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Polynuclear silver(I) complex with thianthrene: structural characterization, antimicrobial activity and interaction with biomolecules

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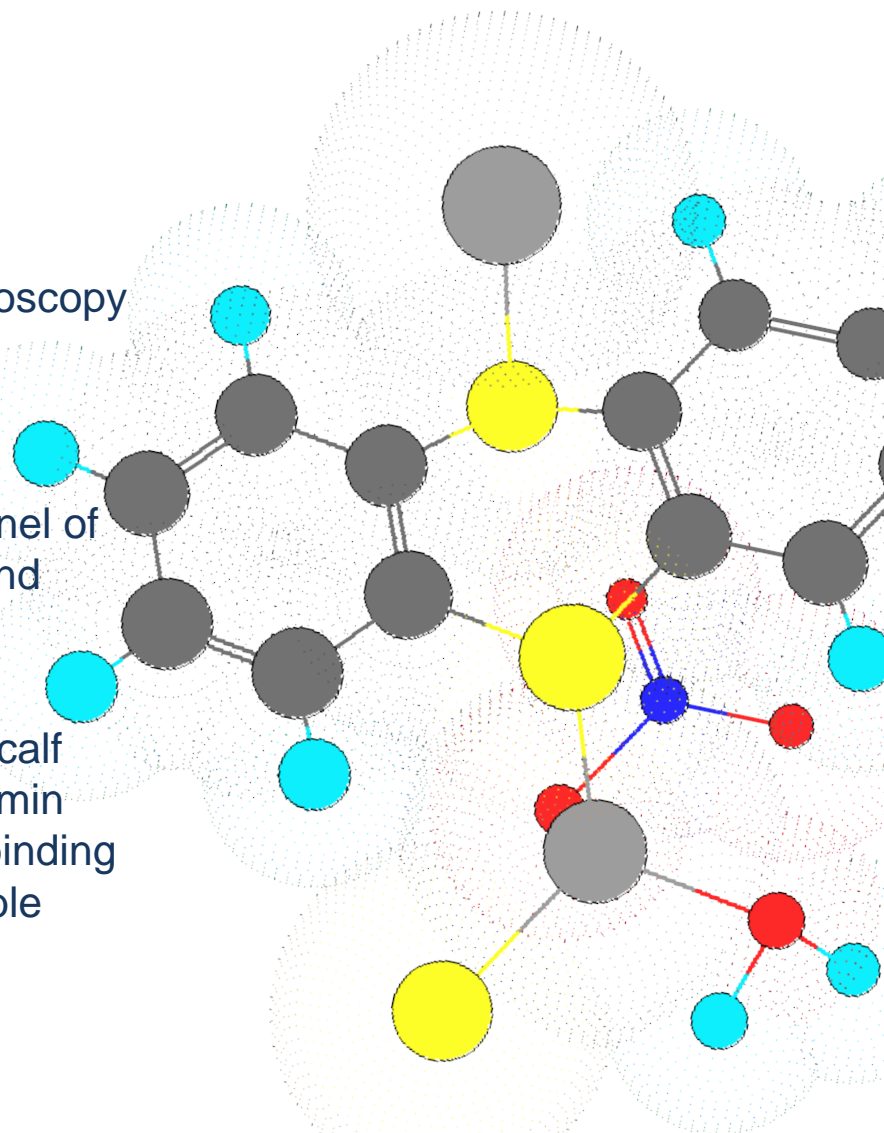
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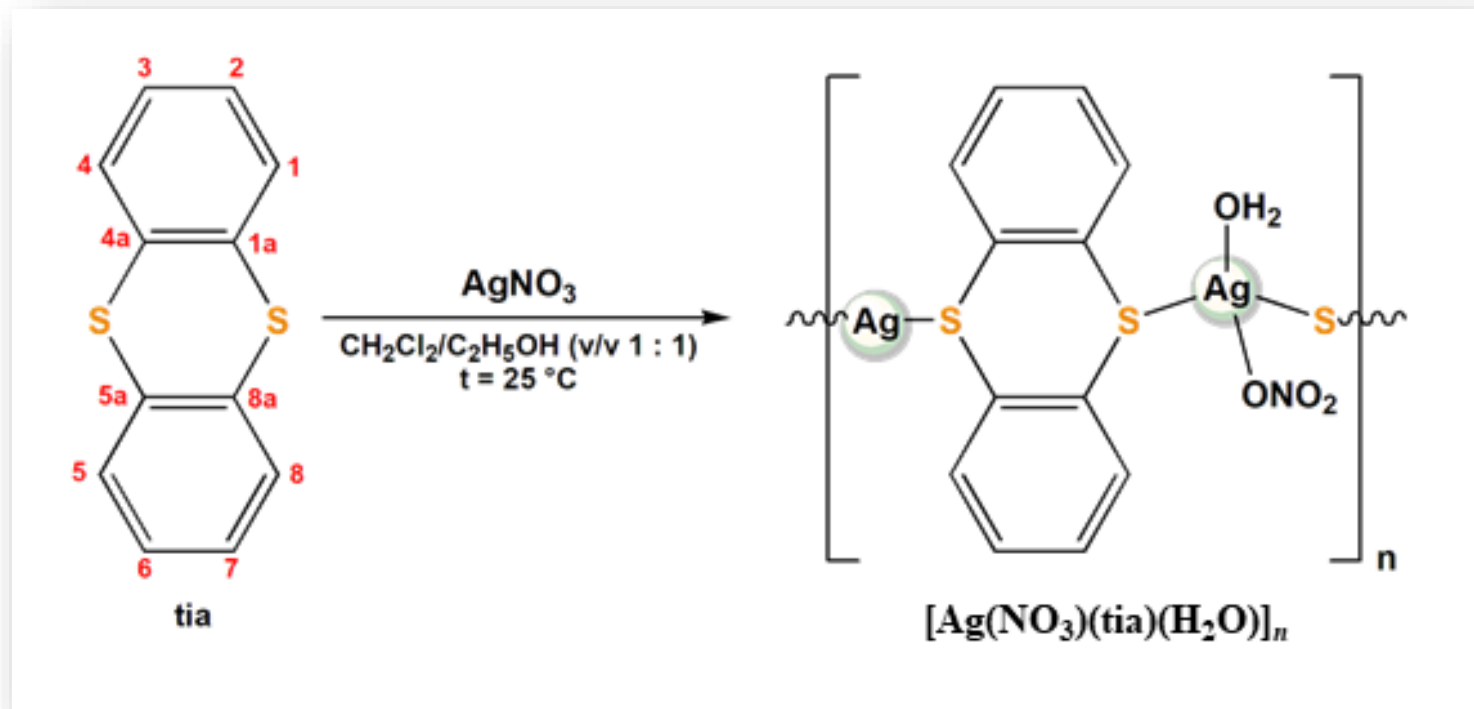
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Abstract

