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Research Article

Anti-microbial resistance studies of silver (I) and copper (II) from the acylation of urea ligand with benzoyl chloride

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ABSTRACT

This research focused on the growing danger of antibiotic resistance, which is a worrying issue for public health, especially in Africa, where the uncontrolled sale of antibiotics and inappropriate use of these medicines promote the development of drug-resistant pathogens. The rise of drug-resistant microbes poses a serious public health challenge, reducing the effectiveness of existing treatments. New antimicrobial compounds based on Ag(I) and Cu(II) amide complexes were synthesized by acylating urea ligands with benzoyl chloride. Spectroscopic and crystallographic properties of the synthesized complexes were analyzed using Fourier-transform infrared (FTIR), X-ray diffraction, and ultraviolet-visible spectroscopy. These compounds demonstrated unique coordination patterns and crystalline structures, which allow the Cu(II) complex to outperform the free ligand control against *Escherichia coli, Staphylococcus aureus, Salmonella typhi and Candida albicans. We* assign these robust antimicrobial properties to the efficient penetration and binding of the metal complexes to the microbial cell membrane due to metal-ligand chelating effects. Although their effectiveness was less than that of the standardized drugs Imipenem and Amphotericin under the tested conditions, their clinical usefulness may be improved with additional refinements and create alternative pathways for the development of effective antimicrobial agents. The inference from the finding is that the complexes have shown promise as alternative antimicrobial compounds, especially in cases of drug resistance where conventional antibiotics fail. These results have expanded the search for new metal-based antimicrobial agents, with a strong foundation for future drug development against resistant infections, as there are limited studies using these metals.

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INTRODUCTION

Antimicrobial resistance (AMR) represents one of the most significant threats to global health as it has accelerated over the past few years and borders on the edge of being undefinable [1–3]. It is immensely lethal to developing countries because antibiotics are increasingly becoming ineffective [4]. Drug-resistant pathogens are evolving at an unprecedented pace due to uncontrolled use of antibiotics and unrestricted commercialization of healthcare services [5]. This calls for new methods with more promising means of conducting novel treatments targeting the mechanisms of action of these medications. Transition metal complexes, particularly those of copper (II) and silver (I), are receiving attention due to their potentially useful antimicrobial activity [6, 7]. These metals can form stable coordination compounds with ligands, which further improve their biological activity due to enhanced penetration and binding to microbial membranes [7]. It is important to note that urea and its derivatives possess coordinated versatility and therefore can be used for complexation with bioactive metals [8-10]. The presence of transition metals enables them to engage in electron transfer redox reactions and generate reactive oxygen species, which are crucial to antimicrobial processes [11]. For example, silver has been reported to act by destabilizing the cell walls of microbes and inhibiting key metabolic activities [11]. Such key intrinsic properties, combined with the presence of organic ligands possessing flexible structures, offer a new approach to dealing with the problem of drug resistance. In the present work, novel N-substituted Ag(I) and Cu(II) amide complexes were synthesized and characterized in which urea ligands were acylated with benzoyl chloride.

MATERIALS AND METHODS

Materials

Ligand synthesis: 0.013 mol of freshly prepared substituted benzoyl chloride was mixed dropwise into a 20 mL acetonic solution of 0.013 mol of ammonium thiocyanate under constant stirring for approximately 20 mins. Afterward, 25 mL of an acetonic solution of 0.0065 mol of 4-chloro-1,2-phenylenediamine was added to the aliquot, heated to 50 °C, and the reaction was allowed to proceed for 3 h under reflux. The resulting solution was transferred into a 250 mL beaker and placed in an ice bath for crystallization. The precipitated samples were collected by vacuum filtration and washed several times with cold 1:1 ethanol/water mixture to purify them. Further purification was performed by recrystallization using a 1:1 mixture of ethanol and dichloromethane [12].

Acylation of urea: A solution of 0.013 mol benzoyl chloride in 25 mL anhydrous acetone was added drop by drop to a solution containing 0.013 mol of urea in 25 mL dry acetone under constant stirring using a magnetic stirrer. Some pieces of anti-bumping chips were added to the obtained colorless solution and heated under a reflux condenser for 3 h, followed by cooling to about 25 °C. Vacuum filtration was used to collect the precipitated sample, which was washed using a cold ethanol/water mixture to remove any unreacted impurities. Using a 1:1 ethanol/dichloromethane combination, the white crystals of benzoylurea were recrystallized, filtered, and desiccated [12].

Synthesis of Cu(II) and Ag(I) amide complexes: Cu(II) and Ag(I) amide complexes were prepared by the template method using the techniques employed by Nur Illane et al. [12]. For the synthesis of the N-benzoylurea Cu(II) amide complex, 20 mL of ethanolic solution of blue Cu(II) acetate monohydrate (0.0005 mol) was added to 40 mL stirring solution of 0.0003 mol N-benzoylurea in dichloromethane. Some pieces of anti-bumping granules were then added, and the now dark green solution was heated at 50 °C for 6 h under reflux. The solution containing the Cu(II) complex crystals was cooled to room temperature, and the Cu(II) complex crystals were filtered out and repeatedly washed using a cold ethanol/water mixture before being recrystallized using a mixture of 1:1 ethanol and dichloromethane. The purified dark green crystals were filtered and desiccated.

For the synthesis of N-benzoylurea Ag(I) amide Complex, a 20 mL ethanolic solution containing 0.0005 mol of Ag(I) acetate was gently poured into a round-bottom flask containing 40 mL solution of 0.0003 mol N-benzoylurea in DCM. This was followed by the addition of anti-bumping granules to the light orange mixture, after which the reaction was left to proceed for 6 h under reflux. After cooling to room temperature, the white crystals of N-benzoylurea Ag(I) amide Complex were obtained, filtered out, washed with a cold water/ethanol mixture, and then recrystallized in a 1:1 DCM/ethanol mixture. The light brown crystals were obtained by filtration, dried in a desiccator, and stored in an amber bottle.

