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# Synthesis, spectral characterization and biological studies of copper(II) complexes bearing azomethine thiourea ligands

Quang Trung Nguyen\*  | Phuong Nam Pham Thi | Van Tuyen Nguyen

*Institute of Chemistry, Vietnam Academy of Science and Technology, Hanoi, Vietnam*

Cytotoxic metal complexes have drawn significant attention from biochemists nowadays. These bioactive coordination compounds of potential ligands with biological functional groups and suitable metal ions have garnered considerable interest. In this study, hybrid azomethine thiourea ligands and their copper(II) complexes were prepared and studied using modern physicochemical techniques. The spectral data have shown that the coordination was carried out through N, N, O, and S atoms. One unpaired electron  $d^9$  configuration and the distorted square-planar environment were suggested for the synthetic copper(II) complexes. The electrochemical properties of the Schiff base thiourea copper(II) complexes were investigated. The antioxidant activities of all azomethine thiourea copper(II) complexes were identified by DPPH method using curcumin as a positive control. *In vitro* cytotoxic activity against human cancer cell lines, hepatocellular carcinoma (HepG-2) and human lung adenocarcinoma (A549) of the received copper(II) complexes was examined. The obtained results have indicated that  $[Cu(II)LCl]$  possessed the best cytotoxicity for HepG-2 and A549 with 50% inhibitory concentration ( $IC_{50}$ ) = 2.41 and 1.88  $\mu g/ml$ , respectively.

**\*Corresponding Author:**

Quang Trung Nguyen

EMAIL: [trungquang\\_cnhh@yahoo.com](mailto:trungquang_cnhh@yahoo.com)

Tel.: +840909901871

**KEYWORDS**

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**Introduction**

Coordination complexes of potential ligands with bioactive functional groups and suitable metal ions have received intensive interest recently [1-4]. Thioureas belong to organic compounds containing thiourea group which are very diverse in their structure and various applications [5,6]. They are essential commercially, industrially, and academically. Thioureas are usually used in the film and plastic industry, elastomers, dyes, textiles, and solar cells [7,8]. Thiourea derivatives could be applied as pharmaceuticals, preservatives, herbicides, and insecticides [9-11]. Thioureas possess biological activities effectively.

They are described to have antioxidant, antifungal, antiviral, antibacterial, antitubercular, anti-inflammatory, anti-convulsant, anticancer, and anti-thyroid activities [12-15]. Azomethine compounds or Schiff base compounds are reported to be some of the most widely used compounds [16,17]. They can be applied as optical materials, photosensitizers, urease inhibitors [18-20]. Schiff bases have also exhibited a broad range of biological activities. They have herbicidal, antibacterial, antifungal, anti-inflammatory, antitubercular, antiviral, and antitumor properties [21-24]. Both thiourea and azomethine compounds can coordinate with transition metals to create

potential metal complexes which could be found in various structures [25-30], and also useful applications such as luminescent complexes, antibacterial agents, antioxidant compounds, cytotoxic compounds, etc. [30-33]. The combination of thiourea and Schiff base moieties with various substituted groups can create new hybrid ligands and induce interesting metal complexes. Therefore, in this study, some Schiff base thiourea compounds and their copper(II) complexes were prepared and studied by spectral and physical methods. The antioxidant and anticancer activity of the synthetic copper(II) complexes were estimated.

### Materials and methods

Chemical reagents including *o*-phenylenediamine (98%), phenyl isothiocyanate (98%), aldehydes and other chemicals such as anhydrous  $\text{Na}_2\text{CO}_3$  (98.5%), and  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  (99.0%) were purchased from commercial companies and used without more purification.

#### *Synthesis of Schiff base thiourea ligands*

Ligands  $\text{H}_2\text{L}$ - $\text{H}_2\text{L3M}$  (Table 1) were synthesized following the modified known method [34] by mixing equimolar amounts of *o*-phenylenediamine and phenylisothiocyanate in ethanol. The reaction was carried out for several hours until it ran completely. After that, the respective equimolar aldehyde in ethanol was dropped into the reaction solution and ran for 3 hours more. The observed solid precipitates were collected and dried under vacuum. The spectral data of the synthetic azomethine thiourea ligands such as TOF-MS,  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR, and FTIR were recorded and presented in Tables 1-4.

