

# Synthesis and Characterization of Metals Complexes with Uracil and Uracil Derivatives (A Review)

S. R. Al-Ayash<sup>a</sup>, T. H. Al-Noor<sup>a</sup>, and A. Abdou<sup>b,\*</sup>

<sup>a</sup> Department of Chemistry, College of Education for Pure Science, Ibn-Al-Haithem, University of Baghdad, Baghdad, 10071 Iraq

<sup>b</sup> Chemistry Department, Faculty of Science, Sohag University, Sohag, 82524 Egypt

\*e-mail: aly\_abdou@science.sohag.edu.eg

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**Abstract**—Previous studies on the synthesis and characterization of metal chelates with uracil by elemental analysis, conductivity, IR, UV-Vis, NMR spectroscopy, and thermal analysis were covered in this review article. Reviewing these studies, we found that uracil can be coordinated through the electron pair on the N<sup>1</sup>, N<sup>3</sup>, O<sup>2</sup>, or O<sup>4</sup> atoms. If the uracil was a mono-dentate ligand, it will be coordinated by one of the following atoms: N<sup>1</sup>, N<sup>3</sup> or O<sup>2</sup>. But if the uracil was bi-dentate ligand, it will be coordinated by atoms N<sup>1</sup> and O<sup>2</sup>, N<sup>3</sup> and O<sup>2</sup> or N<sup>3</sup> and O<sup>4</sup>. However, when uracil forms complexes in the form of polymers, coordination occurs through the following atoms: N<sup>1</sup> and N<sup>3</sup> or N<sup>1</sup> and O<sup>4</sup>.

**Keywords:** uracil, metal chelates, metal complexes, coordination polymers

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## 1. INTRODUCTION

Uracil is a naturally occurring pyrimidine derivative found in nucleic acids. It is a pyrimidine base composed of four different binding sites and was first isolated by hydrolysis of materials including RNA [1, 2]. Other names of uracil are 2-oxy-4-oxypyrimidine or 2,4-dihydroxypyrimidine or 2,4-pyrimidinediol [3, 4]. Uracil structure is shown in Scheme 1.

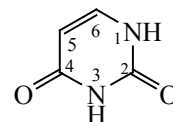
In recent years, uracil and its derivatives and their complexes have been used in the synthesis of antibacterial, antiviral and antitumor reagents [5, 6]. Uracil belonged to a group of the most important pyrimidines that played a fundamental role in the structure and function of enzymes and drugs. Uracil has been used in the synthesis of antitumor drugs [7, 8]. Among all the derivatives of pyrimidine nucleobases, the derivatives of uracil deserve special attention. The 6-aminouracil and 6-amino substituted derivatives of thymine have been shown to be competitive inhibitors of human thymidine phosphorylase [9, 10]. Also 5-fluorouracil is a known anticancer agent [11, 12], 5-nitouracil and derivatives are used as antiviral agents inhibiting thymidylate synthetase [13, 14]. The interaction of metal ions with nucleic bases

is of great interest because of its relevance to the essential, medicinal or toxic bioactivity of metal centers [15, 16]. Therefore, researchers became interested in the synthesis of new complexes of metal ions and uracil.

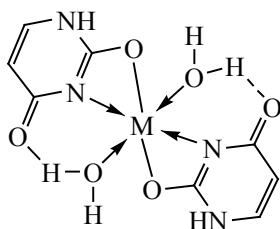
## 2. SYNTHESIS AND CHARACTERIZATION OF METAL COMPLEXES WITH URACIL AND URACIL DERIVATIVES

Ghosh et al. (1984) [17] have been synthesized Cu(II), Ni(II), Co(II), Fe(II), and Mn(II) complexes of uracil. The complexes were characterized by conductivity, elemental analysis, UV-Vis, melting point, FT-IR spectroscopy and magnetic susceptibility measurements. It was found that the coordination was through the oxygen atom of carbonyl group C<sup>2</sup>=O and N<sup>3</sup> of uracil with metal ions (Scheme 2).

