{Br}_2\text{NiN}_4\text{O}_{10}$, 546.73): C, 17.60 (17.57); H, 3.03 (2.95); Ni, 10.81 (10.74); N, 10.34 (10.25).

$[\text{Ag}(\text{Br}-\text{U})(\text{Br}-\text{U}-\text{H})] \cdot 2\text{H}_2\text{O}$ (**6**). Yield: (88.40%). M.P.: $278\text{ }^\circ\text{C}$. Colour: white silvery. Analysis found% (calculated % for $\text{C}_8\text{H}_9\text{AgBr}_2\text{N}_4\text{O}_6$, 524.86): C, 17.98 (18.31); H, 1.79 (1.73); Ag, 21.05 (20.55); N, 10.36 (10.67).

Antimicrobial activity

The *in vitro* antibacterial effects of the compounds were tested against four bacterial strains, i.e. *E. coli* and *P. aeruginosa* (Gram-negative bacteria) and *B. subtilis* and *S. aureus* (Gram-positive bacteria), by an agar well diffusion method using nutrient agar medium [21-23]. All bacteria were inoculated into nutrient broth and incubated for 24 h (1.0 mL of inoculant was added to 50 mL of agar media (50 °C) and mixed). The agar was poured into 120 mm petri dishes and allowed to cool to room temperature. In the agar well diffusion method, the dilution plate method was used to enumerate microorganisms for 24 h [24, 25]. Using a sterilized cork borer (7 mm diameter), wells were dug into the culture plates. The compounds dissolved in DMSO (0.1 mL, 250 µmol/mL) were added to these wells. The petri dishes were left at 5 °C for 2 h, and then, the plates were incubated at 35 °C for bacterial growth (24 h). At the end of the period, the inhibition zones formed on the medium were evaluated in millimetres (mm). DMSO (0.1 mL) was used as a control under similar conditions. The inhibition zones based on the zone size around the discs were measured and calculated as means of triplicates and are reported as average values of three experiments.

RESULTS AND DISCUSSION

Free ligand and complexes

All the prepared complexes are insoluble in many organic solvents (methanol, ethanol, acetonitrile, chloroform, carbon tetrachloride) and water. Complexes **1**, **4** and **6** are soluble in DMF, while the other complexes **2**, **3** and **5** are slightly or sparingly soluble in DMF. These complexes were characterized by IR, ¹H NMR spectroscopy, melting point measurements, elemental analyses and TGA. The complexes have a 1:2 metal-to-ligand stoichiometry.

Conductance

The conductivity values measured at 25 °C in DMF for 10⁻³ M solutions of the free ligand and its complexes are very small, and their values lie in the range of 3.17– 8.2 µs·cm⁻¹, indicating the non-electrolytic nature of the complexes [26].

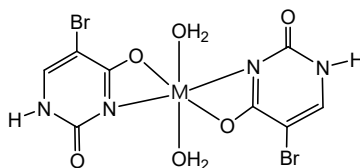
IR spectra

The infrared spectrum of the free ligand (Table 1) shows a strong broad band at 1677 cm⁻¹ characteristic of (C(4)=O) and a shoulder at 1617 cm⁻¹ corresponding to (C(2)=O), which are practically overlapped. Two weak/medium bands are observed at 3360 and 3168 cm⁻¹, which may be assigned to (N(3)-H) and (N(1)-H) stretching vibrations, respectively.

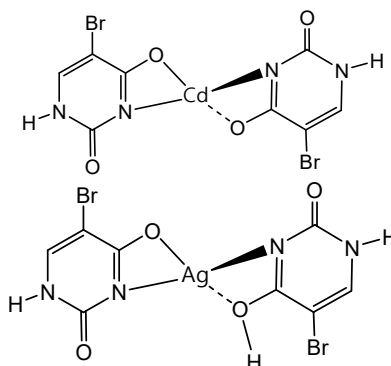
The assignments of the well-defined bands in the infrared spectra of the complexes are summarized in Table 1. The ν(C=O) of the free ligand is observed at 1677 cm⁻¹, while the corresponding vibrations in the metal complexes are observed in the range of 1611–1640 cm⁻¹. A shift of 30-50 cm⁻¹ to lower frequencies is observed for the carbonyl band after coordination with the metal ions, clearly indicating the coordination of the carbonyl group to the metal ions. The disappearance of the absorption band at 3360 cm⁻¹ (N(3)-H in the free ligand spectrum) in the complex spectra indicates that the N(3) atom is bound to the metal ions. The complex spectra show an absorption band in the range of 1590-1525 cm⁻¹. This band is not observed in the spectrum of the free ligand and may be attributed to the stretching motion associated with the C=N bond resulting from the transformation of the ligand from the keto form to the enol form upon complexation. The observation of such a band in the complex spectra support the assumption that 5-bromouracil is coordinated with the metal ions as a mononegative bidentate

