

Scientific report

Regarding the implementation of the PN-III-P1-1.1-PD-2016-0409 project

SILVER COORDINATION POLYMERS FOR ANTIBACTERIAL PAPER (SILVAPAPER)

January – December 2019 (Phase 2)

The objective, related activities and expected results, for this reporting period, are given in the table below:

Phase	Objective	Activities	Phase deadline	Expected results
2	Synthesis and characterization of some silver coordination polymers and their incorporation into paper matrices	A1. Synthesis of new silver coordination polymers based on the organic ligands obtained in Phase 1 A2. Structural and spectroscopic characterization of the obtained silver coordination polymers A3. Study of the antibacterial action of the obtained silver coordination polymers A4. Incorporation of the obtained silver coordination polymers into paper matrices A5. Dissemination of the research results: publication of 1 ISI paper and preparation of 1 poster presentation for an international conference	20 December 2019	- new silver coordination polymers with antibacterial action - new composite paper materials incorporating silver coordination polymers - 1 ISI paper - 1 participation at an international conference

This phase was dedicated to the synthesis, characterization and antibacterial activity of some new silver coordination polymers, as well as their incorporation into paper matrices.

In the following, the results obtained per each activity are briefly presented.

Activity 1. Synthesis of new silver coordination polymers based on the organic ligands obtained in Phase 1

The organic compounds from the class of quaternary ammonium salts (QAs), which were synthesized and reported in Phase 1, unfortunately, did not show good coordinative aptitudes towards silver(I) ions. However, this issue was successfully managed by replacing them with one resynthesized nitrogen ligand from the class of azoles, scarcely exploited towards the preparation of coordination polymers, which was further used in the synthesis of new silver coordination polymers with antibacterial properties.

To this aim, the chemical precipitation method was employed to synthesize a new family of six silver coordination polymers (CPs), having the general stoichiometric formulation $[\text{Ag}(\text{H}_2\text{DMPMB})(\text{X})]$ ($\text{X} = \text{NO}_3$, **1**; CF_3CO_2 , **2**; CF_3SO_3 , **3**; BF_4 , **4**; ClO_4 , **5**; and PF_6 , **6**), based on the flexible nitrogen ligand 4,4'-bis((3,5-dimethyl-1H-pyrazol-4-yl)methyl)biphenyl (H_2DMPMB). In a general procedure, 1 equivalent of H_2DMPMB was dissolved in methanol under gentle warming. Then, the silver(I) salt was added, and the resulting white suspension was left under stirring at room temperature for 2 h, obtaining a white precipitate that was filtered off, washed twice with methanol, and dried under a vacuum. The obtained Ag CPs are insoluble in chlorinated solvents, alcohols, acetone, acetonitrile, dimethylformamide, dimethylsulfoxide, and water. All products were obtained in reasonable good yields, are remarkably air- and moisture-stable for long times, and possess high thermal stabilities.

Infrared and analytical data:

[Ag(H₂DMPMB)(NO₃)] (1). IR (cm^{-1}): 3199(mbr) $\nu(\text{N-H})$; 3100-3000(vw) $\nu(\text{C-H}_{\text{aromatic}})$, 3000-2900(w) $\nu(\text{CH}_3, \text{CH}_2)$, 1748(w), 1582(w), 1528(w), 1499(w) $\nu(\text{C=C+C=N})$, 1387(vs) $\nu_{\text{asym}}(\text{NO}_3)$, 1347(vs) $\nu_{\text{asym}}(\text{NO}_3)$, 1210(w), 1006(w), 905(w), and 754(vs). Elemental analysis calcd. for $\text{C}_{24}\text{H}_{26}\text{AgN}_5\text{O}_3$ (FW = 540.36 g/mol): C, 53.34; H, 4.85; N, 12.96%. Found: C, 53.03; H, 4.67; N, 12.38%.

[Ag(H₂DMPMB)(CF₃CO₂)] (2). IR (cm^{-1}): 3186(mbr), $\nu(\text{N-H})$, 3092(vw), 3028(vw) $\nu(\text{C-H}_{\text{aromatic}})$, 2921(vw) $\nu(\text{CH}_3, \text{CH}_2)$, 1668(vs) $\nu(\text{C=O})$, 1579(vw), 1528(vw), 1494(m) $\nu(\text{C=C+C=N})$, 1431(m), 1201-1140(vs) $\nu(\text{CF}_3\text{CO}_2)$, 1058(m), 1005(m), 905(m), 806(m), 719(s). Elemental analysis calc. for $\text{C}_{26}\text{H}_{26}\text{AgF}_3\text{N}_4\text{O}_2$ (FW = 591.38 g/mol): C, 52.81; H, 4.43; and N, 9.47%. Found: C, 52.35; H, 4.25; N, 9.08%.

