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Antimicrobial activity and DNA/BSA binding affinities of silver(I) and gold(III) complexes with 1,6-naphthyridine

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pharmaceuticals MDPI

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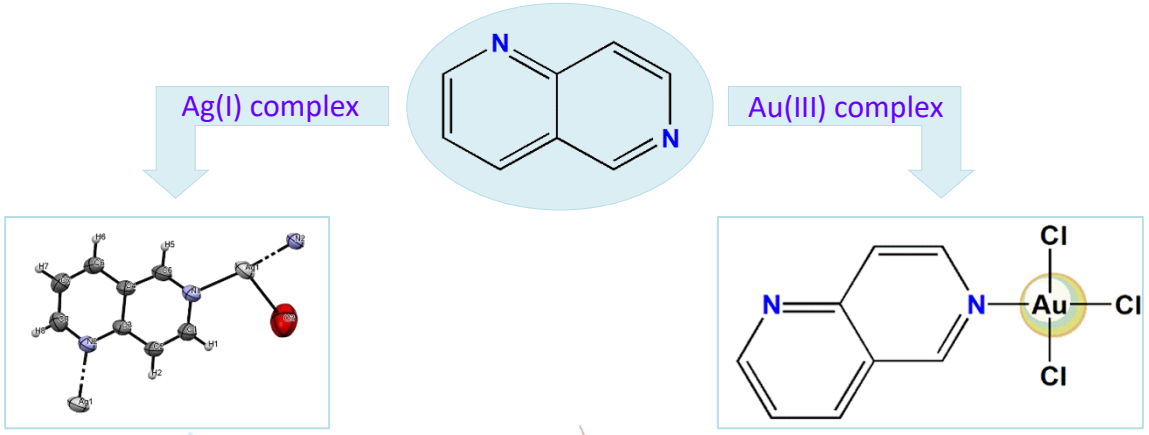
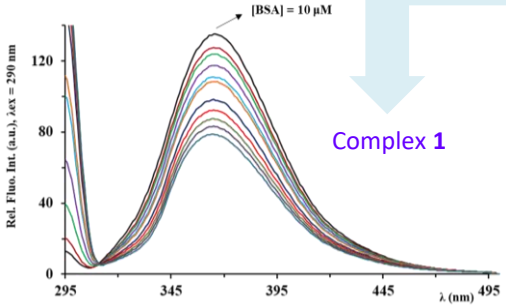
САНУ
СРПСКА АКАДЕМИЈА НАУКА И УМЕТНОСТИ

Antimicrobial activity and DNA/BSA binding affinities of silver(I) and gold(III) complexes with 1,6-naphthyridine