#### *Preparation of azomethine thiourea copper(II) complexes*

Azomethine thiourea copper(II) complexes were prepared according to the modified literature procedure [35] using  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  and synthetic thiourea Schiff base ligands. The methanol solution containing  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  (1.0 mmol) was added to the dichloromethane

solution of the respective ligand (1.0 mmol) and  $\text{Na}_2\text{CO}_3$  (1.0 mmol) was used as the neutralizing reagent under magnetic stirring for overnight. The reaction was observed by TLC until it occurred completely. The obtained precipitates were collected and dried under vacuum. The obtained copper(II) complexes were examined for physicochemical features by ESI-MS, FTIR, and UV-Vis spectroscopy and the result data were exhibited in Tables 1 and 4.

#### *Electrochemical studies*

The electrochemical property of the synthetic complexes was studied. The cyclic voltammograms of the synthetic complexes were obtained on an IM6 Zahner Elektrik instrument using copper(II) complexes' concentration of  $5.0 \times 10^{-2}$  M in DMSO solution and the supporting electrolyte as  $\text{LiClO}_4$  0.1 M. At room temperature, all experiments were run in a cell containing three electrodes (the working electrode was a graphite carbon; the counter electrode was a platinum wire and the reference electrode was  $\text{Ag}/\text{AgCl}$ ) at a scan rate of  $200 \text{ mV s}^{-1}$  and the potential window -3.4 V to +1.3 V.

#### *Biological activities*

##### *Antioxidant assay*

Synthetic Schiff base thiourea copper(II) complexes were examined for their antioxidant activity using DPPH assay. This assay is based on the color change of 1,1-diphenyl-2-picrylhydrazine (DPPH) from violet to yellow when deactivated by antioxidants in a radical scavenging model [36]. DMSO solutions of tested complexes were prepared and adjusted to various concentrations of 128, 32, 8, 2, and 0.5  $\mu\text{g}/\text{ml}$ . A 1 ml methanolic solution (0.3 mM) of DPPH was added to 1 ml of the prepared complexes' solutions and standard compound, curcumin. Each test was kept in the dark for 30 min and the absorbance was determined in triplicate at the wavelength of 517 nm using a Biotek Epoch 2 Microplate Reader. The DPPH scavenging activity (DSA) (%) was estimated following the simple Equation (1) where,  $\text{OD}_b$  was

the absorbance of the control reaction containing all reagents except the test compound and  $OD_t$  was the absorbance of the tested sample and standard.

$$DSA (\%) = [(OD_b - OD_t) / OD_b] \times 100 \quad (1)$$

$EC_{50}$  was determined from the curve plotting between the inhibition percent vs. concentration. The obtained results were presented in Table 6.