Scheme 1.

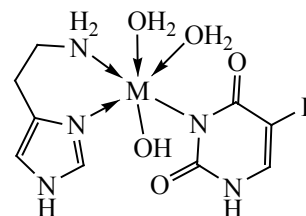


Scheme 2.



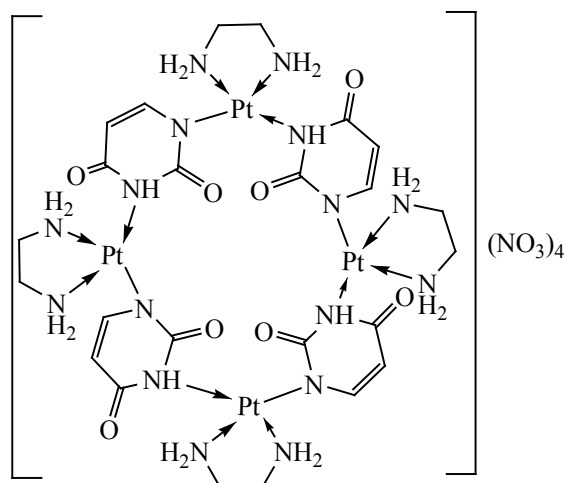
M = Cu(II), Ni(II), Co(II), Fe(II), Mn(II).

Scheme 5.

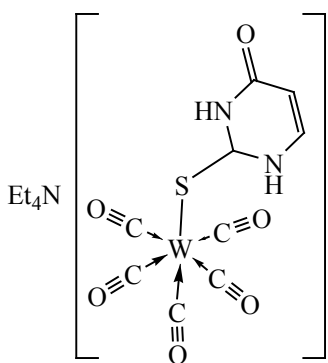


M = Co(II), Ni(II), Cu(II), Zn(II).

Scheme 3.



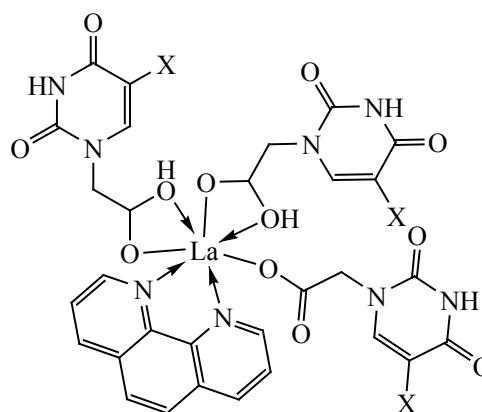
Scheme 4.



Rauter et al. (1992) [18] reported synthesis of  $[\text{Pt}_4(\text{en})_4(\text{uracil})_4](\text{NO}_3)_4$ , en = ethylenediamine, and characterized by X-ray. It was found that the uracil coordinated with Pt(II) via nitrogen atoms and give a cyclic compound (Scheme 3).

Darensbourg et al. (1999) [19] synthesized of 2-thiouracil derivatives and carbonyl of tungsten. The

Scheme 6.



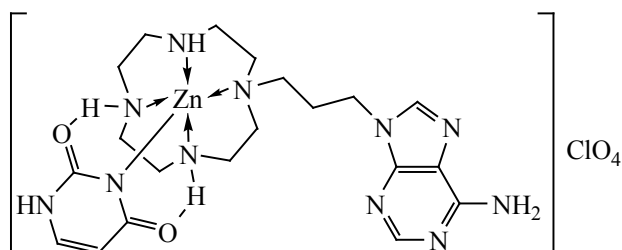
complex  $[\text{Et}_4\text{N}][\text{W}(2\text{-thiouracil})_5(\text{CO})_5]$  formed through bound to the tungsten center by S atom (Scheme 4).