[Ag(H₂DMPMB)(CF₃SO₃)] (3). IR (cm^{-1}): 3233(mbr), $\nu(\text{N-H})$, 3024(vw) $\nu(\text{C-H}_{\text{aromatic}})$, 2923(vw) $\nu(\text{CH}_3, \text{CH}_2)$, 1586(w), 1526(vw), 1498(w) $\nu(\text{C=C+C=N})$, 1240(vs), 1224(vs), 1162(vs), 1029(vs) $\nu(\text{CF}_3\text{SO}_3)$, 905(w), 839(w), and 759(m). Elemental analysis calcd. for $\text{C}_{25}\text{H}_{26}\text{AgF}_3\text{N}_4\text{O}_3\text{S}$ (FW = 627.43 g/mol): C, 47.86; H, 4.18; N, 8.93; S, 5.11%. Found: C, 47.85; H, 3.92; N, 8.34; S, 4.91%.

[Ag(H₂DMPMB)(BF₄)] (4). IR (cm^{-1}): 3316(mbr) $\nu(\text{N-H})$, 3025(vw) $\nu(\text{C-H}_{\text{aromatic}})$, 2923(vw) $\nu(\text{CH}_3, \text{CH}_2)$, 1587(w), 1526(vw), 1494(w) $\nu(\text{C=C+C=N})$, 1057(vs), 1005(vs) $\nu(\text{BF}_4)$, 904(w), 845(m), 799(w), 768(m), and 692(mbr). Elemental analysis calcd. for $\text{C}_{24}\text{H}_{26}\text{AgBF}_4\text{N}_4$ (FW = 565.17 g/mol): C, 51.00; H, 4.64; N, 9.91%. Found: C, 50.86; H, 4.45; N, 9.36%.

[Ag(H₂DMPMB)(ClO₄)] (5). IR (cm^{-1}): 3267(mbr) $\nu(\text{N-H})$, 3025(vw) $\nu(\text{C-H}_{\text{aromatic}})$, 2923(vw) $\nu(\text{CH}_3, \text{CH}_2)$, 1587(w), 1525(vw), 1495(w) $\nu(\text{C=C+C=N})$, 1075(vs), 1040(vs) $\nu(\text{ClO}_4)$, 845(m), 769(m), and 687(mbr). Elemental analysis calcd. for $\text{C}_{24}\text{H}_{26}\text{AgClN}_4\text{O}_4$ (FW = 577.82 g/mol): C, 49.89; H, 4.54; N, 9.70%. Found: C, 49.52; H, 4.46; N, 9.51%.

[Ag(H₂DMPMB)(PF₆)] (6). IR (cm^{-1}): 3410(mbr) $\nu(\text{N-H})$, 3027(vw) $\nu(\text{C-H}_{\text{aromatic}})$, 2926(vw) $\nu(\text{CH}_3, \text{CH}_2)$, 1585(w), 1525(vw), 1495(w) $\nu(\text{C=C+C=N})$, 828(vs) $\nu(\text{PF}_6)$, 768(m), and 667(mbr). Elemental analysis calcd. for $\text{C}_{24}\text{H}_{26}\text{AgF}_6\text{N}_4\text{P}$ (FW = 623.33 g/mol): C, 46.25; H, 4.20; N, 8.99%. Found: C, 46.22; H, 3.98; N, 8.50%.

Activity 2. Structural and spectroscopic characterization of the obtained silver coordination polymers

Fourier transform infrared spectroscopy (FTIR) was employed in order to reveal both the changes in the absorption bands of the ligand upon coordination to silver(I) ions and the binding modes of the counterions. The FTIR spectra of silver(I) CPs **1–6** are given in Figures 1 and 2. The infrared spectrum of the free ligand showed a strong and broad band in the region $2500\text{--}3200\text{ cm}^{-1}$, which was specific to the intermolecular hydrogen bond interactions mediated by the N–H functions of the pyrazolyl rings. Upon coordination to silver(I) ions, the infrared pattern of the ligand was significantly changed, indicating the success of the synthetic methodology adopted for obtaining the new silver(I) CPs.