ligand through one oxygen atom of the carbonyl group and the N(3) atom. This coordination mode is also supported by the observation of two weak bands in the ranges of 609–563 and 550–510 cm^{-1} , which are attributed to M–N and M–O stretching modes, respectively. These two bands are not observed in the spectrum of the free ligand [27-31].

According to the forgoing discussion and based on the proposed molecular formulas, the probable structures of the Mn(II), Co(II), Ni(II), and Co(II) complexes are in octahedral geometries. On other hand, the structures for the Cd(II) and Ag(I) complexes are more likely in tetrahedral geometries, as shown in Scheme 3 [32-36].



where M = Mn(II), Co(II), Ni(II) or Cu(II)



Scheme 3. Suggested structures for the 5-bromouracil-metal ion complexes.

Table 1. Selected IR frequencies (cm^{-1}) and tentative assignments for 5-bromouracil (as a free ligand) and its metal complexes (1-6).

(Br–U–H)	1	2	3	4	5	6	Assignments
3467 w,br	3448 vs	3415 s,br	3409 vs,br	3433 vs,br	3440.3 vs,br	3419 w,br	$\nu(\text{O–H})$, H_2O
3360 sh	-----	-----	-----	-----	-----	-----	$\nu(\text{N3–H})$
3168 m	3187 m	3137 w,br	3202 w	3118 m	3117 s	3150 w	$\nu(\text{N1–H})$
3060 m	3125 m	3020 w,br	3077 vw	3029 vw	3029 vw	3048 vw	$\nu(\text{C–H})$, aromatic
1677 vs	1612 vs	1641 s	1643 vs	1611 s	1618 vs	1640 vs	$\nu(\text{C=O})$
-----	1590 sh	1572 w	1578 sh	1576 s	1573 vs	1525 vs	$\nu(\text{C=N})$
1427 s	1392 s	1454 s	1470 m	1389 vs	1394 vs	1404 m	$\nu(\text{C–C})$; $\delta(\text{N1–H})$
1224 m	1271 m	1274 m	1281 m	1272 vs	1278 m	1273 m	$\nu(\text{C–N})$; $\nu(\text{C–O})$
1054 w	1010 m	1026 s	1063 m	1080 m	1082 w	1068 w	$\nu(\text{C–Br})$
-----	583 w	562 sh	609 sh	586 m	592 w	576 m	$\nu(\text{M–N})$
-----	550 sh	509 sh	536 w	520 w	517 vw	477 w	$\nu(\text{M–O})$

Where, sh = shoulder, s = strong, m = medium, w = weak, br = broad, v = very.

¹H NMR spectra

The ¹H NMR spectral data of free 5-bromouracil and its Cd(II) and Ag(I) complexes in DMSO are summarized in Table 2. The spectra reveal a characteristic signal for the aromatic proton in its expected region of 7.00–8.00 ppm. The N(1)-H signal is located at 11.13 ppm in the spectrum of the free ligand, while the corresponding signals in the spectra of the Cd(II) and Ag(I) complexes are observed at 10.90 and 10.85 ppm, respectively. The N(3)-H signal in the free ligand spectrum (11.51 ppm) is absent in the spectra of the complexes, which is consistent with the forgoing suggestion that 5-bromouracil reacted with the metal ions through its enol form. The Ag(I) complex exhibits a signal at 10.51 ppm, and such a signal is neither present in the spectrum of the free ligand nor in the spectra of the other complexes. This signal may be attributed to the (O-H) proton associated with one of the two ligands coordinated with the Ag(I) ion. Accordingly, one of the two ligands bonded to the Ag(I) ion is a neutral molecule in the enol form, while the other is negatively charged, as shown in Scheme III. The ¹H NMR spectrum of the free ligand confirms the results obtained from the IR spectrum. The obtained data suggests that 5-bromouracil is in the keto form. Dissolving the base with additional KOH converts the keto form to the enol form, forming a soluble salt with the deprotonation of N(3)-H as the pH is raised to 10 [37, 38].