Tyagi et al. (2002) [20] reported synthesis of  $[\text{M}(\text{Furacil})(\text{Hm})(\text{OH})(\text{H}_2\text{O})_2]$ , M = Co(II), Ni(II), Cu(II) and Zn(II), Furacil = 5-fluorouracil, Hm = histamine, and characterized by X-ray. It was found that the uracil coordinated with metal ions via N<sup>3</sup> atom (Scheme 5).

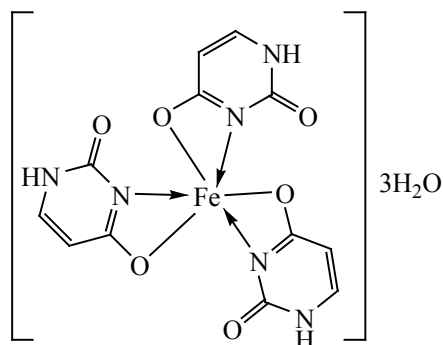
Hu et al. (2006) [21] synthesized two lanthanum(III) complexes of 1,10-phenanthroline (phen) with anionic uracil-1-acetato (uracil-A) and 5-fluorouracil-1-acetato (Furacil-A) ligands,  $[\text{La}(\text{uracil-A})_3(\text{phen})]$  and  $[\text{La}(\text{Furacil-A})_3(\text{phen})]$ , and characterized by spectroscopy methods. From spectroscopy data, the uracil-A, and Furacil-A in the complexes were coordinated with La(III) ion via oxygen atoms (Scheme 6).

Xia et al. (2006) [22] synthesized adenine-cyclen Zn(II) complex with uracil, and characterized by UV-Vis, FT-IR, melting point, elemental analysis and

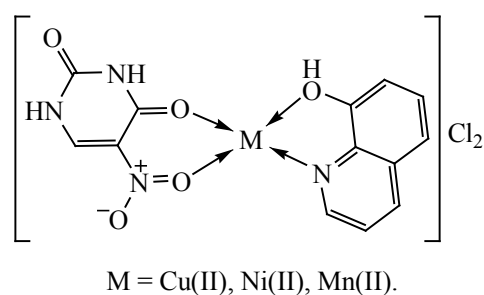
Scheme 7.



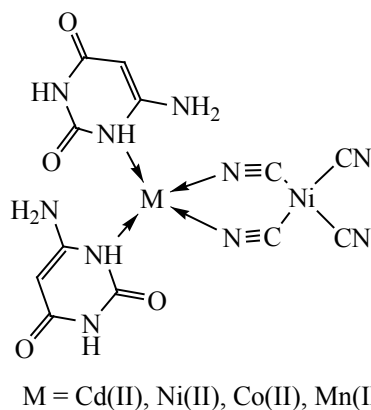
Scheme 8.



Scheme 9.



Scheme 10.



conductivity. Through spectra data, it was found that the uracil coordinated with Zn(II) via N<sup>3</sup> atom (Scheme 7).

Masoud et al. (2007) [23] prepared Fe(II) complex with uracil. The complex has been characterized through IR, electronic spectra, magnetic susceptibility and elemental analyses. The formula of the complex was [Fe(uracil)<sub>3</sub>·3H<sub>2</sub>O]. By the spectroscopy measurements, it was found that the uracil is coordinated bi-dentately via the oxygen and nitrogen atoms (Scheme 8).

Prachayasittikul et al. (2012) [24] synthesized Cu(II), Ni(II) and Mn(II) complexes [M(5-Nuracil)(8-HQ)]Cl<sub>2</sub> of 8-hydroxyquinoline with 5-nitro-uracil. The complexes were characterized by conductivity, elemental analysis, UV-Vis, melting point, FT-IR. From the spectroscopy data it was found that the 5-nitro-uracil was coordination done through O<sup>4</sup>-carbonyl and O=N-O group (Scheme 9).