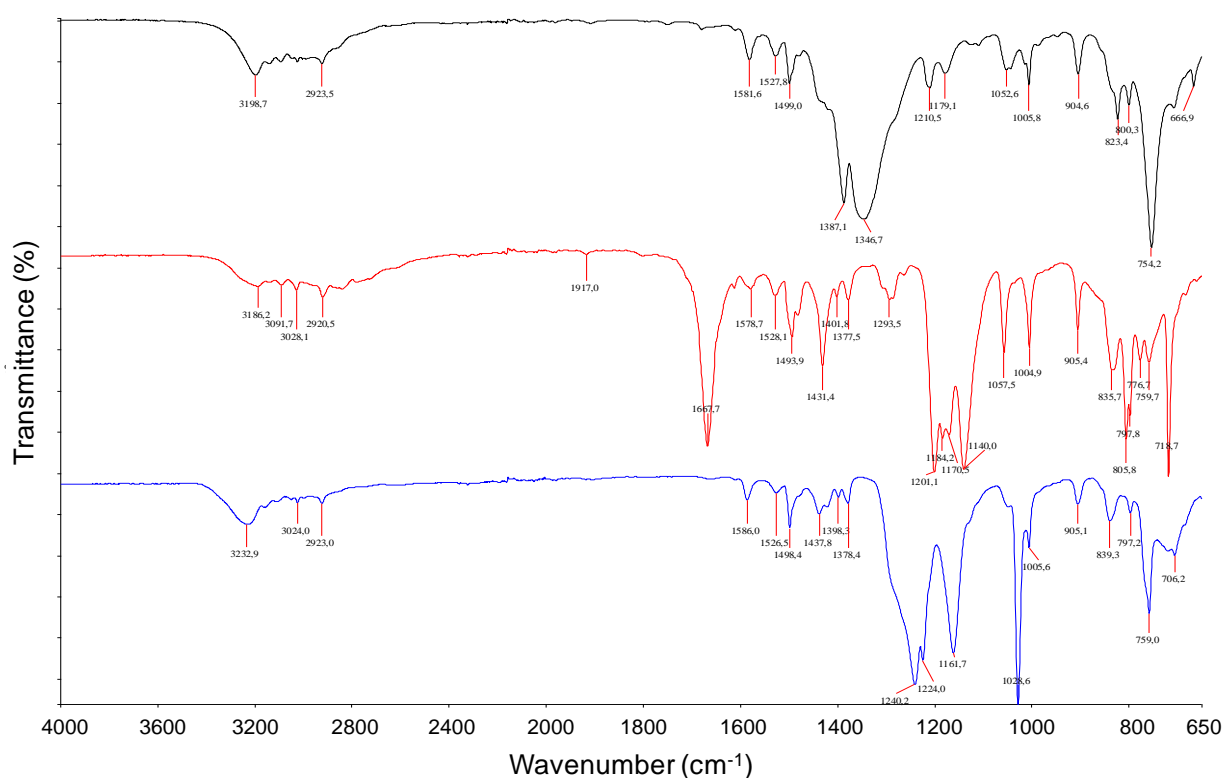


Figure 1. FTIR spectra of silver(I) CPs **1** (black), **2** (red), and **3** (blue).