Table 2. ¹H NMR data in ppm and assignments for 5-bromouracil as a free ligand and its Cd(II) and Ag(I) complexes.

Compound	C ₆ -H	N ₁ -H	N ₃ -H	O-H	H ₂ O
Free ligand (Br-U-H)	7.88 (1H)	11.13	11.51 (1H)	-----	3.35
[Cd(Br-U) ₂].4H ₂ O (2)	7.85 (1H)	10.90	-----	-----	3.34
[Ag(Br-U)(Br-U-H)].2H ₂ O (6)	7.80 (1H)	10.85	-----	10.51(1H)	3.32

Thermal analyses

To confirm the proposed structures of the complexes, thermogravimetric analyses (TGA) were performed. The thermal data for all complexes are summarized in Table 3. The free ligand completely decomposes in one step at approximately 320 °C, as shown in Figure 1, indicating its pure organic structure.

The decomposition reactions of [Mn(Br-U)₂(H₂O)₂].4H₂O, [Cd(Br-U)₂].2H₂O, [Cu(Br-U)₂(H₂O)₂].2H₂O, [Co(Br-U)₂(H₂O)₂].4H₂O, [Ni(Br-U)₂(H₂O)₂].4H₂O and [Ag(Br-U)(Br-U-H)].2H₂O occur in four, five or six steps from 120 °C to 1000 °C, as shown in Figure 1. In these complexes, the first decomposition step proceeds at a temperature between 120 °C and 210 °C with a weight loss ranging from 6.30–13.50%, associated with the loss of the outer-sphere (uncoordinated) water content. The calculated ratio of the outer-sphere water content in the suggested forms is between 6.82% and 13.27%, in good agreement with the observed values (Table 3).

The second thermal decomposition step for complexes **1**, **3**, **4**, and **5** displayed weight loss in the range of 6.71–7.50% at a temperature range of 240–275 °C, which may be attributed to the loss of coordinated water. This result agrees with the calculated coordinated water values of 6.59–6.99% in the suggested formulas of these complexes. The TGA thermograms of complexes **2** and **6** shows no weight loss in this temperature range, indicating the absence of any coordinated water, which is consistent with the suggested formulas of both complexes.