Zaki (2018) [25] synthesized the complexes formed between some metal ions, with 6-aminouracil (6-Auracil) and tetracyanonickelate, [M(6-Auracil)<sub>2</sub>(Ni(CN)<sub>4</sub>)], M = Cd(II), Ni(II), Co(II) and Mn(II), and characterized by FT-IR, far-IR and FT-Raman spectra. From these

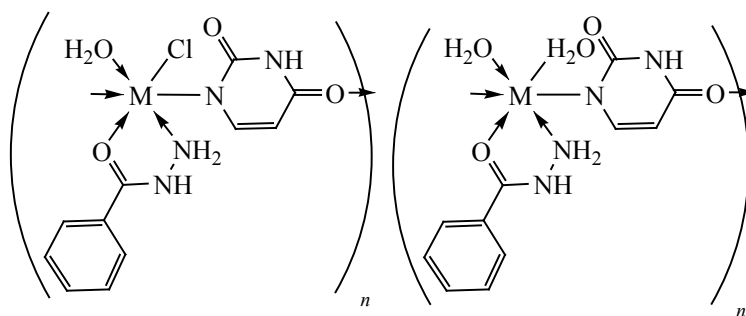
spectroscopic studies, it was found that the 6-aminouracil connected with metal ions via N<sup>3</sup> atom (Scheme 10).

Singh et al. (2013) [26] synthesized the complexes of the type [MCl(Bh)(uracil)(H<sub>2</sub>O)]<sub>n</sub> and [M(Inh)(uracil)(H<sub>2</sub>O)<sub>2</sub>]<sub>n</sub>, where M = Zn(II), Cu(II), Ni(II), and Co(II); Bh = benzoic acid hydrazide, and Inh = isonicotinic acid hydrazide, and characterized through magnetic susceptibility measurements, elemental analyses and FT-IR. Through the FT-IR, it was found that uracil behaves as bi-dentate ligand bonding via N<sup>1</sup> and O atoms of C<sup>4</sup>=O groups with metal ions (Scheme 11).

Singh et al. (2022) [27] reported synthesis of Zn(II) ternary complexes involving L-tryptophan, L-citrulline, L-glutamine with biologically active nucleobase uracil in solution, and were characterized by melting points, magnetic moments, infrared and electronic spectroscopy. Infrared spectral data confirmed that coordination occurred via N and O-carbonyl atoms of uracil (Scheme 12).

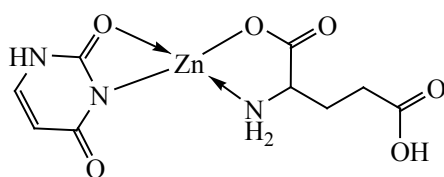
Sinha et al. (2014) [28] reported synthesis of mixed ligand complexes of Co(II), Ni(II), Cu(II), and Zn(II) with

Scheme 11.

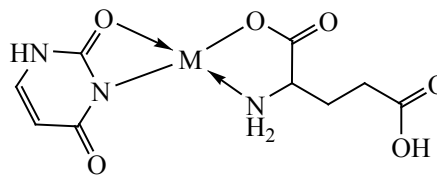


M = Zn(II), Cu(II), Ni(II), Co(II).

Scheme 12.



[(M)uracil (L-Try or L-Cit or L-Glu)]



[M(uracil)(Glu)]

M = Pb(II), Co(II), Cu(II), Ni(II), Zn(II), Cd(II), Hg(II).

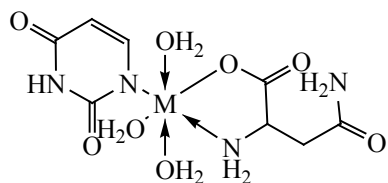
uracil and asparagines (asp), and characterized by FT-IR, UV-Vis, electronic spectroscopy, melting points, and magnetic moments. FT-IR spectral data confirmed that coordination occurred via N atom of uracil (Scheme 13).

Patil and Nethaji (2015) [29] synthesized ternary polymeric complexes of copper (II) with uracil and 1,10-phenanthroline. The complexes  $[\text{Cu}(\text{uracil})(\text{phen}) \cdot (\text{H}_2\text{O})]_n$  were characterized by FT-IR, UV-Vis, electronic spectroscopy, melting points, and magnetic moments.

