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# Spectral studies on a series of metal ion complexes derived from pyrimidine nucleus, TEM, biological and γ-irradiation effect

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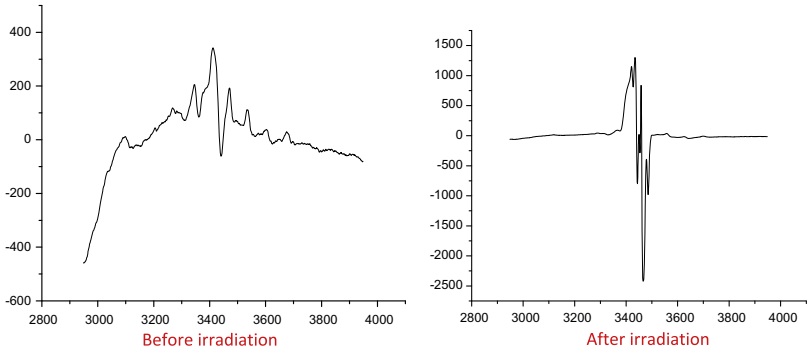
## HIGHLIGHTS

- A series of transition metal ion complexes was prepared using different metal ions with a new derivative of thiouracil.
- The complexes were investigated using all possible tools.
- ESR spectrum of Cu(II) complex was carried out before and after γ-irradiation.
- XRD and TEM were carried out to give insight about the nature of the complexes isolated.
- The biological effect of all investigated compounds was studied on different microorganisms.

## GRAPHICAL ABSTRACT

The EPR spectrum of Cu(II) complex before and after γ-irradiation which may reflect a change in the structural formula of the complex after irradiation.

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## ABSTRACT

A series of thiouracil complexes was prepared, all the prepared compounds are investigated by all possible tools. The ligand coordinates towards two central atoms as a neutral hexadentate mode. The octahedral structure was proposed with Ni(II), Pt(IV) and $UO_2$(II) complexes. Square-pyramidal and square planar with VO(II) and Pd(II) complexes, respectively. VO(II) complex was irradiated by using Gamma radiation to through a light on the probability of geometry changes with the effect of radiation. The parameters calculated from ESR spectra before and after γ-irradiation reflect the rigidity of the complex towards the effect. Such may discuss the unaffected biological behavior before and after irradiation. XRD patterns were carried out to emphasis on the nature of the particles and the purity of products. The ligand, Pt(IV) and Pd(II) are found in nanometer range. TEM is a sensitive tool used to justify on the microstructure and surface morphology. All the investigated compounds are in nanorange. TG curves reflect a lower thermal stability of all investigated complexes due to the presence of water of crystallization. Finally, a toxic effect was observed with all investigated complexes towards Gram positive bacterium as well as a resistant behavior was observed with Gram negative bacteria.



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## Introduction

Compounds containing nitrogen and sulfur as donor atoms have an important role to play as anticancer and antiviral agents [1,2]. Pyrimidine is the parent heterocycle of a very important group of compounds that have been extensively studied due to their occurrence in living systems [3], which exist in nucleic acids, several vitamins, coenzymes and antibiotics. Pyrimidine derivatives are reported to have a broad spectrum of biological activities such as anticancer [4], antiviral, antibacterial, antioxidant [5], anti-inflammatory, analgesic activities, anxiolytic and antidepressant activities [6]. 5-Carbethoxy-2-thiouracil (eitot$H_2$) reacts with copper(I) halides CuX (X ¼Cl, Br, I) to give dinuclear complexes of the formula [CuX(eitot$H_2$)$_2$]$_2$ while mononuclear mixed-ligand complexes of the formula [CuX($PPh_3$)$_2$(eitot$H_2$)] result when the reactions are performed in the presence of two equivalents of triphenylphosphine ($PPh_3$) [7]. New hetero-metallic Cu(II) complexes of thiouracil and report an assessment of their coordination behavior using spectral measurements and thermal studies (TG, DTG and DTA) [8]. Citrazinic acid azo dyes were prepared to dye cellulosic and nylon fibers. Citrazinic acid is used in the field of photography [9,10] as an inhibitor-removing wash bath for direct positive color photographic development. A continuation of my work on the use of thiouracile derivatives to produce metal ion complexes may serve by a distinguish behavior in the biological field [11,12]. The aim in this paper is to investigate the complexes prepared spectrally to emphasis on their chemistry. TEM is a sensitive spectral tool used to give insight about the size of the investigated particles. The structural formula of VO(II) complex was investigated before and after irradiation by Gamma rays to give an insight about the deformation on the complex crystal or reflecting its rigidity which my reflect on the complex biological behavior.