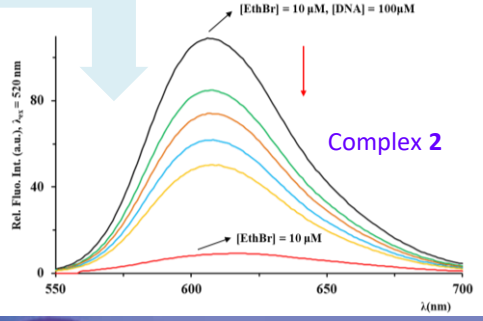


Antimicrobial activity

BSA interaction **DNA interaction**



Complex **1**



Complex **2**

Abstract

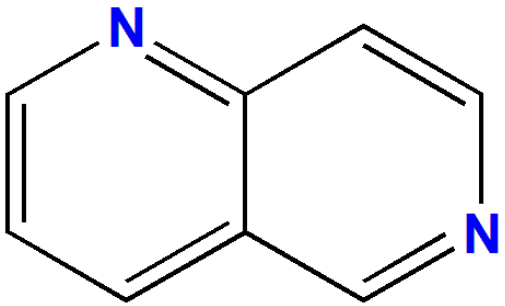
Silver(I) and gold(III) complexes with aromatic nitrogen-containing heterocycles have shown an effective and wide-spectrum antimicrobial activity. The possible mechanism of their antimicrobial activity can be attributed to the interactions of these complexes with biomolecules, including DNA and proteins. In the present study, new silver(I) complex with 1,6-naphthyridine (1,6-naph), $\{[Ag(1,6\text{-naph})(H_2O)](BF_4)\}_n$ (**1**) was synthesized and characterized by NMR, IR and UV-Vis spectroscopy, and its crystal structure was determined by single-crystal X-ray diffraction analysis. The complex **1** and the previously reported analogue gold(III) complex [1], $[AuCl_3(1,6\text{-naph})]$ (**2**), were evaluated for antimicrobial activity against the panel of representative microorganisms, while their cytotoxicity was tested against normal human lung fibroblast cell line (MRC-5). The binding affinity of these complexes with calf thymus DNA (ct-DNA) and bovine serum albumin (BSA) was studied to clarify the mode of their antimicrobial activity [2].

Keywords: Silver(I) complexes; Gold(III) complexes; 1,6-Naphthyridine; Antimicrobial activity; DNA/BSA interaction.

[1] B. Đ. Glišić, B. Warżajtis, M. Hoffmann, U. Rychlewska, M. I. Djuran, RSC Adv. 10 (2020) 44481-44493.
[2] D. P. Ašanin, M. Nenadovic, T. P. Andrejević, S. Vojnovic, M. I. Djuran, B. Đ. Glišić, manuscript in preparation