From these spectroscopic studies; it was found that uracil coordinated through  $\text{N}^1$  and  $\text{N}^3$  atoms, which act as a bidentate bridging ligand (Scheme 14).

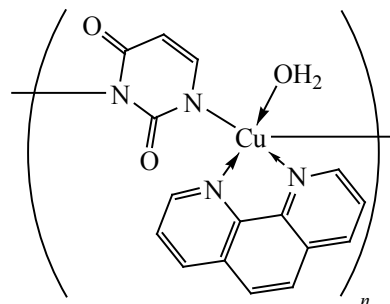
Patil and Nethaji (2015) [29] synthesized of the uracil derivative (uracilnitrosoamine = uracil-N) and used as a colorimetric-chemosensor for the detection of Cu(II) ion among many metal ions [Ag(I), Ba(II), Ca(II), Cd(II), Co(II), Cr(III), Cs(I), Fe(II), Fe(III), Li(I), Mg(II), Mn(II), Na(I), Ni(II), Zn(II), Hg(II), Pb(II), Sr(II), and Al(III)]

Scheme 13.

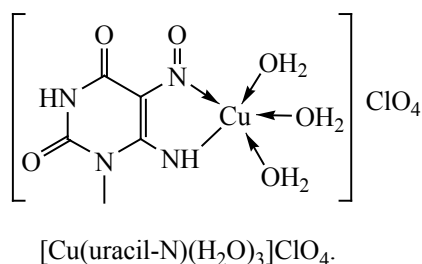


M = Co(II), Ni(II), Cu(II), Zn(II).

Scheme 14.



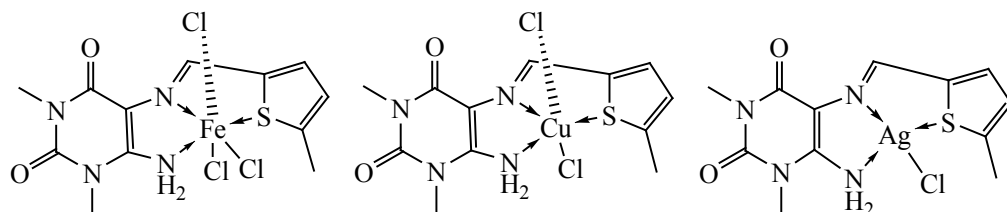
Scheme 15.



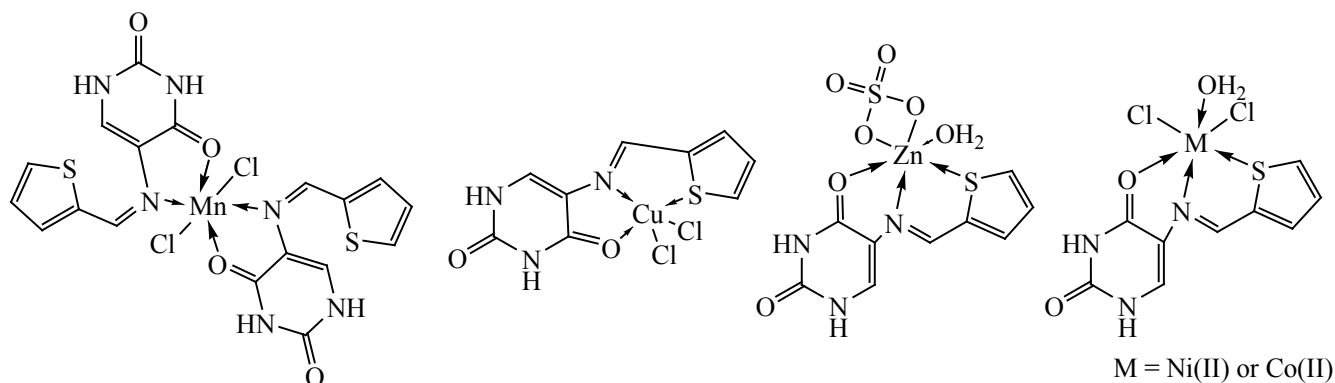
in the aqueous medium. The complex was characterized by FT-IR, UV-Vis, and melting points. FT-IR spectral data confirmed that coordination occurred via N atoms of uracil-N ligand (Scheme 15).