## Experimental

### Reagents

All chemicals used in this study were of analytically reagent grade, commercially available from fulka and used without previous purification as $Ni(NO_3)_2{\cdot}6H_2O$, $VOSO_4{\cdot}2H_2O$, $PdCl_2$, $H_2PtCl_6$ and $UO_2(NO_3)_2$ compounds, which represents the metal ions used in the complexation process. All solvents were used as it is without previous purifications.

### Synthesis of the ligand

The synthesis of thiouracil derivatives was carried out previously [13]. 0.1 mol of 4-chlorobenzene-1,2-diamine was mixed with HCl (0.2 mol in 25 ml distilled water) and diazotized below 5 °C with $NaNO_2$ (0.1 mol) in distilled water (30 ml). The resulting diazonium chloride was coupled with an alkaline solution of 2-thiouracil (0.1 mol) below 5 °C with equimolar ratio (0.02 mol). The reaction mixture was stirred under reflux for ≈1 h. The volume of the resultant solution was reduced to a half by evaporation then the solid product was precipitated, separated, washed with $Et_2O$ and dried in vacuum over calcium chloride (Fig. 1) .

### Synthesis of the metal ion complexes

All metal ion complexes were prepared according to Eqs. (1)-(3), by mixing equimolar (0.01 mol) from each metal salt with the organic ligand (0.01 mol) dissolved previously in ammonia solution (1:1, 25 ml). The reaction mixture was left over night where the resulting solid complexes were isolated by filtration, washed several times with EtOH followed by $Et_2O$ and dried in a vacuum dissector over anhydrous $CaCl_2$.

$$2Ni(NO_3)_2\cdot 6H_2O \text{ or } 2UO_2(NO_3)_2 + H_4L \xleftrightarrow{\text{Solvent}} [M_2(NO_3)_2(H_4L)\cdot 2(H_2O)_2]2(NO_3)2H_2O \quad (1)$$

$$VOSO_4\cdot 2H_2O + H_4L \xleftrightarrow{\text{Solvent}} [(VO)_2(SO_4)(H_4L)(H_2O)]SO_4\cdot 2H_2O \quad (2)$$

$$PdCl_2 \text{ or } H_2PtCl_6 + H_4L \xleftrightarrow{\text{Solvent}} [M_2(X)_n(H_4L)]2X\cdot 2H_2O, \text{ where } n = 2 \text{ and } 6, \text{ respectively} \quad (3)$$

### Molecular modeling

Attempt to obtain an acceptable view about the best orientation of several active sites towards each other's through implemented hyperchem 7.5 program [14]. Molecular modeling structure of the ligand and its complexes were obtained. The geometry optimization in our study is focusing on calculating a total energy content by the use of molecular mechanics ($MM^+$) [15] force-field.

### Biological studies

#### Antibacterial screening

Antibacterial screening is performed in vitro by the agar disc diffusion method [16]. The species used in the screening are *Escherishia coli sp.* and *Klebsiella* sp. as Gram-negative bacteria, *Bacillus subtilis* as Gram-positive bacterium. Stock cultures of the tested organisms are maintained on nutrient agar media by sub culturing in Petri dishes. The media are prepared by adding the components as per manufacturer's instructions and sterilized in the autoclave at 121 °C and atmospheric pressure for 15 min. Each medium is cooled to 45–60 °C, 20 ml of it is poured into a Petri dish and allowed to solidify. After solidification, Petri plates with media are spread with 1.0 ml of bacterial or fugal suspension prepared in sterile distilled water. The wells are bored with cork borer and the agar plugs are removed. To each agar well, unique concentration of 100 μg for each compound in DMSO (75 μl) were applied to the corresponding well (6 mm). All the plates are incubated at 37 °C for 24 h and they are observed for the growth inhibition zones. The presence of clear zones around the wells indicate that the ligand and its complexes are active. The diameter of zone of inhibition is calculated in millimeters. The well diameter is deducted from the zone diameter and the values are tabulated.

#### Genotoxicity

A Calf thymus DNA (2 mg) was dissolved in 1 ml of sterile distilled water and completed to a final concentration of 2 g/l. Stock concentrations of the ligand and their complexes were prepared by dissolving 2 mg/ml in DMSO. An equal volume of each compound and DNA were mixed thoroughly and kept at room temperature for 2–3 h. The effects of the chemicals on the DNA were analyzed by agarose gel electrophoresis. A 2 μl of loading dye was added to 15 μl of the DNA-chemical mixture before being loaded into the wall of an agarose gel. The loaded DNA-chemical mixtures were fractionated by electrophoresis, visualized by UV and photographed.

### Physical measurements

The elements content (carbon, hydrogen and nitrogen) were determined using a Perkin–Elmer CHN 2400 in the Micro-analytical Unit. Chloride and metal contents were determined using standard methods [17]. The $UO_2$ content in its complex was