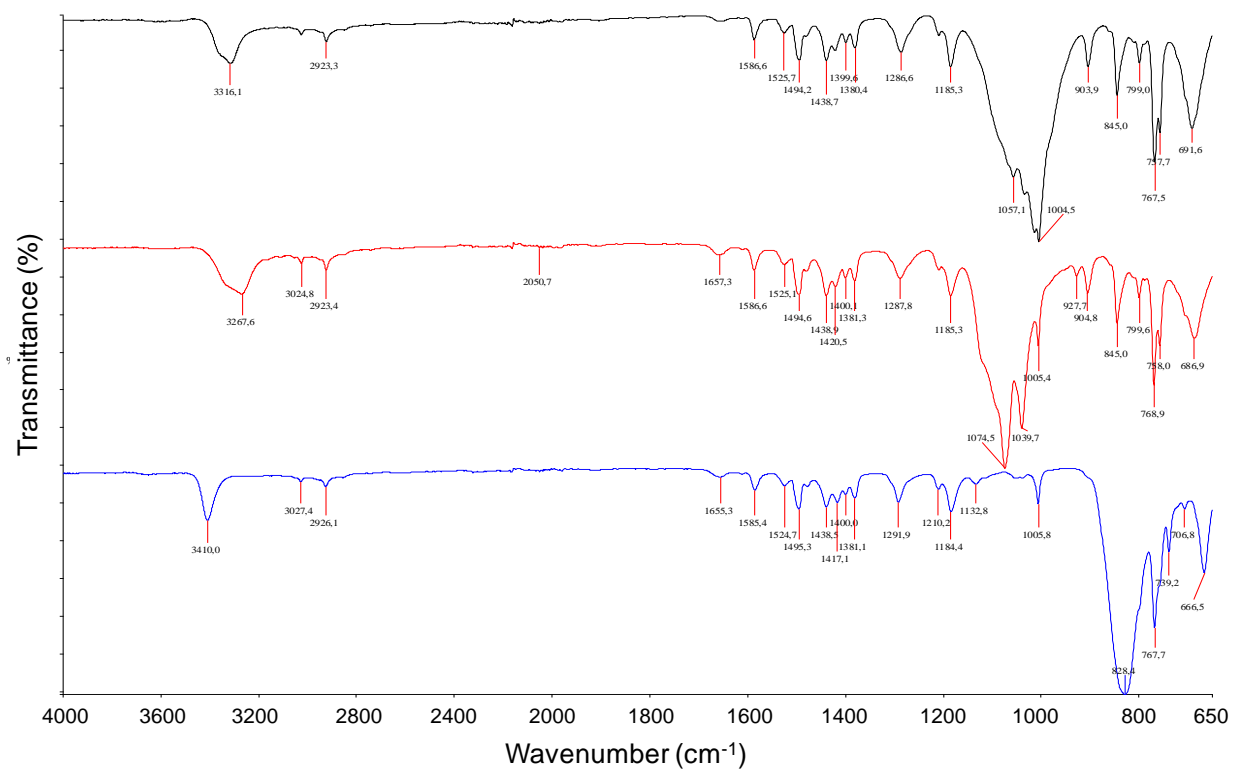
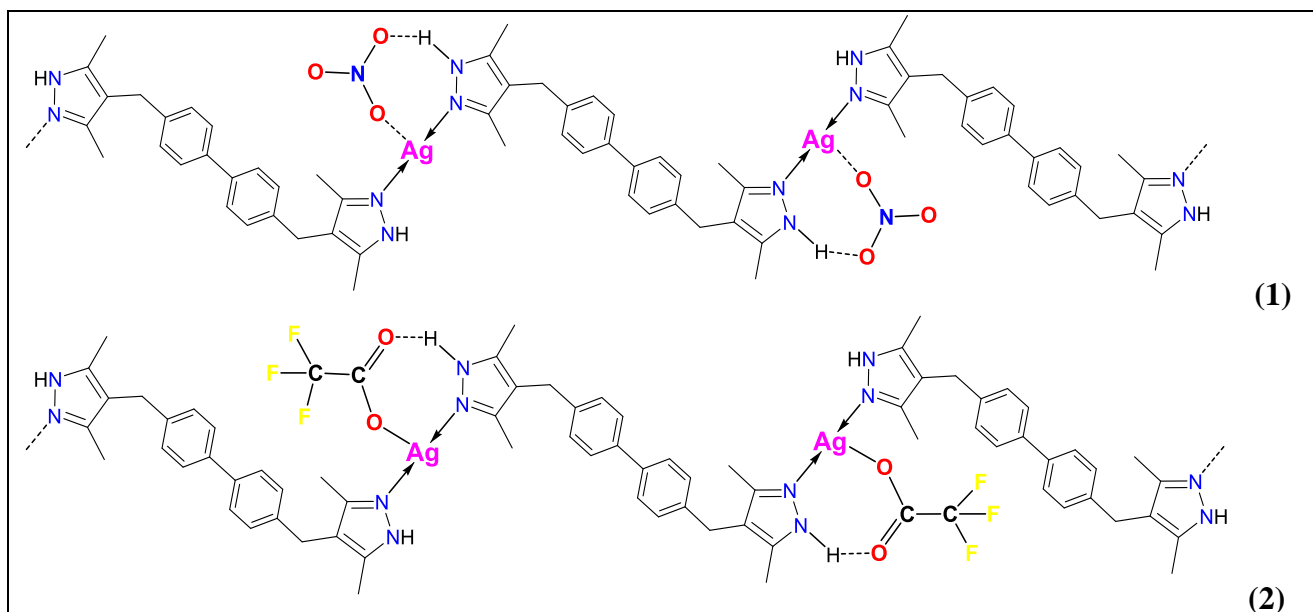


Figure 2. FTIR spectra of silver(I) CPs **4** (black), **5** (red), and **6** (blue).