Hammud et al. (2015) [30] synthesized Cu(II), Ag(I) and Fe(III) complexes of Schiff base, made up of 5-methylthiophene-2-carboxaldehyde and 5,6-diamino-1,3-dimethyluracil. It was used as a colorimetric chemosensor for the detection of Cu(II), Ag(I) and Fe(III) in presence of other cations in natural water by formed of complexes from ions Cu(II), Ag(I) and Fe(III) with Schiff base (Scheme 16).

Scheme 16.



Scheme 17.

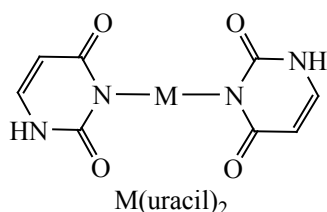


Abdel-Monem and Abouel-Enein (2017) [31] prepared Mn(II), Ni(II), Zn(II), Cd(II), and Cu(II) complexes with 5-(thiophene-2-ylmethineazo)uracil, and characterized by (IR), magnetic moment, elemental analyses, and spectroscopic measurements. The complexes were characterized by FT-IR, UV-Vis, and melting points. FT-IR spectral data confirmed that coordination occurred via O atom of uracil ring, N atom of azomethine, and S atom of thiophene ring of 5-(thiophene-2-ylmethineazo) group. Except Mn, it was coordination via O atom of uracil ring and N atom of azomethine (Scheme 17).

Üngördü and Tezer (2017) [32] studied theoretically, design metal-mediated-uracil pair complexes, by the DFT method. The results of this study revealed that the uracil connected with metal via  $\text{N}^3$  atom (Scheme 18).

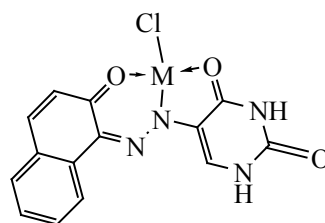
Power et al. (2017) [33] synthesized complexes of the Fe(II), Co(II), Ni(II), Zn(II) and Cd(II), with uracil, and characterized by FT-IR, UV-Vis, magnetic moments and melting points. FT-IR spectral data confirmed that coordination occurred via  $\text{O}^4$  and  $\text{N}^3$  atoms of the deprotonated uracil in addition  $\text{O}^2$  of the neutral uracil (Scheme 19).

Scheme 18.



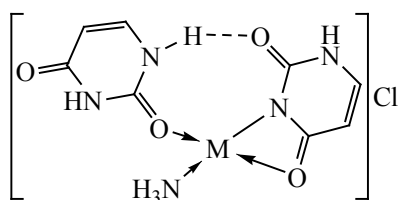
$M = \text{Hg(II)}, \text{Cd(II)}, \text{Zn(II)}, \text{Cu(II)}, \text{Ni(II)}, \text{Pt(II)}, \text{Pb(II)}$ .

Scheme 21.



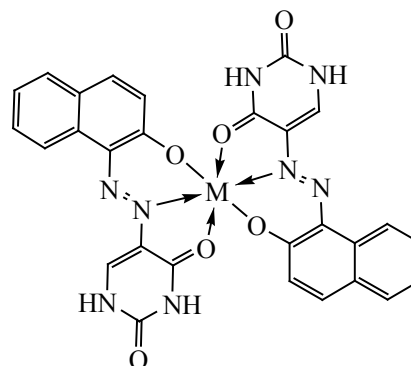
$M = \text{Ni(II)}, \text{Cu(II)}, \text{Zn(II)}$ .

Scheme 19.