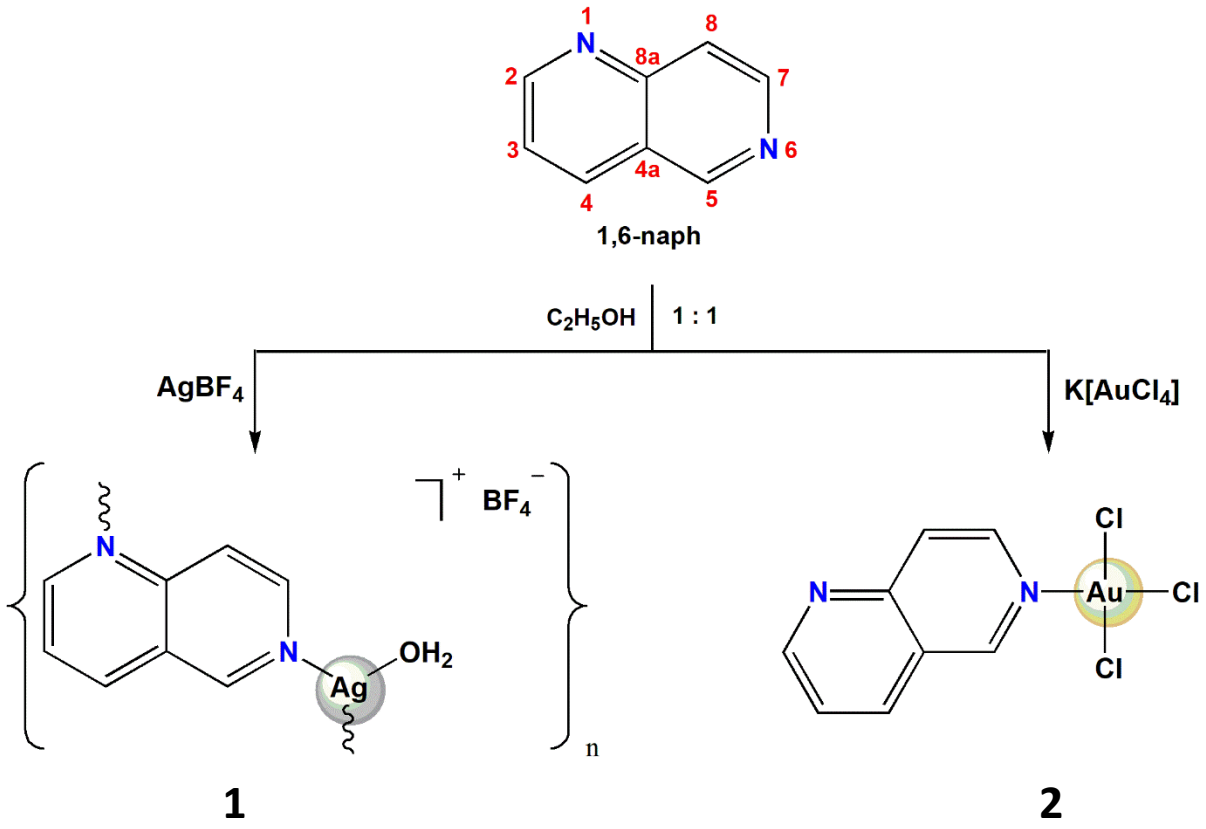
Introduction

- ✓ Silver(I) and gold(III) complexes with aromatic nitrogen-containing heterocycles have shown an effective and wide-spectrum antimicrobial activity
- ✓ One of the possible mechanism of their antimicrobial activity can be attributed to interactions of these complexes with biological targets, including DNA and proteins



1,6-naphthyridine (1,6-naph)

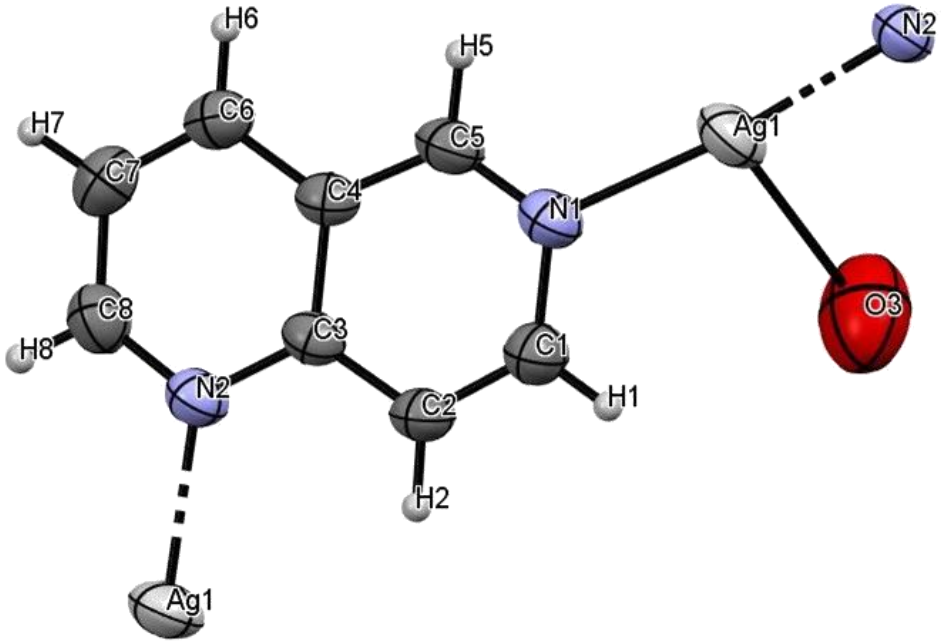
Results and discussion



[1] B. Đ. Glišić, B. Warżajtis, M. Hoffmann, U. Rychlewska, M. I. Djuran, RSC Adv. 10 (2020) 44481-44493.