The infrared spectra of all silver(I) CPs were generally consistent with the proposed formulations, and present all of the required absorption bands for both the ligand and the counterions, finally allowing the proposition of the possible polymeric structures for all silver(I) CPs (Figure 3).



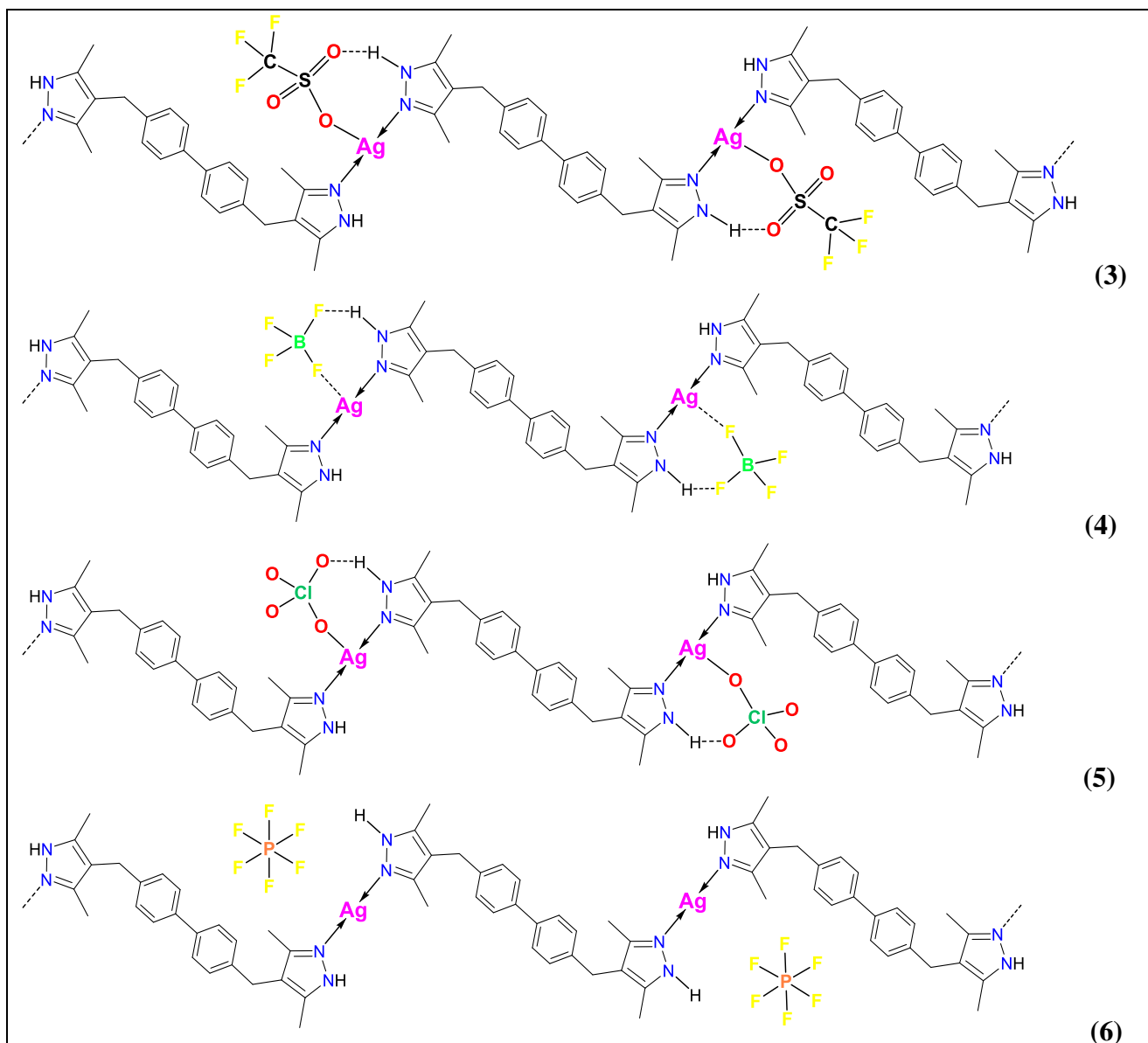


Figure 3. Proposed structures of silver(I) CPs 1-6

Thermogravimetric analyses (TGA) of silver(I) polymeric species **1–6** also were performed in order to investigate their thermal behavior upon heating from 30 to 700 °C, under nitrogen, and the resulting TGA curves were collectively gathered in Figure 4. Compound **1** showed an appreciable thermal stability, resistant up to 275 °C, after which a weight loss of about 12% in the range 275–325 °C was recorded, corresponding to the removal of one nitric acid molecule, which was the result of the proton transfer from one pyrazolyl moiety (theoretical weight loss: 11.66%). This loss was immediately followed by a progressive decomposition of the remaining species.

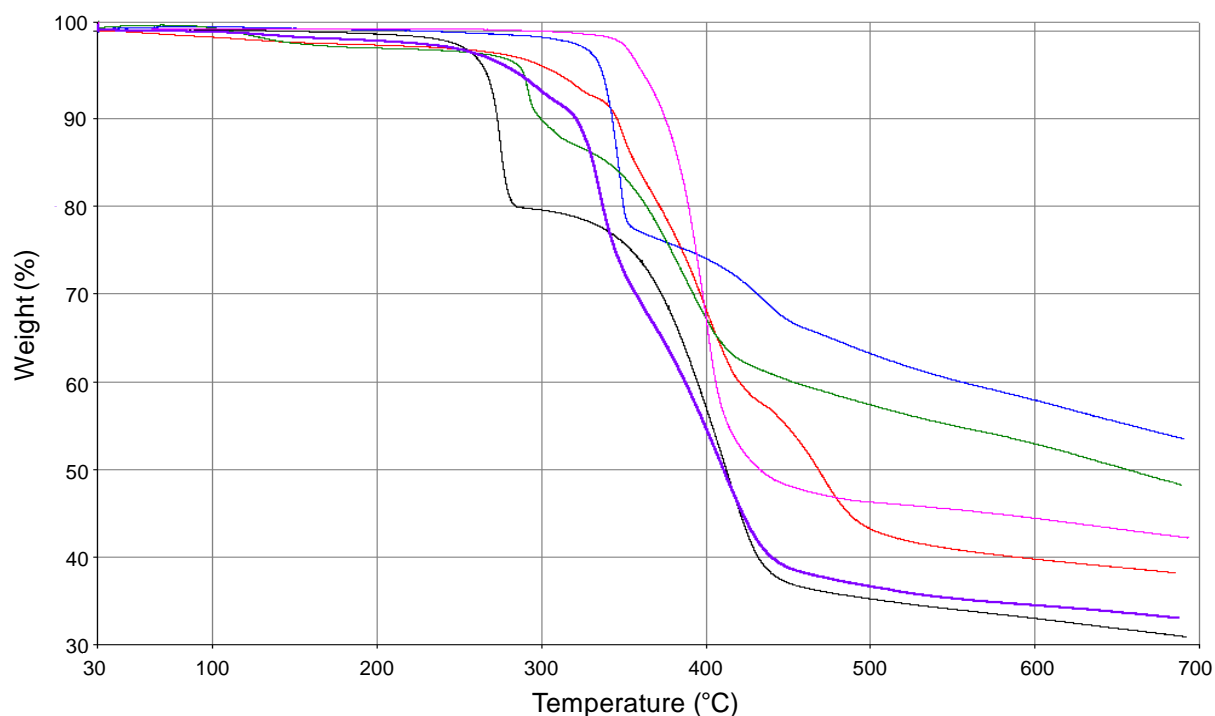


Figure 4. Thermogravimetric analysis (TGA) curves of silver(I) CPs **1** (green), **2** (black), **3** (fuchsia), **4** (red), **5** (blue), and **6** (purple).

Compound **2** was thermally stable up to 250 °C, which then underwent a weight loss of about 20% until 300 °C, which is in a good agreement with the expected theoretical weight loss of 19.28%, corresponding to the evolution of one trifluoroacetic acid molecule, which was the result of the proton transfer from the organic ligand. This event was further continued by a progressive decomposition of the remaining species. Compounds **3** and **5** displayed the highest thermal stabilities, which were resistant up to 350 and 325 °C, respectively. Such remarkable results may be ascribed to the stronger electron-withdrawing effect of both trifluoromethanesulfonate and perchlorate anions, imparting more inertness to the Ag–N coordinative bonds, and thus to the overall polymeric structures. Compounds **4** and **6** showed the lowest thermal stability, which, although still significant, peaked up to 250 °C, followed then by a progressive decomposition.