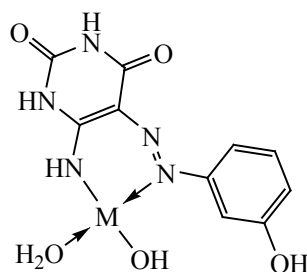
$[M(\text{uracil-H})(\text{uracil})(\text{NH}_3)]\text{Cl}$

$M = \text{Fe(II)}, \text{Co(II)}, \text{Ni(II)}, \text{Zn(II)}, \text{Cd(II)}$ .



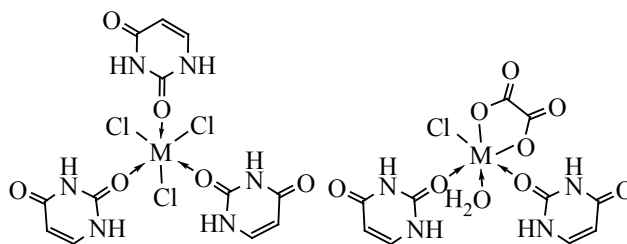
$M = \text{Mn(II)}, \text{Co(II)}$ .

Scheme 20.



$M = \text{Zn(II)}, \text{Cu(II)}, \text{Ni(II)}, \text{Co(II)}$ .

Scheme 22.



$M = \text{Cr(III)}, \text{Fe(III)}$ .

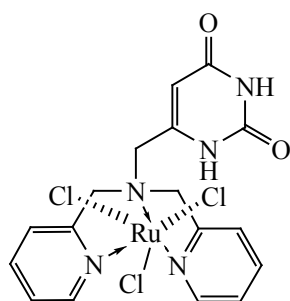
Zaki et al. (2018) [34] prepared Zn(II), Cu(II), Ni(II), and Co(II) complexes with 5-(3-nitrophenylazo)-6-aminouracil, which were characterized by FT-IR, thermal analyses (TGA and DTA), and elemental analysis. FT-IR spectral data confirmed that 5-(3-nitrophenylazo)-6-aminouracil acts as a bi-dentate ligand that binds to the metal ion through both the N=N group and the NH<sub>2</sub> group (Scheme 20).

Philip et al. (2019) [35] synthesized Mn(II), Co(II), Zn(II), Cu(II), and Ni(II) complexes of uracil derivative 1-(2,4-dioxypyrimidine-5-yl)-azonaphth-2-ol (HNAP) and were characterized by UV-Vis, magnetic moments,

melting points and FT-IR. The infrared spectral data confirmed that the HNAP reacts with metal ions via two O-carbonyl and nitrogen atoms (Scheme 21).

Obaid (2019) [36] synthesized mixed ligand metal complexes of the some metal ions with uracil and oxalic acid (Ox),  $[M(\text{uracil})_2(\text{Ox})(\text{OH}_2)\text{Cl}]\cdot\text{H}_2\text{O}$  and  $[M(\text{uracil})_3\text{Cl}_3]$  where  $M = \text{Cr(III)}$  and  $\text{Fe(III)}$ , which were characterized through the FTIR, electronic spectra, and elemental analysis. The structural formula of these chelating agents was obtained by examining these spectra mentioned above (Scheme 22). Also that uracil ligand is

Scheme 23.



[Ru(6-HuracilP)Cl].

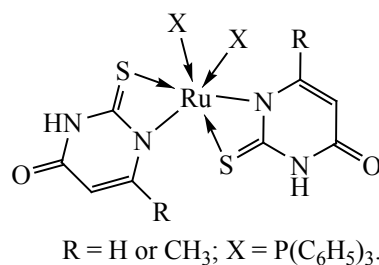
coordinated with Cr(III) and Fe(III) via the O-carbonyl atom.

Gramni et al. (2019) [37] synthesized of new ruthenium(III) complex with uracil derivative, 6-[[bis(pyridin-2-ylmethyl)amino]methyl}uracil (6-HuracilP), and characterized its using physicochemical techniques. It was showed that the 6-HuracilP is connected with ruthenium via N<sup>2</sup>-pyridyl, N-amine, and N-pyridimine coordination mode (Scheme 23).