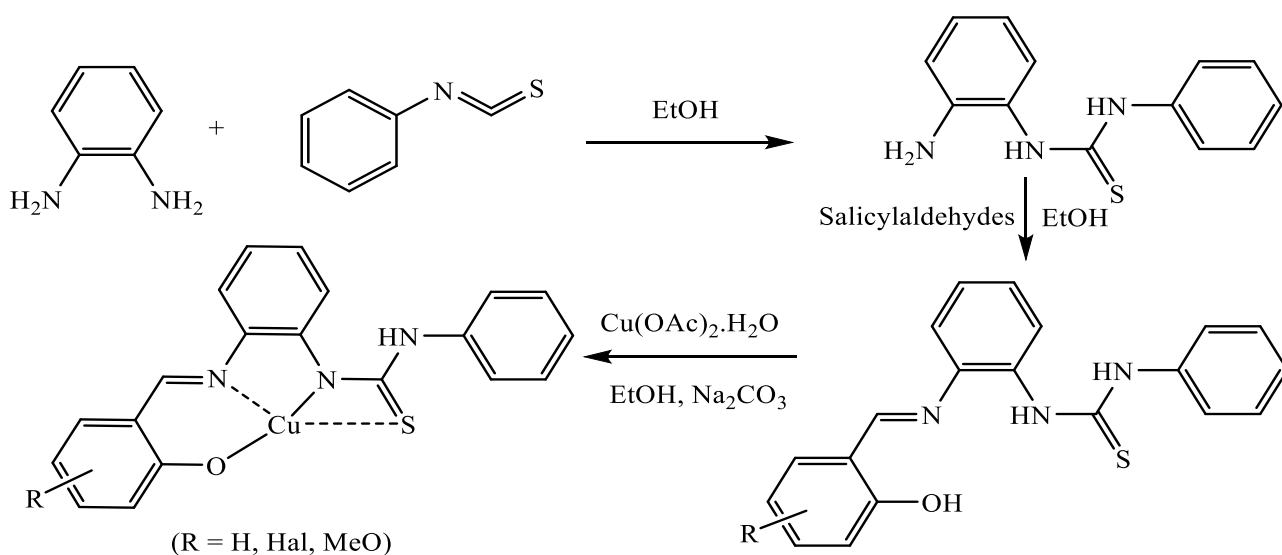
#### *In vitro* cytotoxicity assay

Human cancer cell lines, HepG-2, and A549 were used to evaluate the anticancer activity of the synthetic copper(II) complexes using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) reduction approach according to Mosmann's modified method [37]. Ellipticine was used as the reference drug for comparison. The 50% inhibitory concentration ( $IC_{50}$ ,  $\mu\text{g/ml}$ ) values [38] were estimated and presented in Table 7.

## Results and discussion

### *Chemical and physical studies*

Schiff base thiourea compounds were synthesized by a process including 2 steps (Scheme 1): The initial step was the addition of phenyl isothiocyanate to the diamine, and then it was the condensation of the added product and salicylaldehydes in the second step. The product yields obtained were quite good (65.0-75.0%). The synthetic azomethine ligands may be dissolved in chloroform, ethyl acetate, ethanol, and DMSO. These obtained Schiff base thiourea ligands were studied by HRMS, FTIR,  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectroscopies. The copper(II) complexes were formed by the coordination of these Schiff base thiourea ligands with  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  in the mole ratio of 1:1 with  $\text{Na}_2\text{CO}_3$  as neutralizing agent and ethanol as solvent (Scheme 1). The coordination yields were high (87.5-93.5%). The prepared copper(II) complexes are soluble in some polar solvents such as dichloromethane, acetonitrile, and DMF. The obtained complexes were characterized by the spectroscopies of ESI-MS, FTIR, UV-Vis, and magnetic moment measurements ( $\mu_{\text{eff}}$ ).



**SCHEME 1** Synthesis of azomethine thiourea ligands and their mononuclear copper(II) complexes

**TABLE 1** Azomethine thiourea ligands and their mononuclear copper(II) complexes

R	Compound	Yield (%)	Mol. Weight (Cal.)	$\mu_{\text{eff}}$ (BM)	Geometry
H	H <sub>2</sub> L	68.5	348.1168 (M <sup>+</sup> ) (348.4425)	-	-
	[Cu(II)L]	90.0	409.0 (M <sup>+</sup> ) (409.9)	2.02	Distorted square-planar
F	H <sub>2</sub> LF	73.5	366.0949 (M <sup>+</sup> ) (366.4330)	-	-
	[Cu(II)LF]	91.5	426.9 (M <sup>+</sup> ) (427.9)	1.81	Distorted square-planar
Cl	H <sub>2</sub> LCl	75.0	382.0778 (M <sup>+</sup> ) (382.8873)	-	-
	[Cu(II)LCl]	93.0	442.9 (M <sup>+</sup> ) (444.4)	2.15	Distorted square-planar
Br	H <sub>2</sub> LBr	72.5	426.0134 (M <sup>+</sup> ) (427.3386)	-	-
	[Cu(II)LBr]	93.5	486.8 (M <sup>+</sup> ) (488.8)	1.93	Distorted square-planar
5-MeO	H <sub>2</sub> L5M	67.0	378.1272 (M <sup>+</sup> ) (378.4685)	-	-
	[Cu(II)L5M]	89.0	438.9 (M <sup>+</sup> ) (439.9)	2.10	Distorted square-planar
3-MeO	H <sub>2</sub> L3M	65.0	378.1271 (M <sup>+</sup> ) (378.4685)	-	-
	[Cu(II)L3M]	87.5	438.9 (M <sup>+</sup> ) (439.9)	2.12	Distorted square-planar