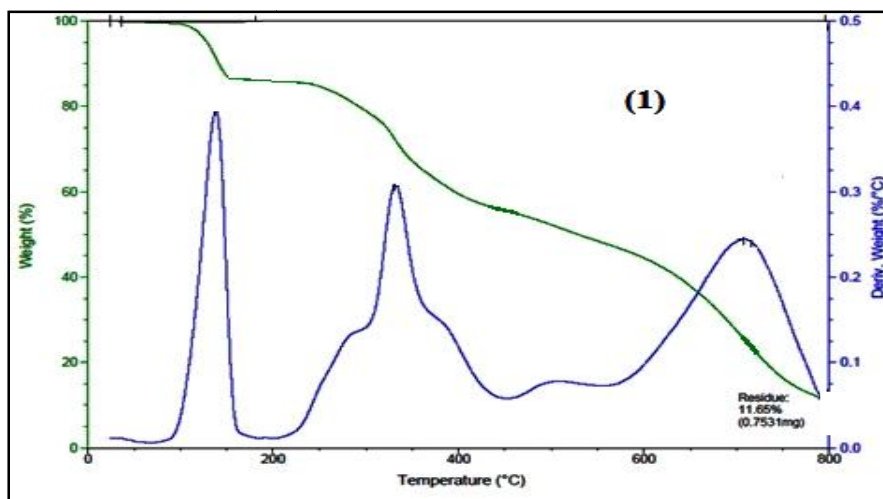
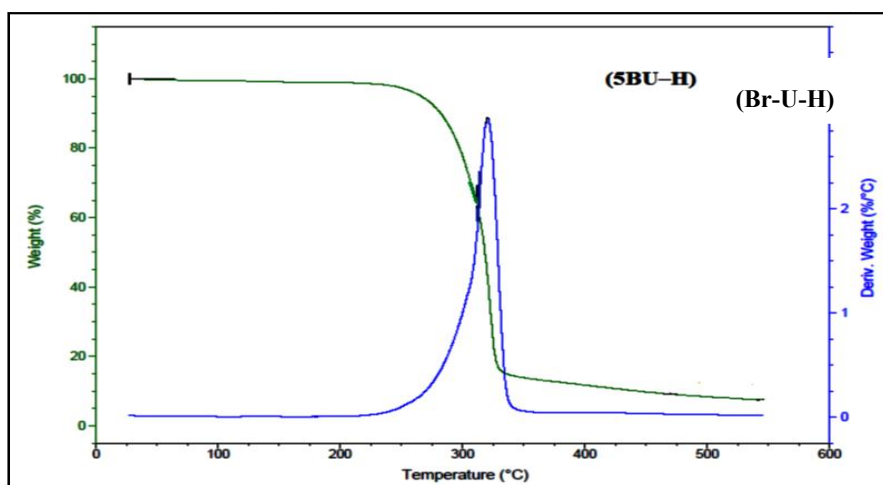
The loss of organic content associated with the ligands occurs in the next two to six decomposition steps at maximum temperatures between 283 °C and 925 °C. The weight loss associated with these decomposition steps (65.75–78.49%) is in agreement with the calculated values (66.54–72.59%). The total weight loss throughout the decomposition process lies in the

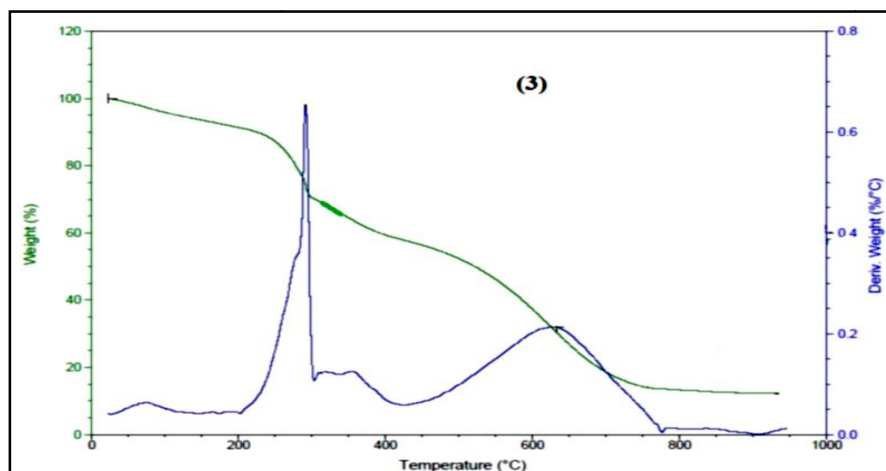
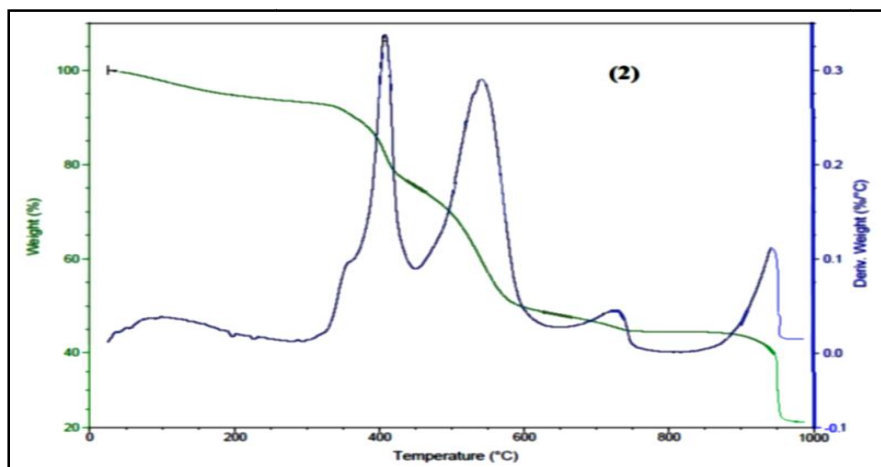
Table 3. The maximum temperature values for the decomposition along with the species lost in each step of the decomposition reactions of 5-bromouracil and its complexes.