Ultraviolet-Visible Spectrophotometric Analysis of the Ligands and Metal Complexes was conducted using the Pasco spectrometer PS-2600 (wireless spectrometer & fluorometer) [13]. Approximately 0.01 g of each as-synthesized sample was weighed into a 20 cm test tube and dissolved in 10 mL of ethanol. Then, a portion of this diluted solution was introduced into the spectrometer's cuvette and put in the instrument for analysis. The samples were scanned between 400 and 950 nm using a digital UV-visible spectrophotometer, and the interfaced computer was used to print the spectrum. The same procedure was repeated for all the as-synthesized metal complexes and ligands.

Infrared Spectrophotometric Analysis of the Complexes was carried out using an Agilent Cary 630 FTIR spectrophotometer. Approximately 2 mg of each as-synthesized sample was added to a drop of Nujol and ground to powdery particles using a small agate mortar. The resulting powdery substances were mixed with KBr, placed in the FTIR cell, and the data were collected between the frequencies

of 4000-650 cm^{-1} at 32 scans per minute. The spectrometer and computer were in phase as the chart was plotted.

X-ray diffraction spectroscopy of the Complexes was performed using a Bruker D8 Advance diffractometer that was equipped with a LynxEye detector and a monochromator. Cu $K_{\alpha 1}$ (1.5406Å) radiation was used to capture the powder PXRD data throughout a 2θ range of 5–70° for 43 minutes, with a step size of 0.022°.

Antimicrobial studies were carried out at Charis Rhema Diagnostic and Research Laboratories in Makurdi, Nigeria, using the agar-well diffusion technique [14]. The examined bacteria were *Salmonella typhi, Staphylococcus aureus*, *Escherichia coli*, and the fungus *Candida albicans*. These microorganisms were selected due to their frequent isolation from patients suffering from blood, skin, and intestinal diseases. All the examined microbes were acquired from the microbiology laboratory of the Benue State University Teaching Hospital, Makurdi, Nigeria.

Preparation of sample concentrations for antimicrobial study: Eight concentrations (0.78, 1.56, 3.13, 6.25, 12.5, 25, 50, and 100 mg/mL) were obtained by dissolving about 1.00 g of each ligand and metal complex in 10.00 mL of dimethyl sulfoxide using a two-fold serial dilution method. These were applied in the test for microbes.

Media used: The major medium employed for the tube dilution to ascertain the minimum inhibitory concentration of every test microorganism was Mueller-Hinton broth. Mueller-Hinton agar plates were used to plate out agar for well diffusion experiments.

Preparation of bacteria and fungi suspension: The test fungus and bacteria were mixed with peptone water in a 20 cm test tube and placed over an open flame using a sterilized wire loop. The inoculum had a concentration of 0.5 McFarland's standard or roughly 1×10^8 CFU/mL [14, 15].

Tube dilution assay: Two-fold broth microdilution was used to create the sample concentrations of 0.78, 1.56, 3.13, 6.25, 12.5, 25, 50, and 100 mg/mL to determine the MIC values of as-synthesized ligands and metal complexes. 1.00 mL of each sample was then placed in a test tube that had 1.00 mL of sterile MH medium. A drop of suspension of these microbes was inoculated, followed by incubation of the tubes at 37 °C for 24 hours. Positive control experiments for fungus and bacterium, respectively, used 0.05 mg/mL amphotericin and 0.05 mg/mL imipenem. Water was used for the negative control.

After 24 h of incubation, MIC values were determined and compared with the growth and sterility controls [14, 16]. After that, six sections of MH plates were created and designated with various concentrations on the plate base to plate out the contents of the tubes in the appropriate part of each plate. Each plate was subjected to 24-hour incubation at 37 °C. Then, minimum bactericidal or fungicidal concentrations (MBCs/MFCs) –– the lowest concentrations at which no growth of the organism was observed –– were measured.

Well-diffusion assay test for inhibitory zones: The well-diffusion method was employed for antimicrobial susceptibility testing to identify any antifungal or antibacterial properties of the ligand-metal complexes. Bacterial or fungal culture was equally distributed across the suitable medium using a sterile swab. Before testing, the plates were given fifteen minutes to dry. A sterile cork borer of 6 mm diameter was used to drill wells in the plate. Then, 30.00 µL of the ligands and metal complexes were added to each well using a micropipette. Two plates were utilized for each analyzed sample. Each plate consisted of two wells designated for positive and negative controls, in addition to wells for the ligand and its respective metal complexes. The experimental procedure utilized both positive and negative controls similar to those in the tube dilution assay. After incubating for 24 h at 37 °C, the plates were inspected for inhibitory zones, which were then measured using a caliper.