From +IDA-TOF-MS spectra which were recorded on a Sciex X500 QTOF spectrometer, the pseudo-molecular ion signals of the obtained ligands are observed as [M<sup>+</sup>] which clearly indicated the molecular masses are well suitable to the supposed formulae. In ESI-MS spectra of synthetic copper(II) complexes conducted on Agilent 6310 Ion Trap spectrometer, pseudo-molecular ion peaks are assigned to [M<sup>+</sup>] which show that mononuclear coordination compounds are quite well in agreement with the proposed formulae (Table 1). Due to the molecular structure feature, the obtained Schiff base thiourea ligands can be observed in the forms of keto-amine or enol-imine [39]. On <sup>1</sup>H-NMR spectra of the ligands, there were single peaks at 11.98-12.69 ppm attributed to the protons of OH and single peaks at 8.84-8.88 ppm attributed to the protons of CH=N which induced the

synthesized ligands in the enol-imine form (Scheme 1) [34]. A single peak at 9.87-9.93 ppm could be assigned to the proton of NH-Phenyl, while the proton of the NH-o-phenylene appeared at 9.43-9.46 ppm as a single signal. Three protons of methoxy groups could be observed at 3.74 and 3.82 ppm as single peaks (Table 2).

On <sup>13</sup>C-NMR spectra of the ligands, there were typical peaks at 179.82-180.05 ppm assigned to the carbon of C=S, at 161.18-163.37 ppm attributed to the carbon of C=N, at 150.37-160.08 ppm attributed to the carbon of C-OH, at 133.06-144.16 ppm to the carbons of C-N bondings. The carbon signals of phenyl and salicyl rings should be found at 114.78- 133.37 ppm. The carbons of methoxy groups have appeared at 55.54 and 55.89 ppm (Table 3).

**TABLE 2** Typical <sup>1</sup>H-NMR data of Schiff base thiourea ligands

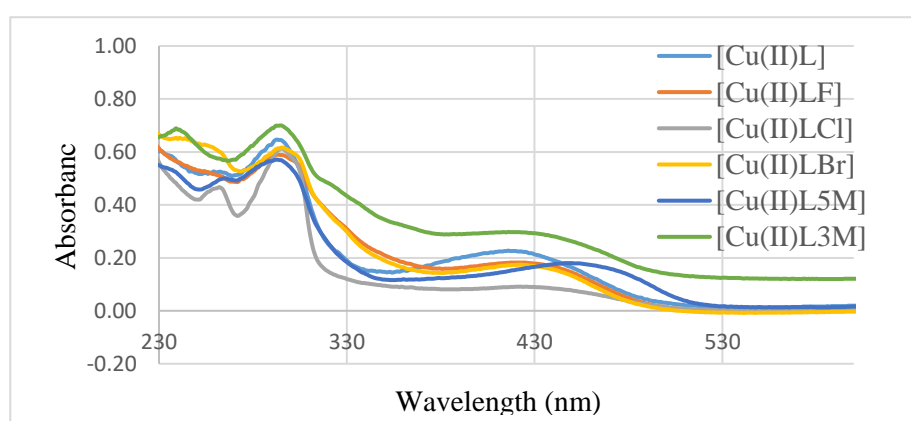
Compound	$\delta$ (ppm), protons of				
	OH	NH	CH=N	Ph, Sal	MeO
H <sub>2</sub> L	12.62 (s, 1H)	9.87 (s,1H); 9.45 (s,1H)	8.88 (s, 1H)	7.65 – 6.96 (13H)	-
H <sub>2</sub> LF	12.17 (s, 1H)	9.93 (s,1H); 9.46 (s,1H)	8.86 (s, 1H)	7.75 – 6.98 (12H)	-
H <sub>2</sub> LCl	12.55 (s, 1H)	9.90 (s,1H); 9.45 (s,1H)	8.86 (s, 1H)	7.76 – 7.00 (12H)	-
H <sub>2</sub> LBr	12.59 (s, 1H)	9.90 (s,1H); 9.45 (s,1H)	8.85 (s, 1H)	7.89 – 6.95 (12H)	-
H <sub>2</sub> L5M	11.98 (s, 1H)	9.88 (s,1H); 9.43 (s,1H)	8.84 (s, 1H)	7.65 – 6.90 (12H)	3.74 (3H)
H <sub>2</sub> L3M	12.69 (s, 1H)	9.89 (s,1H); 9.44 (s,1H)	8.87 (s, 1H)	7.66 – 6.90 (12H)	3.82 (3H)