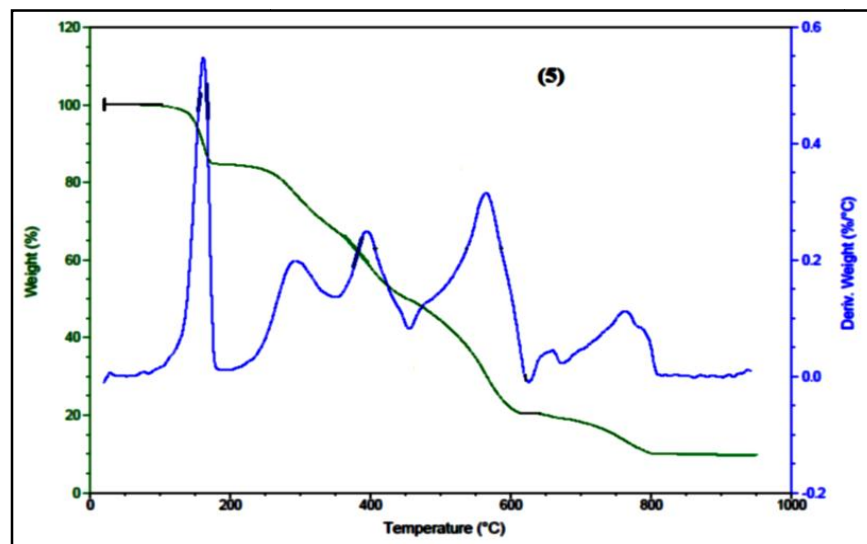
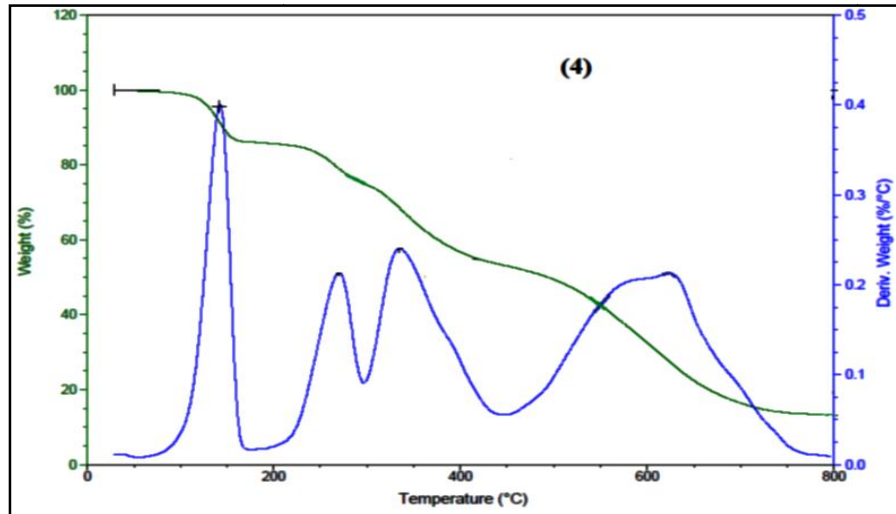
Complex	Decomposition	T _{max} (°C)	Lost species	% of weight loss	
				Found	Calcd
Free ligand (Br–U–H)	one step	320	C ₄ H ₂ N ₂ O ₂ Br	99.60	100
[Mn(Br–U) ₂ (H ₂ O) ₂].4H ₂ O (1)	1 st step	138	4H ₂ O	13.32	13.27
	2 nd step	280	2H ₂ O	6.71	6.63
	3 rd step	331	---	---	---
	4 th step	510	---	---	---
	5 th step	707	C ₈ H ₄ Br ₂ N ₄ O ₃	68.07	67.03
	Total loss	----	C ₈ H ₁₆ Br ₂ N ₄ O ₉	88.10	86.93
	Residue	----	MnO	11.90	13.04
[Cd(Br–U) ₂].2H ₂ O (2)	1 st step	210	2H ₂ O	6.30	6.82
	2 nd step	407	----	----	----
	3 rd step	539	---	----	---
	4 th step	724	---	----	---
	5 th step	925	C ₈ H ₄ Br ₂ N ₄ O ₃	71.20	68.88
	Total loss	----	C ₈ H ₈ Br ₂ N ₄ O ₅	77.50	75.70
	Residue	----	CdO	22.50	24.30
[Cu(Br–U) ₂ (H ₂ O) ₂].2H ₂ O (3)	1 st step	120	2H ₂ O	6.50	6.99
	2 nd step	240	2H ₂ O	7.00	6.99
	3 rd step	283	---	---	---
	4 th step	355	---	---	---
	5 th step	627	C ₈ H ₄ Br ₂ N ₄ O ₄	75.00	70.59