Activity 3. Study of the antibacterial action of the obtained silver coordination polymers

The assessment of antibacterial activity of all prepared silver(I) CPs against Gram-negative bacteria *E. coli* and Gram-positive bacteria *S. aureus* was performed by using the Tetrazolium/Formazan test (TTC) as a qualitative assay, by measuring the bacterial viability at different time intervals (2, 4, 6, and 24 h).

Figure 5 shows the bacterial viability of the two bacterial strains, *S. aureus* and *E. coli*, in the presence of silver(I) CPs **1–6**, and silver(I) nitrate (AgNO_3) used as a standard antibacterial agent, after 2, 4, and 6 h. The TTC test indicated, as expected in the presence of an antibacterial agent, the bacterial reduction in time with respect to the control (untreated cells). In the case of *S. aureus*, after 2 h, the values of bacterial viability significantly decreased to 8%–19%, and after 6 h the values went down to 1%–4%.

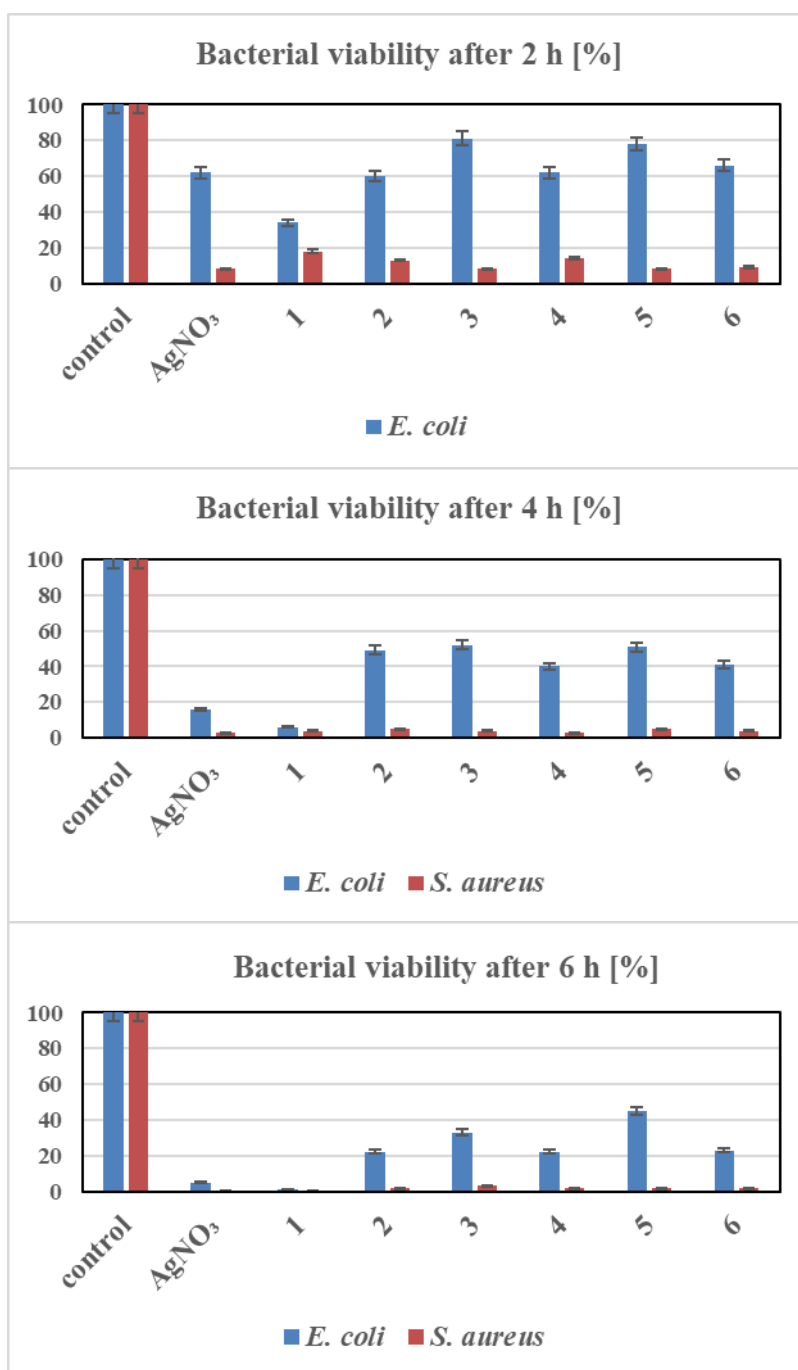


Figure 5. Bacterial viability of *S. aureus* and *E. coli* in the presence of silver(I) CPs 1–6 and standard AgNO₃.