**TABLE 3**  $^{13}\text{C}$ -NMR data of azomethine thiourea ligands

Compound	$\delta$ (ppm), carbons of						
	C=S	CH=N	C-O	C-Hal or C-OCH <sub>3</sub>	C-N	Ph, Sal	CH <sub>3</sub> O
H <sub>2</sub> L	180.04	163.18	160.08		143.94; 139.11; 133.33	133.10 – 116.75 (14 C)	-
H <sub>2</sub> LF	179.82	161.18	156.19	155.71 and 154.16	143.53; 139.03; 133.30	128.48 – 116.12 (13 C)	-
H <sub>2</sub> LCl	179.99	161.36	158.68	122.53	143.68; 139.07; 133.27	132.77 – 118.59 (13 C)	-
H <sub>2</sub> LBr	180.01	161.36	159.09	109.89	143.72; 139.08; 135.53	133.37 – 118.82 (13 C)	-
H <sub>2</sub> L5M	180.04	162.73	154.16	151.82	144.16; 139.16; 133.08	128.40 – 114.78 (13 C)	55.54
H <sub>2</sub> L3M	180.05	163.37	150.37	147.92	143.75; 139.13; 133.06	128.42 – 115.63 (13 C)	55.89

**TABLE 4** Some selected IR data of Schiff base thiourea ligands and their copper(II) complexes

Compound	$\nu_{\text{N-H}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{N-H}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{C=N}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{C-N}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{C-O}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{C=S}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{Cu-O}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{Cu-S}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{Cu-N}}$ ( $\text{cm}^{-1}$ )
H <sub>2</sub> L	3280	3140	1615	1383	1259	1152	-	-	-
[Cu(II)L]	3300	-	1608	1365	1245	1147	603	535	498
H <sub>2</sub> LF	3267	3155	1617	1358	1253	1172	-	-	-
[Cu(II)LF]	3223	-	1609	1310	1243	1144	603	535	492
H <sub>2</sub> LCl	3265	3157	1615	1356	1274	1179	-	-	-
[Cu(II)LCl]	3303	-	1608	1311	1243	1159	611	560	491
H <sub>2</sub> LBr	3269	3159	1615	1355	1273	1177	-	-	-
[Cu(II)LBr]	3198	-	1608	1301	1245	1157	610	555	491
H <sub>2</sub> L5M	3262	3148	1622	1377	1272	1156	-	-	-
[Cu(II)L5M]	3316	-	1606	1292	1261	1152	607	528	492
H <sub>2</sub> L3M	3316	3145	1612	1369	1254	1188	-	-	-
[Cu(II)L3M]	3270	-	1603	1309	1244	1182	604	504	479

**FIGURE 1** UV-Vis absorption spectra of Schiff base thiourea Cu (II) complexes

On IR spectra of the synthetic Schiff base thioureas, there were typical signals presented for two N-H vibrations, one at 3262- 3316  $\text{cm}^{-1}$  [40] and one at 3140-3159  $\text{cm}^{-1}$ . The signals were

observed at 1612-1622  $\text{cm}^{-1}$  presented for C=N, at 1355-1383  $\text{cm}^{-1}$  performed for C-N and at 1253-1274  $\text{cm}^{-1}$  exhibited for C-O [27,41] stretching vibrations. There were typical signals