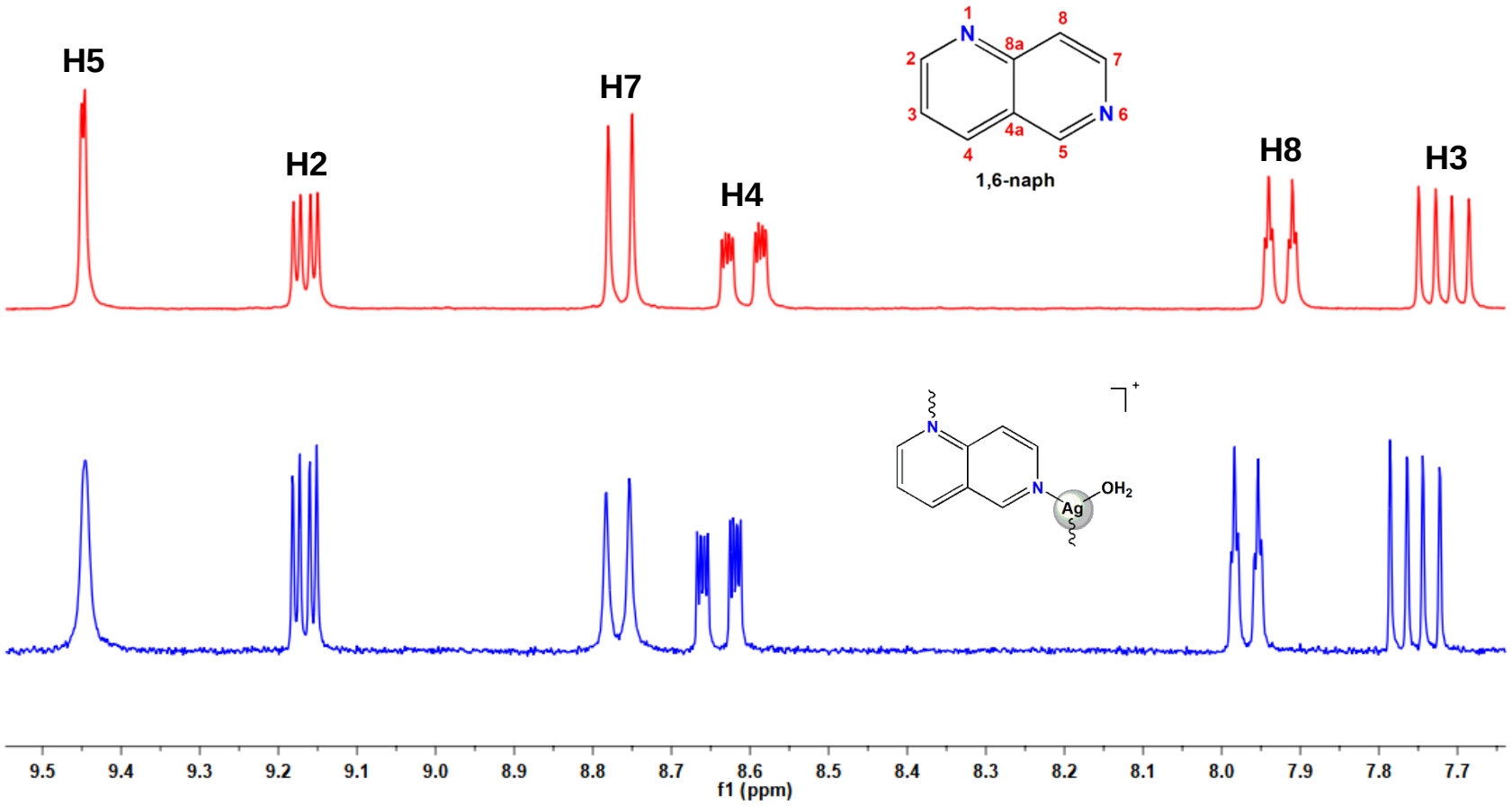
Structural characterization

✓ *Crystal structure of silver(I) complex 1*

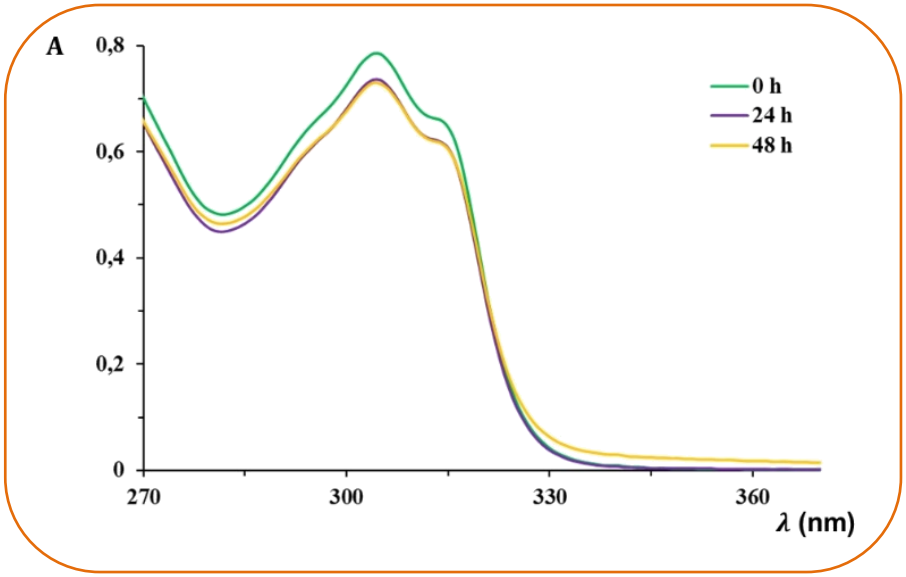


1

✓ *^{1}H NMR spectroscopic characterization of 1*

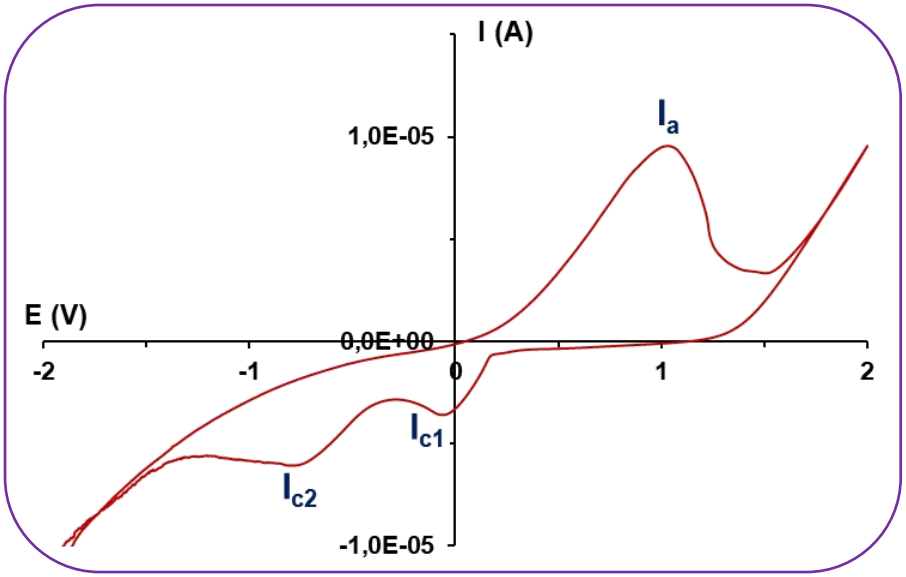


✓ *UV-Vis stability of 1*



Time stability of complex **1** followed by UV-Vis spectrophotometry at room temperature in DMSO

✓ *Electrochemical characterization of 1*



Cyclic voltammogram of complex **1** recorded at the GC electrode in DMSO and 0.1 M tetrabutylammonium hexafluorophosphate (TBAHP) as a supporting electrolyte at a scan rate of 50 mV/s. The conditions are given as follows: E_{begin} = −2.0 V, E_{end} = 2.0 V and E_{step} = 0.002 V

Antimicrobial activity

✓ Antimicrobial activity of silver(I) **1** and gold(III) **2** complexes and the corresponding ligand expressed as MIC (µg/mL) in comparison to their cytotoxicity against healthy human fibroblasts MRC-5 (IC_{50}, µg/mL)