Correa et al. (2019) [38] synthesized four Ru(II) complexes containing uracil derivatives, 6-methyl-2-thiouracil (MT-uracil) and 2-thiouracil (T-uracil), and characterized using physicochemical techniques. It was found that the complexes containing T-uracil and MT-uracil are coordinated via N<sup>1</sup> and S atoms (Scheme 24).

Teleb et al. (2019) [39] synthesized six complexes of the Mn(II), Co(II), Ni(II), Cu(II), Cd(II), and Ag(I) with uracil derivative 5-bromouracil (Br-uracil). The complexes were characterized using physicochemical techniques. The data showed the all metal ions were

Scheme 24.



R = H or CH<sub>3</sub>; X = P(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>.

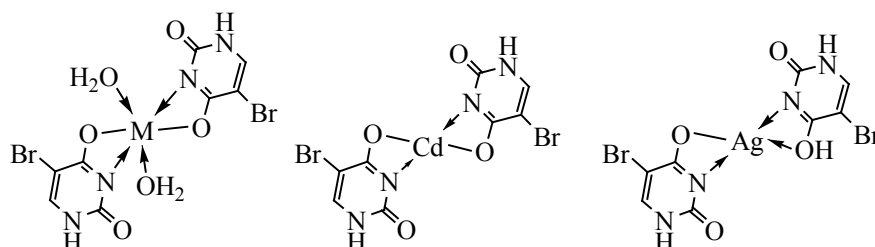
coordinated with 5-bromouracil via N<sup>3</sup> and O<sup>4</sup> atoms (Scheme 25).

Khoshsoroor et al. (2020) [40] synthesized the uracil derivative (uracil-CS), which were used to detect of the copper(II) in the presence of some metals (K<sup>+</sup>, Ag<sup>+</sup>, Cd<sup>2+</sup>, Fe<sup>2+</sup>, Hg<sup>2+</sup>, Ni<sup>2+</sup>, Ba<sup>2+</sup>, Ca<sup>2+</sup>, Co<sup>2+</sup>, Zn<sup>2+</sup>, Cu<sup>2+</sup>, Pb<sup>2+</sup>, Al<sup>3+</sup>, Fe<sup>3+</sup> and Cr<sup>3+</sup>) in an aqueous medium by coordinating the (uracil-CS) with Cu(II) (2 : 1) via the nitrogen and oxygen atoms (Scheme 26).

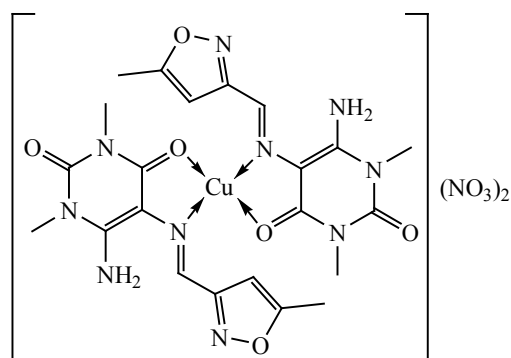
### 3. CONCLUSIONS

Development of new uracil complexes is now attracting the attention of scientists. Uracil and its derivatives are considered as a very important class of organic compounds due to their ability to form complexes with various transition and lanthanide metal ions. Uracil metal complexes have been of much interest over the last years, largely because of its ease of preparation various applications, and variety of coordination numbers. This review aims to cover the prior investigations on the

Scheme 25.



Scheme 26.

[Cu(uracil-CS)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>.

coordination of uracil and its derivatives with various metal ions to form complexes and the donor atoms involved. After reviewing, one can conclude that uracil may be controlled by the electron pair on the N<sup>1</sup>, N<sup>3</sup>, O<sup>2</sup>, or O<sup>4</sup> atoms. This review compiles examples of the most promising uracil complexes.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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