at 1152 – 1188  $\text{cm}^{-1}$  for C=S stretching vibrations probably. On IR spectra of the synthetic Schiff base thiourea copper(II) complexes, there were still the typical signals at 3198 – 3316  $\text{cm}^{-1}$  which could represent for vibrations of the last N–H bonding [32]. The typical peaks were at 1603-1609  $\text{cm}^{-1}$  presented for C=N, at 1292 -1365  $\text{cm}^{-1}$  for C–N, at 1243-1261  $\text{cm}^{-1}$  for C–O, and at 1144-1182  $\text{cm}^{-1}$  for C=S vibrations (Table 4). The signals of one N–H vibration were disappeared and there were new signals at 603-611, 504-560 and 479-498  $\text{cm}^{-1}$  for Cu–O, Cu–S, and Cu–N stretching vibrations, respectively, which have demonstrated the coordination of  $\text{Cu}^{2+}$  with the ligands through N, N, O, and S atoms. Electronic spectra of the synthetic complexes (200 – 600 nm) in  $6.0 \times 10^{-5}$  M methanol solution were recorded on a Perkin Elmer Lambda UV-35 spectrophotometer and displayed in Figure 1. The absorption bands at 230-270 nm could be attributed to high-energy intraligand transition of  $\pi \rightarrow \pi^*$  [42]. The maximum absorption wavelength at 270-320 nm could perform for  $n \rightarrow \pi^*$  free electronic transitions of imine, thiourea and phenoxy groups. A low band was observed at 350-500 nm, which could be attributed to LMCT transition or d-d transition band in the structure of studied copper(II) complexes [43,44]. The LMCT absorption band in  $[\text{Cu}(\text{II})\text{L5M}]$  bearing substituted electron-donating methoxy was shifted to a quite longer wavelength relative to  $[\text{Cu}(\text{II})\text{L}]$ . In addition, the effective magnetic moments of studied copper(II) complexes were determined in the range of 1.81-2.15 B.M (Table 1) which were suitable to the electron  $d^9$  configuration and indicate a distorted square-planar geometry around Cu(II) center [45-47].

#### *Electrochemical analysis*

The electrochemical behaviors of the synthetic Schiff base thiourea copper(II) complexes were studied. The cyclic voltammograms of azomethine thiourea copper(II) complexes are studied in DMSO solution containing  $\text{LiClO}_4$  0.1 M as supporting electrolyte and at a scan rate of 200  $\text{mV}\cdot\text{s}^{-1}$ . In the reductive scan, all the complexes

showed one reductive peak at  $E_{pa} = (-1.07)$ - $(-0.546)$  V. On the reverse scan, the complexes showed an oxidative peak, respectively, at  $E_{pc} = (-1.22)$ - $(-0.91)$  V. The reductive and oxidative waves could be assigned to metal centred electron transfer reactions and reversible redox couple of  $\text{Cu}(\text{II}) \leftrightarrow \text{Cu}(\text{I})$  (Table 5) probably [42]. Some shifts in the reductive and oxidative peaks of the Cu(II) complexes bearing substituted groups to higher or lower field regard to  $[\text{Cu}(\text{II})\text{L}]$  would be expected from the electronic and stereochemical influence of the substituted groups.

#### *Antioxidant activity of the synthetic Schiff base thiourea complexes*

The antioxidant activities of synthetic Schiff base thiourea copper(II) complexes were evaluated using DPPH method. The biological results showed that all prepared complexes exhibited good antioxidant activity with  $\text{EC}_{50} < 20$   $\mu\text{g}/\text{ml}$ . This activity may depend on imine, hydroxyl and thiourea groups. The substituted groups of both halogens and methoxy enhanced their antioxidant activity. The best one belonged to  $[\text{Cu}(\text{II})\text{LF}]$  with  $\text{EC}_{50} = 3.91$   $\mu\text{g}/\text{ml}$  which was much better than standard compound, curcumin with  $\text{EC}_{50} = 7.64$   $\mu\text{g}/\text{ml}$ .

#### *In vitro Cytotoxicity of Schiff base thiourea copper(II) complexes*

The obtained Cu(II) complexes were evaluated for their cytotoxicity against human cancer cell lines, HepG-2 and A549 using MTT assays. The standard drug, ellipticine, was used for comparison.  $\text{IC}_{50}$  values for the tested complexes were estimated and exhibited in Table 7. They revealed that all synthetic azomethine thiourea copper(II) complexes had quite good activity for tested human cancer cell lines with  $\text{IC}_{50} < 15$   $\mu\text{g}/\text{ml}$ .  $[\text{Cu}(\text{II})\text{LCl}]$  containing chloro group and  $[\text{Cu}(\text{II})\text{L3M}]$  possessing methoxy group performed the best antitumor activity for HepG-2 with  $\text{IC}_{50} = 2.41$  and 3.0  $\mu\text{g}/\text{ml}$ , respectively.  $[\text{Cu}(\text{II})\text{LCl}]$  and  $[\text{Cu}(\text{II})\text{L3M}]$  also showed the best antitumor activity against A549 with  $\text{IC}_{50} = 1.88$

and 1.81  $\mu\text{g/ml}$  which was quite near to the activity of ellipticine with  $\text{IC}_{50} = 0.48 \mu\text{g/ml}$ . It is notable that the cytotoxicity of the obtained mononuclear complexes for HepG-2 and A549

was in the arrangement of  $[\text{Cu(II)LCl}] \sim [\text{Cu(II)L3M}] > [\text{Cu(II)L}] \sim [\text{Cu(II)L5M}] > [\text{Cu(II)LBr}] > [\text{Cu(II)LF}]$ .