RESULTS AND DISCUSSION

Physical Characteristics of the Prepared Complexes

The physical properties of ligands and metal complexes revealed that they are all crystalline solids, as can be seen in Table 1. The complexes exhibit different colors typical of transition metals, with [Cu(II)L] appearing dark green and [Ag(I)L] manifesting a light brown color. The melting points for both the ligands and their corresponding complexes are also listed in the table. The melting point of the ligand is 178.5 °C, which is higher than that of Cu(II) complex (158.8 °C). Ag(I) complex has the highest melting point of 184.4 °C. The increase or decrease in melting points between the complexes and their ligands suggests effective complexation [17, 18]. The observations are consistent with findings by Gun et al. [17] and Iorungwa et al. [18], indicating that successful ligand-metal complexation

Table 1. Physical characteristics of the ligand and its metal complexes

Ligand/Complex	Colour	M.Pt (°C)	Yield %	Physical appearance
L	White	178.5	89	Crystalline
[Cu(II)L]	Dark-green	158.8	80	Crystalline
[Ag(I)L]	Light Brown	184.4	74	Crystalline

Table 2. Solubility of the ligand and metal complexes in different solvents

L/Cplx	D.H_2O	EtOH	DMSO	DCM	ace	$CHCl_3$	CCl_4	DCM/EtOH
L	NS	SS, +Δ, S	NS, +Δ, S	NS, +Δ, SS	NS	S	S	S
[Cu(L)]	NS	NS, +Δ, S	NS	NS	NS	SS	S, +Δ, NS	NS, +Δ, S
[Ag(L)]	NS	SS, +Δ, S	NS, +Δ, S	NS	NS	SS	SS	NS

S = Soluble, SS = slightly soluble, NS = Not soluble, +Δ = plus heat, L/Cplx = ligand/complex, EtOH = ethanol, ace = acetone

significantly influences melting points and contributes to these complexes' stability.

Solubility

The solubility of as-synthesized complexes and their ligands was determined using selected solvents as detailed in Table 2. The results indicate that both ligands and complexes exhibit sparing solubility in weakly polar solvents like ethanol and tetrachloromethane. However, full solubility is achieved upon heating. Specifically, the ligand N-benzoylurea demonstrated minimal solubility in ethanol but achieved complete dissolution in a 1:1 mixture of dichloromethane and ethanol. These findings indicate that the complexes are of low polarity, as they are immiscible with water and only sparingly soluble in less polar solvents. Weak dispersion forces among the particles of a nonpolar compound hinder its ability to dissolve in polar solvents such as water, aligning with the observations reported by Yiase et al. [19].

UV-Visible Spectrophotometric Results

The UV-visible spectrophotometric analysis of N-benzoyl urea and its metal complexes was conducted in ethanol within the wavelength range of 400 to 950 nm at room temperature. The results given in Table 3 indicate that the ligand exhibited a maximum absorption wavelength (λ_{max}) at 903.1 nm, whereas the Ag(I) and Cu(II) complexes displayed sharp bands at 904.2 nm and 715.8 nm, respectively. The decrease in the absorption maximum of the Cu(II) complex compared to the ligand (903.1 to 715.8 nm) indicates metal–ligand coordination, leading to the observed color change, whereas the Ag(I) complex (904.2 nm) shows no appreciable shift. The bands noted within the visible spectrum could be largely attributed to electronic transitions, including metal charge transfers, d-d transitions, or ligand-centered transitions, as noted by Yiase et al. [19] and Gajendra et al. [20]. These transitions are typically $n\rightarrow\sigma^*$, $n\rightarrow\pi^*$, and $\pi\rightarrow\pi^*$ and have been highlighted as contributing factors to the observed spectral features [16–18] (Table 4).

Fourier-transform Infrared (FTIR) Spectroscopic Analysis

The Fourier-transform infrared (FTIR) spectra of the free acylated ligand and its corresponding metal complexes were analyzed to investigate the chelation of Ag(I) and Cu(II) ions by the ligand. FTIR spectroscopic analysis was performed using as-synthesized samples mixed with KBr, and data were acquired from 4000 to 600 cm^{-1}. The FTIR spectra signatures are typical of N–H stretching vibrations in the amide group. Additionally, the observed bands ranging from 1643 cm^{-1} to 1690 cm^{-1} are ascribed to υ(C=O) stretching vibrations in carbonyl groups. The results observed here agree very well with findings by Nur Illane et al. [12]. Notably, these υ(C=O) bands exhibited a decrease in frequency post-complexation, indicating the successful coordination of the metal centers to the ligand. The evidence of successful coordination is further buttressed by a pronounced peak around 1420–1595 cm^{-1}, which we attribute to C–O stretching vibrations associated with coordination. Furthermore, an intense absorption band in the range of 1600–1703.4 cm^{-1} is due to the presence of C–N groups, aligning with previously reported observations [17, 21, 22].

X-Ray Diffraction Analysis

The XRD patterns of the synthesized metal complexes exhibited sharp diffraction peaks, confirming that both are crystalline in nature. The XRD patterns of the Cu(II) and Ag(I) complexes (Figures 1–4) show sharp and well-resolved reflections over the 5–70° 2θ range. Most of the intensity was observed below 30°, and the two patterns differ markedly from each other. The [Cu(II)L] pattern is dominated by a strong reflection at 2θ = 12.11° (d = 7.307 Å), which is accompanied by intense reflections at 13.2°, 13.9°, 23.8°, 25.6° and

Table 3. UV-vis data for the ligand and metal complexes

S/N	Ligand/Complexes	λmax (nm)
1	N-Benzoylurea (L)	903.1
2	[Cu(L)]	715.8
3	[Ag(L)]	904.2

Table 4. IR-spectral data of the ligands and complexes

Peaks	L	[Cu(L)]	[Ag(L)]
υ(N-H)	3261.4	3339.7	3339.7
υ(C=O)	1664.9	1420 (C-O)	1509.6(C-O)
υ(C-N)	1095.8	1602.8	1602.8