	Total loss	----	C ₈ H ₁₂ Br ₂ N ₄ O ₇	87.50	84.57
	Residue	----	CuO	12.50	15.43
[Co(Br–U) ₂ (H ₂ O) ₂].4H ₂ O (4)	1 st step	167	4H ₂ O	13.50	13.17
	2 nd step	269	2H ₂ O	7.50	6.59
	3 rd step	334	----	----	----
	4 th step	624	C ₈ H ₄ Br ₂ N ₄ O ₃	65.75	66.54
	Total loss	----	C ₈ H ₁₆ Br ₂ N ₄ O ₉	86.75	86.30
	Residue	----	CoO	13.25	13.70
	[Ni(Br–U) ₂ (H ₂ O) ₂].4H ₂ O (5)	1 st step	170	4H ₂ O	13.50
2 nd step		275	2H ₂ O	6.90	6.59
3 rd step		290	----	----	----
4 th step		393	----	----	----
5 th step		564	----	----	----
6 th step		762	C ₈ H ₄ Br ₂ N ₄ O ₃	67.10	66.57
Total loss		-----	C ₈ H ₁₆ Br ₂ N ₄ O ₉	87.50	86.34
Residue		-----	NiO	12.50	13.66
[Ag(Br–U)(Br–U–H)].2H ₂ O (6)	1 st step	160	2H ₂ O	6.37	6.86
	2 nd step	299	----	----	----
	3 rd step	393	----	----	----
	4 th step	625	----	----	----
	5 th step	819	C ₈ H ₃ Br ₂ N ₄ O ₄	78.49	72.59
	Total loss	----	C ₈ H ₉ Br ₂ N ₄ O ₆	82.49	79.45
	Residue	----	Ag	18.94	20.55