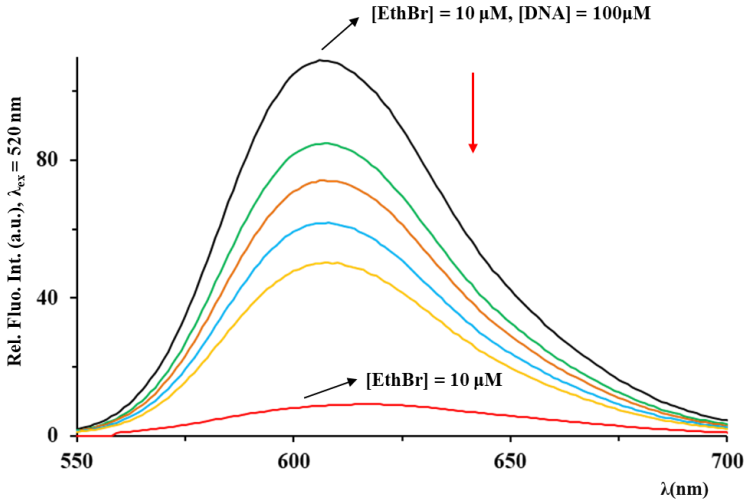
Test organism / Compounds	1	2	1,6-naph
Staphylososus aureus **NCTC 6571**	**31.25**	**62.50**	**>500**
Listeria monocytogenes **NCTC 1194**	**31.25**	**62.50**	**>500**
Pseudomonas aeruginosa **NCTC 10338**	**31.25**	**62.50**	**>500**
Escherichia coli **NCTS 9001**	**7.81**	**62.50**	**>500**
Candida albicans **ATCC 10231**	**3.90**	**>500**	**>500**
Candida parapsilosis **ATCC 22019**	**0.49**	**>500**	**>500**
Klebsiella pneumoniae **ATCC BAA**	**15.62**	**>500**	**>500**
MRC-5	**12 ± 0.8**	**120 ± 8**	**500 ± 10**

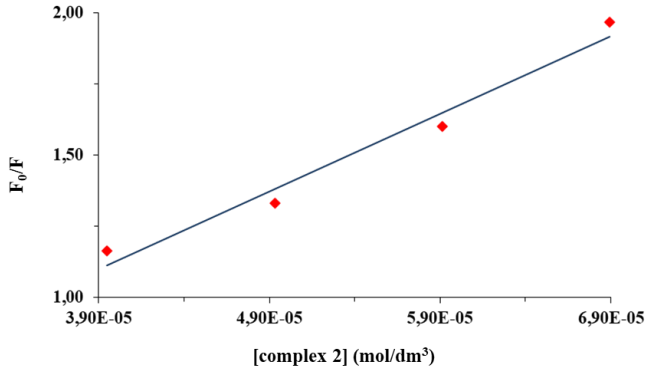
DNA binding study

✓ *DNA interaction of complexes 1 and 2 was studied by florescence spectroscopy*

Complex	K_{sv} (M^{-1})	Hypochromism (%)	K_q ($M^{-1}s^{-1}$)	K_A (M^{-1})	*n*
1	$(9.89\pm0.02)\cdot10^2$	11.90	$9.89\cdot10^{10}$	$6.11\cdot10^3$	1.21
2	$(7.75\pm0.01)\cdot10^5$	53.92	$7.75\cdot10^{13}$	$4.57\cdot10^{10}$	2.55

[complex 2] = 0 – 70 µM, Phosphate buffer saline (pH = 7.4)