A markedly different behavior was appreciated against *E. coli*, that is, all six silver(I) CPs were less effective in the first period of exposure with a slower action rate compared to *S. aureus*. As such, after 2 h, the values of bacterial viability decreased to 37% (1), 60%–64% (2, 4, and 6), and 79%–81% (3 and 5). The decreasing trend was maintained after 4 h, and after 6 h, the values decreased to 2% (1), 21%–22% (2, 4, and 6), 37% (3), and 42% (5). After 24 h of exposure, a complete bacterial reduction was observed. However, no neat influence of the counter-anions upon the bactericidal effect of the related silver(I) CPs could also be noticed.

For the standard AgNO₃, the bactericidal effect against *S. aureus* was strong during the first 2 h of exposure (8%), while the bacterial reduction was complete after only 6 h, compared to *E. coli*, where the bacterial reduction was only 62% after 2 h and 5% after 6 h of exposure. Thus, a difference in the rate of action as a function of the bacteria types could be appreciated.

It can be observed that the bactericidal effect of the standard AgNO₃ was comparable with that of our silver(I) CPs. However, the high insolubility of these CPs would bring the advantage of applying them for much longer time intervals, compared to the highly soluble AgNO₃ (2160 g/L at 20 °C), which underwent faster silver(I) ions release into the environment, thus leading to an increased level of toxicity.

Activity 4. Incorporation of the obtained silver coordination polymers into paper matrices

Considering the obtained results and based on the fact that there are no applications of these new synthesized compounds into paper matrix, an activity regarding their study is necessary for obtaining papers with enhanced bioactive potential. The main properties of these new compounds for paper applications, such as structural affinity inherent for cellulose fibres, which increases the bonding potential and resistance properties, as well as other particular properties for specific applications. The specific feature of these compounds, given by the antibacterial properties, will be tested in the case of cellulose and paper materials obtained to follow their ability of maintaining the antibacterial properties.

In this context, researches were focused on finding the optimum formulas for the treatment of cellulose material, based on the study of physico-chemical interactions of the components in order to get a permanent (irreversible) immobilization of the bioactive compounds onto paper surfaces for obtaining functional properties with maximum efficiency. To this aim, several processes (printing, coating, spraying) were identified.

Activity 5. Dissemination of the research results

- The results presented within the above mentioned activities, together with the results previously reported in Phase 1, made the subject of 2 ISI published papers:
 - 1) **Aurel Tabacaru**, Andreea Veronica Dediu Botezatu, Georgiana Horincar, Bianca Furdui, Rodica Mihaela Dinica, „*Green accelerated synthesis, antimicrobial activity and seed germination test of quaternary ammonium salts of 1,2-bis(4-pyridyl)ethane*”, *Molecules* **2019**, 24(13), 2424. DOI: 10.3390/molecules24132424. **IF = 3.060 (Q2)**. <https://www.mdpi.com/1420-3049/24/13/2424>
 - 2) **Aurel Tabacaru**, Claudio Pettinari, Mariana Busila, Rodica Mihaela Dinica, „*New antibacterial silver(I) coordination polymers based on a flexible ditopic pyrazolyl-type ligand*”, *Polymers* **2019**, 11(10), 1686. DOI: 10.3390/polym11101686. **IF = 3.164 (Q1)**. <https://www.mdpi.com/2073-4360/11/10/1686>
- 1 poster presentation:

Aurel Tabacaru, Rodica Mihaela Dinica, Mariana Busila, Claudio Pettinari, „*Novel antibacterial silver(I) coordination polymers based on a flexible bis(pyrazolyl)-type ligand*”, 21st Romanian International Conference on Chemistry and Chemical Engineering (RICCCE21), 4-7 September **2019**, Constanta – Mamaia, Romania.