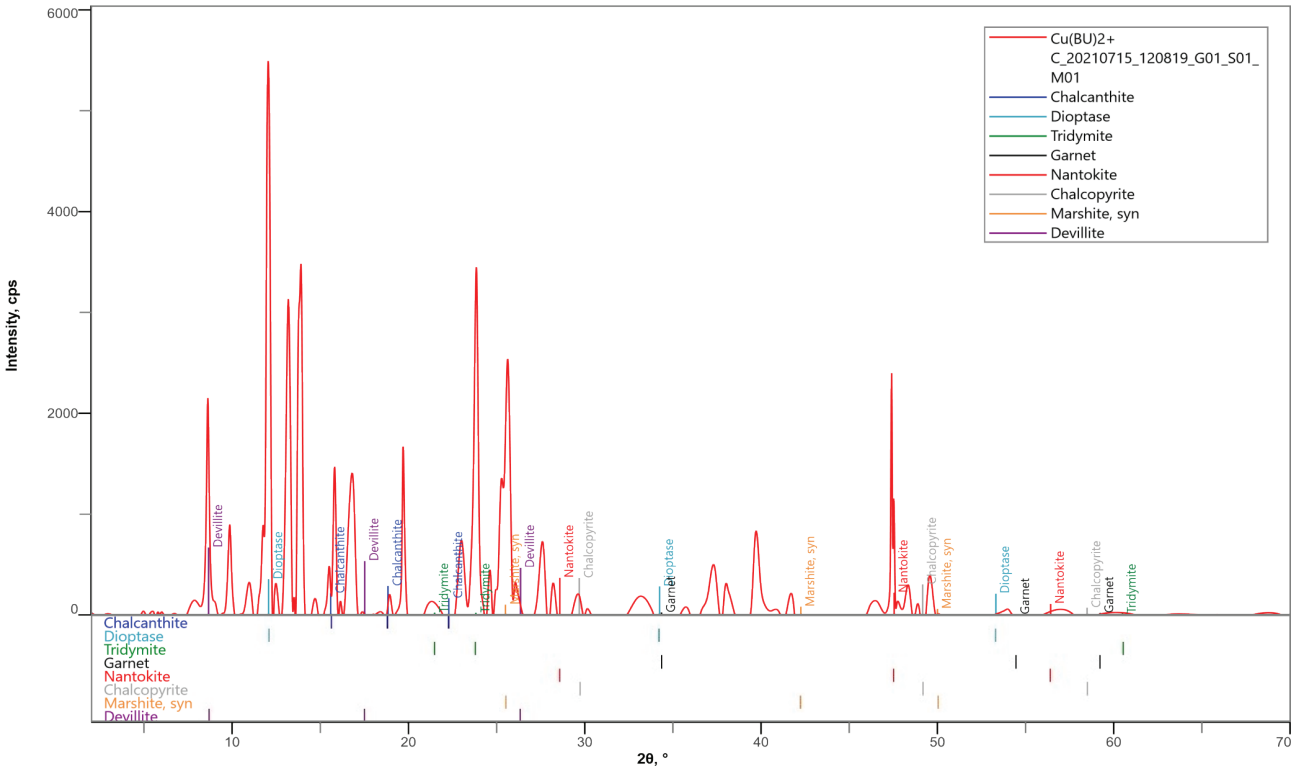


Figure 1. Phase data view of Cu(II) N-Benzoylurea complex with International Centre for Diffraction Data.

General information

Analysis date	2021-07-15 14:44:04	Measurement start time	2021-07-15 12:08:19
Analyst	Administrator	Operator	Administrator
Sample name	Cu(BU)2+ C	Comment	
Measured data name	C:\WallPaper\15-07-2021\Cu(BU)2+ C_20210715_120819_G0...	Memo	

Multiple Profile

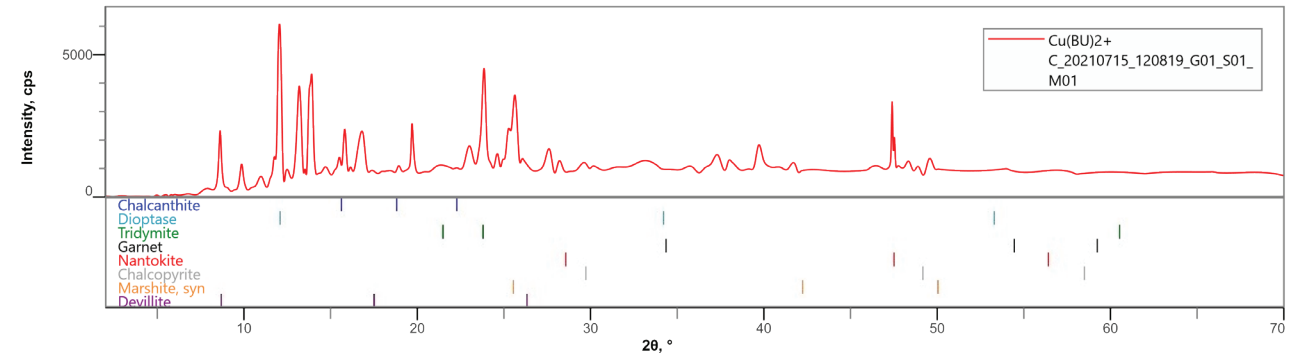
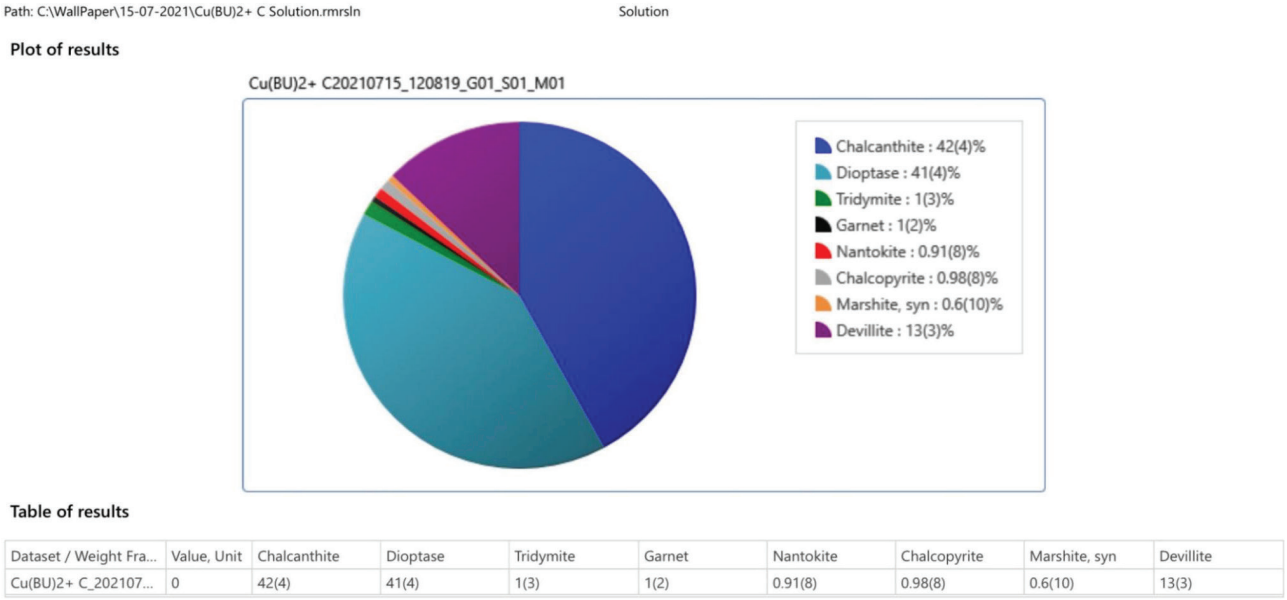