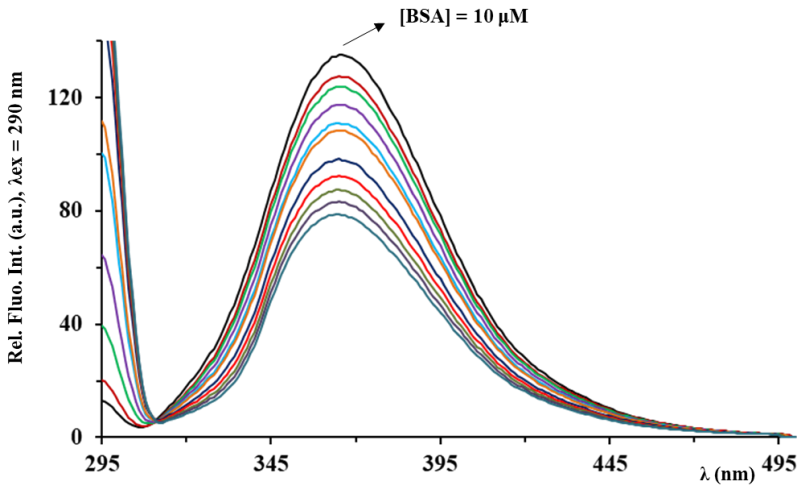


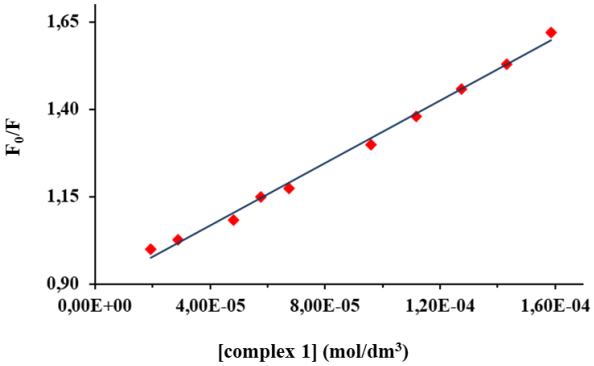
BSA binding study

✓ *BSA interaction of complexes 1 and 2 was studied by florescence spectroscopy*

Complex	K_{sv} (M^{-1})	Hypochromism (%)	K_q ($M^{-1}s^{-1}$)	K_A (M^{-1})	*n*
1	$(5.05\pm0.01)\cdot10^3$	41.96	$5.05\cdot10^{11}$	$2.12\cdot10^4$	1.18
2	$(4.90\pm0.05)\cdot10^4$	61.50	$4.90\cdot10^{12}$	$1.26\cdot10^6$	1.45

[complex 1] = 0 – 160 µM, Phosphate buffer saline (pH = 7.4)