range of 77.50–88.10%, which in good agreement with the theoretical values for the suggested structures (75.70–86.94%). The decomposition processes for the Mn(II), Cd(II), Cu(II), Co(II) and Ni(II) complexes left residue of the corresponding metal(II) oxides. The TGA thermograms show that the ratios of these metal oxide residues are in the range of 11.90–22.50% of the total weight, where the theoretical ratio calculated for the metal oxides resulting from the suggested

structures is between 13.04–24.30%. The decomposition process for the Ag(I) complex left residue of silver metal (Ag), corresponding to 18.94% of the total weight of complex, in good agreement with the calculated ratio of silver metal in the suggested Ag(I) complex (20.55%) [39].







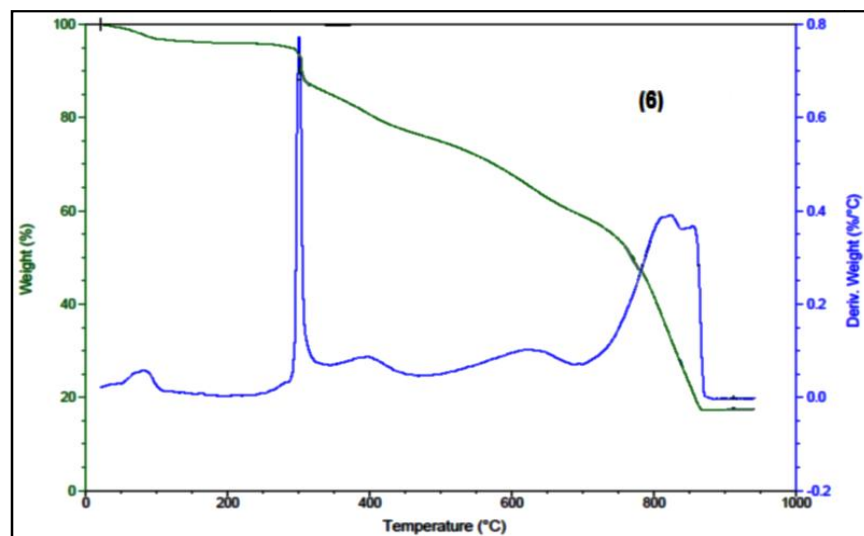


Figure 1. Thermogravimetric Analyses (TGA, DTG) of free ligand (Br–U–H) and its complexes (1–6).

Antimicrobial activity

The *in vitro* antibacterial activities of the compounds under investigation were tested against four bacterial strains, i.e. two Gram-positive bacteria (*B. subtilis* and *S. aureus*), and two Gram-negative bacteria (*E. coli* and *P. aeruginosa*), by an agar well diffusion method (Table 4).

Complexes **1**, **3** and **4** showed good activities against the Gram-positive bacterial strains *B. subtilis* and *S. aureus* and moderate activity against Gram-negative bacterial strains *E. coli* and *P. aeruginosa*. Complex **5** showed good activities against the selected bacterial strains. Complexes **2** and **6** showed excellent activities compared to the positive control against Gram-positive *B. subtilis* and *S. aureus* and moderate activity against Gram-negative *E. coli* and *P. aeruginosa*. The remarkable activities of the complexes may be due to structural changes in the geometries of the molecules and the type of metal ion [40].

Table 4. Antibacterial activities for the 5-bromouracil complexes (1–6).

Compounds	Inhibition zone diameter in mm			
	Gram-positive		Gram-negative	
	<i>Bacillus subtilis</i>	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>
[Mn(Br–U) ₂ (H ₂ O) ₂].4H ₂ O (1)	17	17	12	12
[Cd(Br–U) ₂].2H ₂ O (2)	18	18	13	13
[Cu(Br–U) ₂ (H ₂ O) ₂].2H ₂ O (3)	15	15	12	12
[Co(Br–U) ₂ (H ₂ O) ₂].4H ₂ O (4)	14	14	13	13
[Ni(Br–U) ₂ (H ₂ O) ₂].4H ₂ O (5)	15	16	14	14
[Ag(Br–U)(Br–U–H)].2(H ₂ O) (6)	20	18	13	14
DMSO	0.0	0.0	0.0	0.0
Ampicillin	21	19	23	17

Standard error ± 1.

CONCLUSION

In our study, we have prepared different types of 5-bromouracil–metal ion complexes by the reaction of 5-bromouracil with $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{CdCl}_2 \cdot 2.5\text{H}_2\text{O}$, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, $(\text{CH}_3\text{COO})_2\text{Co} \cdot 4\text{H}_2\text{O}$, $(\text{CH}_3\text{COO})_2\text{Ni} \cdot 4\text{H}_2\text{O}$ and AgNO_3 , respectively. The complexes were structurally characterized by melting point, elemental analyses measurements, electrical conductivity, IR and ^1H NMR spectroscopy. The obtained data indicated that the ligand interacted with the metal ions in its mononegatively charged enol form in a bidentate fashion and the complexes have a 1:2 metal-to-ligand stoichiometry. Thermogravimetric analyses (TGA and DTG) were also achieved. The data obtained agreed with the proposed structures and showed that the complexes were finally decomposed to the corresponding metal oxide or metal. The prepared 5-bromouracil– M^{2+} complexes were screened for their antimicrobial activities by an agar-well diffusion technique using DMSO as a solvent and showed that the complexes were potent antimicrobial.

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