Figure 2. Peak of [Cu(II)L] at full width half maximum.

47.4°, and additional reflections at 8.6°, 15.8°, 16.8° and 19.7°. The [Ag(I)L] pattern is dominated by a single intense reflection at 2θ = 9.60° (d = 9.21 Å), with weaker reflections at 8.7°, 18.6° and 29.9°. Both patterns have a common reflection near 8.6–8.7° (d ≈ 10.2 Å).

Automated phase matching against the International Center for Diffraction Data (ICDD) database gave reference entries consistent with the principal reflections of each pattern. The Cu(II) sample was matched to ICDD card No. 00-001-0301 and the Ag(I) sample to card No. 01-073-4489. The matched entries correspond to a triclinic lattice with



Dataset / Weight Fra...	Value, Unit	Chalcanthite	Dioptase	Tridymite	Garnet	Nantokite	Chalcopyrite	Marshite, syn	Devillite
Cu(BU)2+ C_202107...	0	42(4)	41(4)	1(3)	1(2)	0.91(8)	0.98(8)	0.6(10)	13(3)

Figure 2b. Peak of [Cu(II)L] at full width half maximum - Plot and table of results.

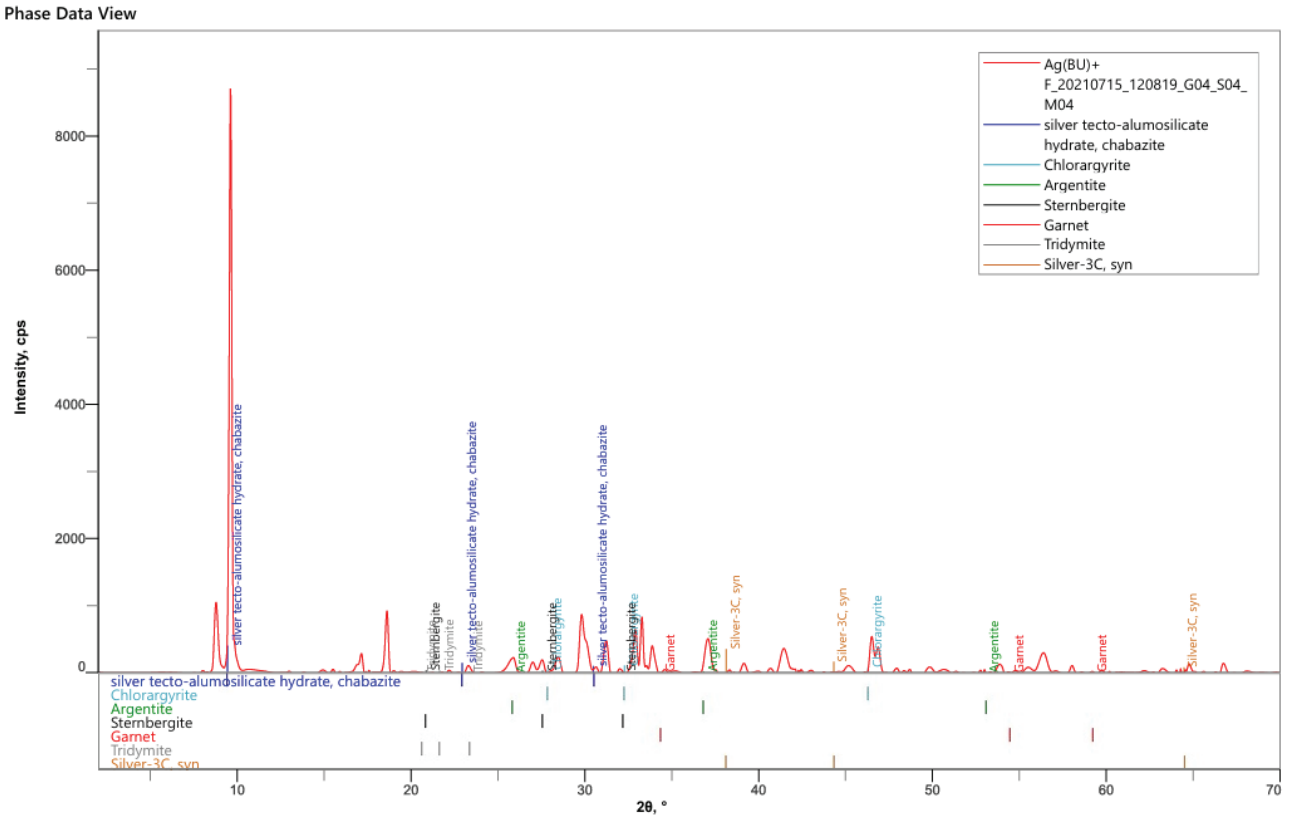


Figure 3. Phase matching of silver (I) N-benzoylurea complex with International Centre for Diffraction Data.

space group P-1 (no. 2) for the Cu(II) sample and a trigonal lattice with space group R-3m (no. 166) for the Ag(I) sample (Table 5). The parameters of the unit cell (a, b, c, α, β, γ) define point lattices and hence the classification of the crystals [21]. The space groups and crystal data in Table 5 follow standard crystallographic sources [24–26], and the crystallite size notably influences the lattice symmetry of these complexes [23–27].

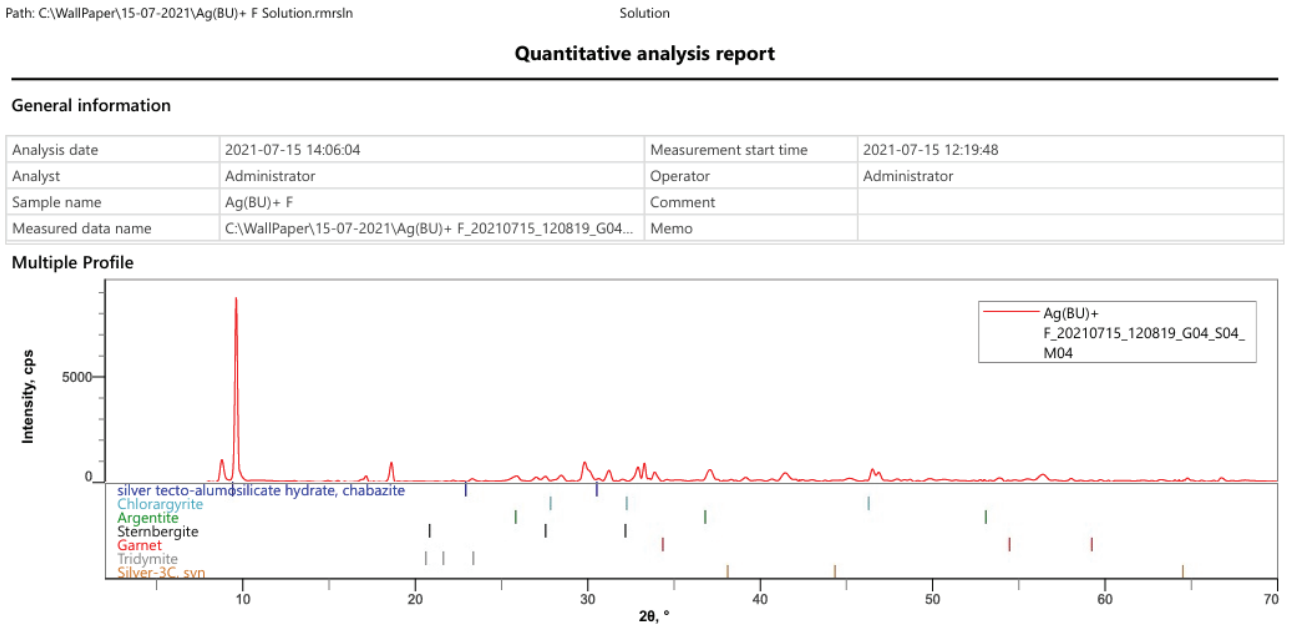
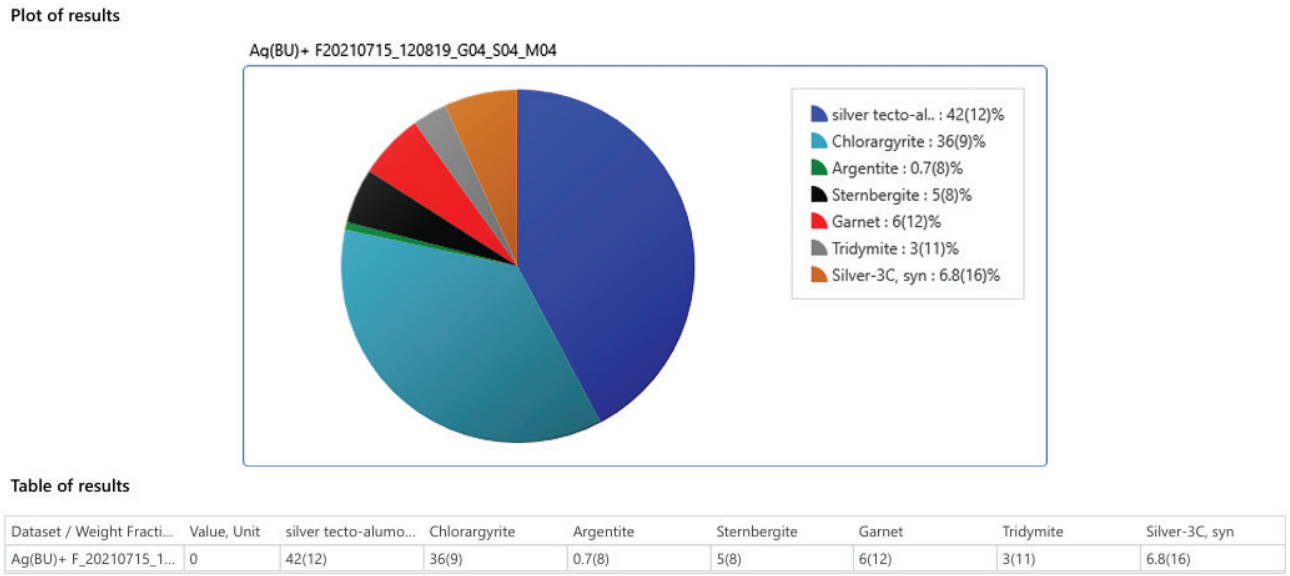