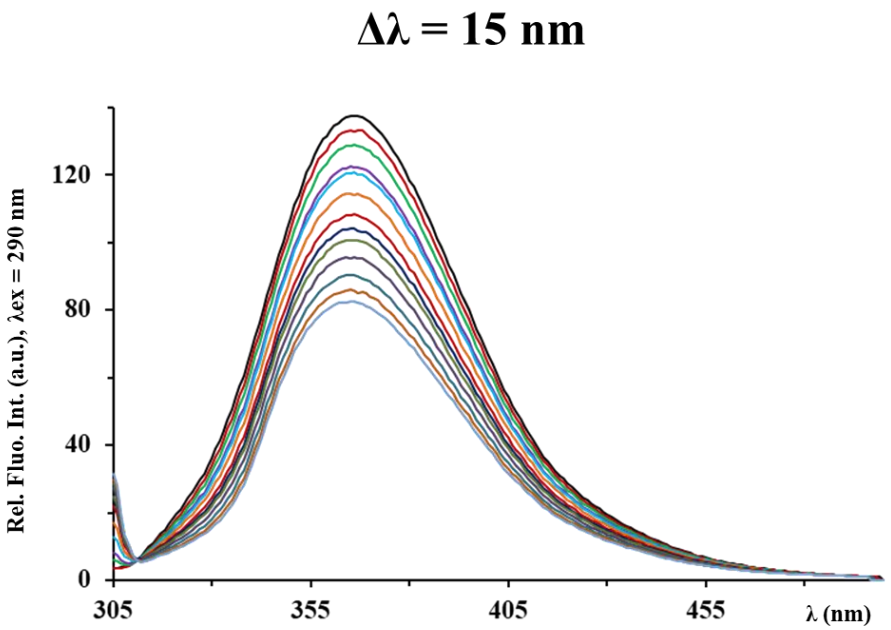


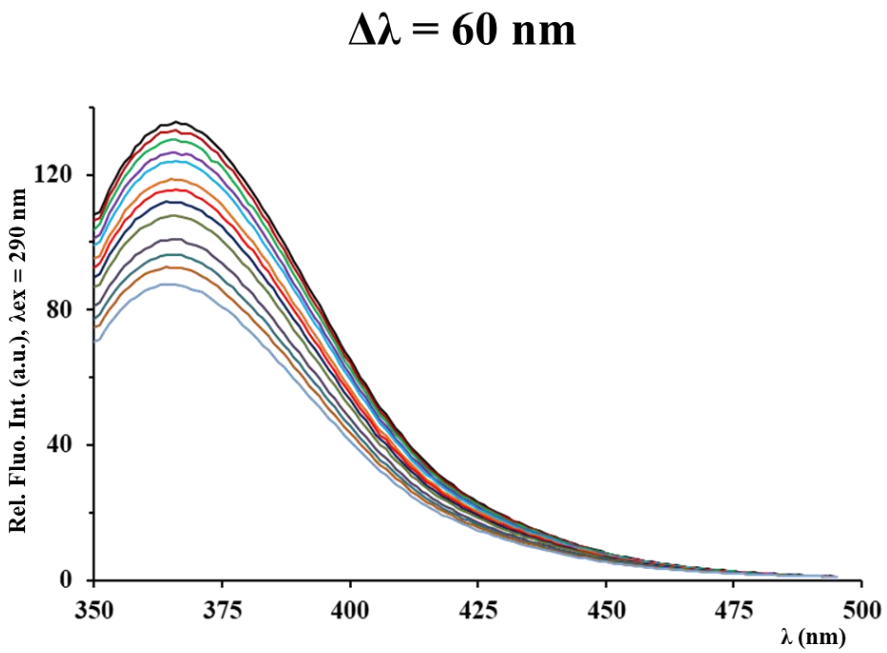
Synchronous fluorescence spectroscopy

- ✓ Synchronous fluorescence spectroscopy was used to explore the structural changes in BSA in the presence of the investigated complexes
- ✓ When Δλ is 15 nm, the synchronous fluorescence is characteristic of the tyrosine (Tyr) residue, while a larger Δλ value of 60 nm is due to tryptophan (Trp)

	Complex	K_{sv} (M^{-1})	Hypochromism (%)	K_q ($M^{-1}s^{-1}$)	K_A (M^{-1})	*n*
Δλ = 15 nm	1	$(4.32\pm0.01)\cdot10^3$	39.99	$4.32\cdot10^{11}$	$7.85\cdot10^3$	1.07
	2	$(2.12\pm0.06)\cdot10^5$	69.28	$2.12\cdot10^{13}$	$6.88\cdot10^7$	1.86
Δλ = 60 nm	1	$(3.70\pm0.01)\cdot10^3$	35.56	$3.70\cdot10^{11}$	$2.34\cdot10^4$	1.22
	2	$(1.02\pm0.04)\cdot10^5$	68.86	$1.02\cdot10^{13}$	$1.27\cdot10^7$	1.68

✓ Synchronous fluorescence spectra of BSA in the absence and presence of increasing concentrations of complex **1**





Conclusions

- ✓ New silver(I) complex with with 1,6-naphthyridine (1,6-naph), $\{[Ag(1,6\text{-naph})(H_2O)](BF_4)\}_n$ (**1**) was synthesized and structurally characterized
- ✓ 1,6-naph ligand is monodentately coordinated to the Ag(I) ion through the nitrogen atom, leading to the formation of $[Ag(1,6\text{-naph})(H_2O)]^+$ complex cation
- ✓ The synthesized silver(I) complex **1** has shown a good antimicrobial activity, especially against *Candida* strains, being, in all cases, more active than gold(III) analogue **2**
- ✓ Both Ag(I) and Au(III) complexes, **1** and **2**, respectively, have the ability to interact with DNA and BSA, with Au(III) complex being more reactive towards these two biomolecules

МИНИСТАРСТВО ПРОСВЕТЕ,
НАУКЕ И ТЕХНОЛОШКОГ РАЗВОЈА

САНУ

Acknowledgments

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