**TABLE 5** Reduction and oxidation potential of Schiff base thiourea copper(II) complexes

Complex	$E_{pc}$ (V)	$E_{pa}$ (V)	$\Delta E$ (mV)
[Cu(II)L]	- 1.09	- 0.999	91
[Cu(II)LF]	- 0.91	- 0.546	364
[Cu(II)LCl]	- 1.12	- 1.07	50
[Cu(II)LBr]	- 1.05	- 0.895	155
[Cu(II)L5M]	- 1.22	- 1.07	150
[Cu(II)L3M]	- 1.01	- 0.938	72

**TABLE 6** Antioxidant activity of the synthetic azomethine thiourea copper(II) complexes

Compound	$\text{EC}_{50}$ ( $\mu\text{g/ml}$ )
[Cu(II)L]	$18.98 \pm 2.0$
[Cu(II)LF]	$3.91 \pm 0.25$
[Cu(II)LCl]	$5.64 \pm 0.50$
[Cu(II)LBr]	$6.62 \pm 0.50$
[Cu(II)L5M]	$4.98 \pm 2.0$
[Cu(II)L3M]	$12.44 \pm 0.82$
Curcumin	$7.64 \pm 0.50$

**TABLE 7** *In vitro* Cytotoxicity of Schiff base thiourea Cu (II) complexes

Compound	$\text{IC}_{50}$ ( $\mu\text{g/ml}$ )	
	HepG-2	A549
[Cu(II)L]	$4.0 \pm 0.08$	$6.28 \pm 0.59$
[Cu(II)LF]	$8.91 \pm 0.72$	$12.65 \pm 0.95$
[Cu(II)LCl]	$2.41 \pm 0.08$	$1.88 \pm 0.05$
[Cu(II)LBr]	$8.3 \pm 0.63$	$10.17 \pm 0.89$
[Cu(II)L5M]	$4.92 \pm 0.01$	$5.87 \pm 0.12$
[Cu(II)L3M]	$3.0 \pm 0.12$	$1.81 \pm 0.12$
Ellipticine	$0.37 \pm 0.05$	$0.48 \pm 0.03$

## Conclusion

In this study, the synthesis of six mononuclear copper(II) complexes bearing Schiff base thiourea ligands was carried out and characterized by spectroscopies. The synthetic mononuclear complexes were created by the coordination of  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  and the hybrid ligands in the presence of  $\text{Na}_2\text{CO}_3$ . Schiff base

thiourea ligands could act as tetradentate ligands with N, N, O, and S atoms in coordination. The coordination geometry around the central ion was confirmed to be distorted square-planar. Their electrochemical behaviors were conducted. In the received cyclic voltammograms of synthetic Cu(II) complexes, the redox couple waves were observed to indicate the reversible reaction of  $\text{Cu(II)} \leftrightarrow \text{Cu(I)}$  probably. The

synthetic Schiff base thiourea complexes were examined for their antioxidant activity with curcumin as the standard compound. The results indicated that their antioxidant activity was enhanced with substituted groups. In addition, HepG-2 and A549 cancer cell lines were used to estimate the *in vitro* anticancer activity of the received mononuclear copper(II) complexes. All prepared azomethine thiourea copper(II) complexes showed good cytotoxicity with  $IC_{50} < 15 \mu\text{g/ml}$  in which  $[\text{Cu}(\text{II})\text{LCl}]$  containing chloride group exhibited the best activity for tested cancer cell lines with  $IC_{50} = 2.41$  and  $1.88 \mu\text{g/ml}$ , respectively.

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### Authors' Contributions

Quang Trung Nguyen contributed conception, methodology, the data analysis and article preparation; Phuong Nam Pham Thi obtained the data; Van Tuyen Nguyen supervised the research.

### Conflict of Interest

The authors declare that there is no conflict of interest in publishing this article.

### Orcid:

Quang Trung Nguyen\*:

<https://www.orcid.org/0000-0002-6882-4124>

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