Figure 4. Peak of silver (I) N-benzoylurea complex.



Dataset / Weight Fracti...	Value, Unit	silver tecto-alumo...	Chlorargyrite	Argentite	Sternbergite	Garnet	Tridymite	Silver-3C, syn
Ag(BU)+ F_20210715_1...	0	42(12)	36(9)	0.7(8)	5(8)	6(12)	3(11)	6.8(16)

Figure 4b. Peak of silver (I) N-benzoylurea complex - Plot and table of results.

Scherrer's equation was employed to determine the complexes' crystallite sizes from the strongest reflection in each pattern [23], expressed as:

$$D = \frac{K\lambda}{\beta cos\theta}$$

In this equation, "*D*" represents the average size of the crystallite, "*K*" is a dimensionless shape factor with a value of 0.9, "*λ*" denotes the X-ray wavelength (CuKα = 1.5406Å), β represents the line broadening at full width at half maximum (FWHM) measured in radians, and "θ" indicates Bragg's angle in degrees.

Peak fitting of the strongest reflection gives 2θ = 12.1125°, FWHM = 0.00984°, and d = 7.30714 Å for the Cu(II) complex. The corresponding results for the Ag(I) complex are 2θ = 9.6022°, FWHM = 0.1574°, and d = 9.21102 Å. The crystallite sizes for Cu(II) and Ag(I) complexes from the Scherrer equation are 84.8 nm and 52.9 nm, respectively.

Table 5. Crystal data of the complexes

Parameters	L	Cu(L)	Ag(L)
Crystal formula	$C_8H_8N_2O_2$	$C_8H_8N_2CuO_2$	$C_8H_8N_2AgO_2$
Formula weight(g/mol)	164.16	227.71	272.03
Crystal size (nm)		84.8	52.9
Crystal system		Triclinic	Triagonal
Space group		p-1(2)	R-3m:H (166)
a (Å)		6.736	7.403
b (Å)		7.830	7.403
c (Å)		10.353	7.403
α (°)		100.571	22.956
β (°)		100.159	22.956
γ (°)		109.774	22.956
Final magnetic moment (μB)		0.000	0.008
Formation energy/atom eV		-0.771	0.000

Antimicrobial studies

The antimicrobial sensitivity of metal complexes and ligands, particularly benzoylamides, was quantitatively evaluated through Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal or Fungicidal Concentration (MBC/MFC) tests, as indicated in Tables 6-8. The susceptibility of targeted bacterial pathogens, including the Gram-positive *S. aureus* and the Gram-negative strains *E. coli* and *S. typhi*, along with the fungus *Candida albicans,* was investigated. The broth microdilution and agar-well diffusion methods were employed to measure the minimum concentrations necessary to inhibit or kill the microorganisms. The results presented in Table 6 detail the diameters of the inhibition zones, where clear areas surrounding the wells indicated antimicrobial activity. The tested amide ligands and their metal complexes exhibited varying levels of effectiveness, with notable antimicrobial effects observed, particularly when the ligand was chelated to Cu(II), as its activity was enhanced far more than when in its free form. For example, Cu(II) complexes were effective against all tested organisms, whereas Ag(I) complexes showed limited activity, being inactive against *Escherichia coli* and *Salmonella typhi*, but demonstrating some inhibitory effect on *Staphylococcus aureus* and *Candida albicans*. Specifically, the ligand exhibited MICs of 6.25 and 12.5 mg/mL against *Staphylococcus aureus* and *Candida albicans*, respectively, with inhibition zones measuring 12 mm and 11 mm. Conversely, the Ag(L) complex demonstrated a lower MIC of 1.56 mg/mL for both *Staphylococcus aureus* and *Candida albicans*, with inhibition zones of 8 mm and 9 mm, although these are smaller than those of the free ligand (12 mm and 11 mm). This indicates that while both the ligand and the complex exhibit biological activity, their effectiveness varies significantly depending on the organism tested (Fig. 5).

Table 6. Zones of inhibition of the ligand along with their metal complexes (mm)

Compound	EC	ST	SA	CA
L	NA	NA	12	11
[Cu(II)L]	17	14	18	23
[Ag(I)L]	NA	NA	8	9
Imipenem	28	24	26	-
Amphotericin	-	-	-	27

EC=Escherichia coli, ST=Salmonella typhi, SA=Staphylococcus aureus, CA=Candida albicans

Table 7. Minimum inhibitory concentrations of the as-prepared ligand and metal complexes (mg/mL)

S/N	Compound	EC	ST	SA	CA
1	L	NA	NA	6.25	12.5
2	[Cu(II)L]	1.56	6.25	6.25	6.25
3	[Ag(I)L]	NA	NA	1.56	1.56

EC=Escherichia coli, ST=Salmonella typhi, SA=Staphylococcus aureus, CA=Candida albicans

Table 8. Minimum bactericidal/fungicidal concentrations of the as-prepared ligand and metal complexes (mg/mL)

S/N	Compound	EC	ST	SA	CA
1	L	NA	NA	25	100
2	[Cu(II)L]	12.5	12.5	6.25	25
3	[Ag(I)L]	NA	NA	1.56	25

ST=Salmonella typhi, EC=Escherichia coli, CA=Candida albicans, SA=Staphylococcus aureus,

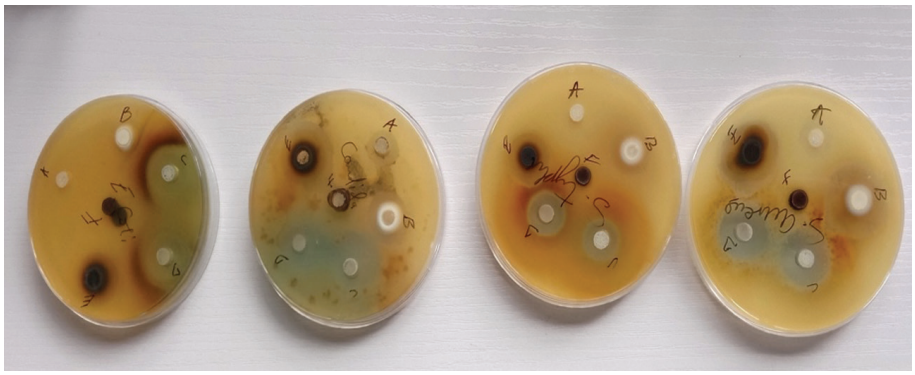


Figure 5. Zones of inhibition of ligands and metal complexes.

The study presents findings on the antimicrobial efficacy of a ligand and its metal complexes against various microorganisms, including *Staphylococcus aureus*, *Candida albicans*, *Escherichia coli*, and *Salmonella typhi*. The minimum inhibitory concentration (MIC) for *Staphylococcus aureus* ranged from 1.56 mg/mL to 6.25 mg/mL, with inhibition zones measuring between 8 mm and 18 mm. In contrast, the antibiotic Imipenem achieved higher inhibition zones of 24–28 mm. The Cu(II) complex also displayed antifungal activity against *Candida albicans*, with a zone (23 mm) approaching that of amphotericin, the antifungal control, which exhibited a zone of inhibition of 27 mm at 0.05 mg/mL, whereas the Ag(I) complex gave a zone of 9 mm; these results are in line with the literature, specifically Chenielle et al. [15].

The results suggest the potential of using these N-benzoylurea complexes as lead antimicrobial agents against prevalent infections. The interaction of ligands with metal ions appears to enhance efficacy by increasing the lipophilicity of the complexes, thereby improving penetration through microbial membranes [27]. This could obstruct important enzyme binding sites in pathogens, which is supported by claims from Gajendra et al. [20] regarding interference in respiratory functions and proteomic processes in cells.

The results illustrate that microorganism type significantly influences the microcidal efficacy of the ligand and complexes. For instance, while *Staphylococcus aureus* showed sensitivity at low concentrations of the complexes, *Escherichia coli* was resistant to the ligand and the Ag(I) complex, whereas the Cu(II) complex was active against it (17 mm; MIC 1.56 mg/mL). The MBC/MFC values, as shown in Table 8, indicated that Cu(II) and Ag(I) complexes had lower minimal bactericidal/fungicidal concentrations than the free ligand against *Staphylococcus aureus* and *Candida albicans*. Notably, the ligand itself was inactive against *Escherichia coli* and *Salmonella typhi*, with MBC values of 25 and 100 mg/mL against *S. aureus* and *C. albicans*, respectively.

On the other hand, its complex, Cu(II)L, has MBC values of 12.5 mg/mL against *Escherichia coli* and *Salmonella typhi*, as well as MBC values of 25 and 6.25 mg/mL for *Candida albicans* and *Staphylococcus aureus*. These indicate the antimicrobial potency of the complexes [19, 20, 27].

In summary, the ligand and its complexes exhibit antibacterial and antifungal activity, with the Cu(II) complex active against all four test organisms, whereas the ligand and the Ag(I) complex had no effect on *Escherichia coli* and *Salmonella typhi*.

CONCLUSION

The study indicated that urea ligands are acylated to form bidentate ligands, which can be used to synthesize transition metal complexes of mono-substitutions. These complexes, according to XRD analysis, are of triclinic, trigonal, and cubic lattice symmetry. The ligand was indicated to be chelated to Cu(II), as the free ligand's electronic band shifted to a higher frequency after complexation with metal ions. The Cu(II) complex was active against the Gram-positive *S. aureus*, the Gram-negative *S. typhi* and *E. coli*, and the fungus *C. albicans*, whereas the Ag(I) complex was active only against *S. aureus* and *C. albicans*; MBC/MFC and MIC values are given in Tables 7 and 8. This study involved comparing the ligands' antimicrobial activities with those of their corresponding metal complexes against standard antibiotics, imipenem and Amphotericin. The metal complexes inhibited microbial growth, although less effectively than the standard drugs at the concentrations tested.

AUTHORSHIP CONTRIBUTIONS

Authors equally contributed to this work.

DATA AVAILABILITY STATEMENT

The authors confirm that the data that supports the findings of this study are available within the article. Raw data that support the finding of this study are available from the corresponding author, upon reasonable request.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ETHICS

There are no ethical issues with the publication of this manuscript.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence was not used in the preparation of the article.

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