- New silver(I) complex with thianthrene (tia), $[\text{Ag}(\text{NO}_3)(\text{tia})(\text{H}_2\text{O})]_n$, was synthesized and characterized by NMR, IR and UV-Vis spectroscopy and single-crystal X-ray diffraction analysis
- The antimicrobial activity of the synthesized complex was evaluated against the broad panel of Gram-positive and Gram-negative bacteria and *Candida* spp.
- The interactions of $[\text{Ag}(\text{NO}_3)(\text{tia})(\text{H}_2\text{O})]_n$ with calf thymus DNA (ctDNA) and bovine serum albumin (BSA) were studied in order to evaluate the binding affinity towards these biomolecules for possible insights on the mode of antimicrobial activity



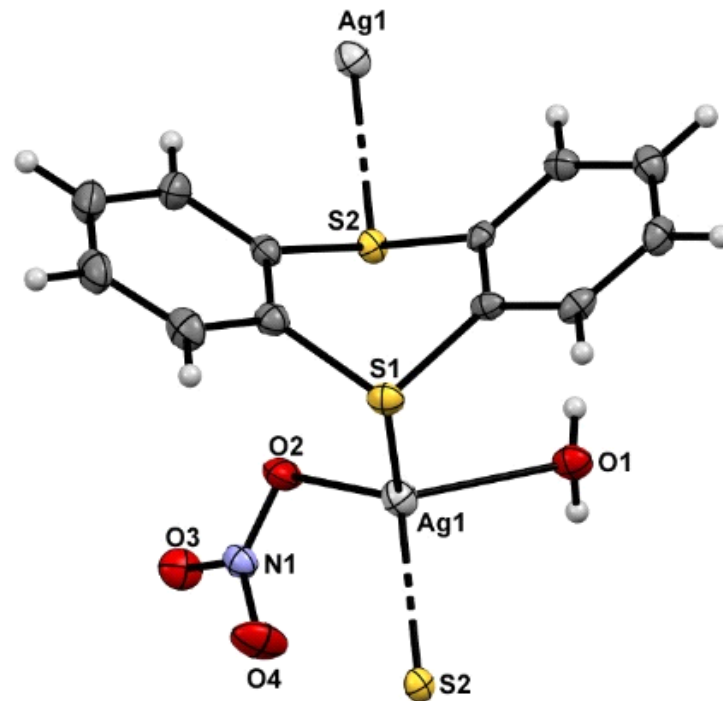
Synthesis of silver(I) complex



Silver(I) complex with thianthrene (tia), $[\text{Ag}(\text{NO}_3)(\text{tia})(\text{H}_2\text{O})]_n$, was synthesized by the reaction of AgNO_3 with an equimolar amount of tia in ethanol/dichloromethane (v/v 1:1) at room temperature

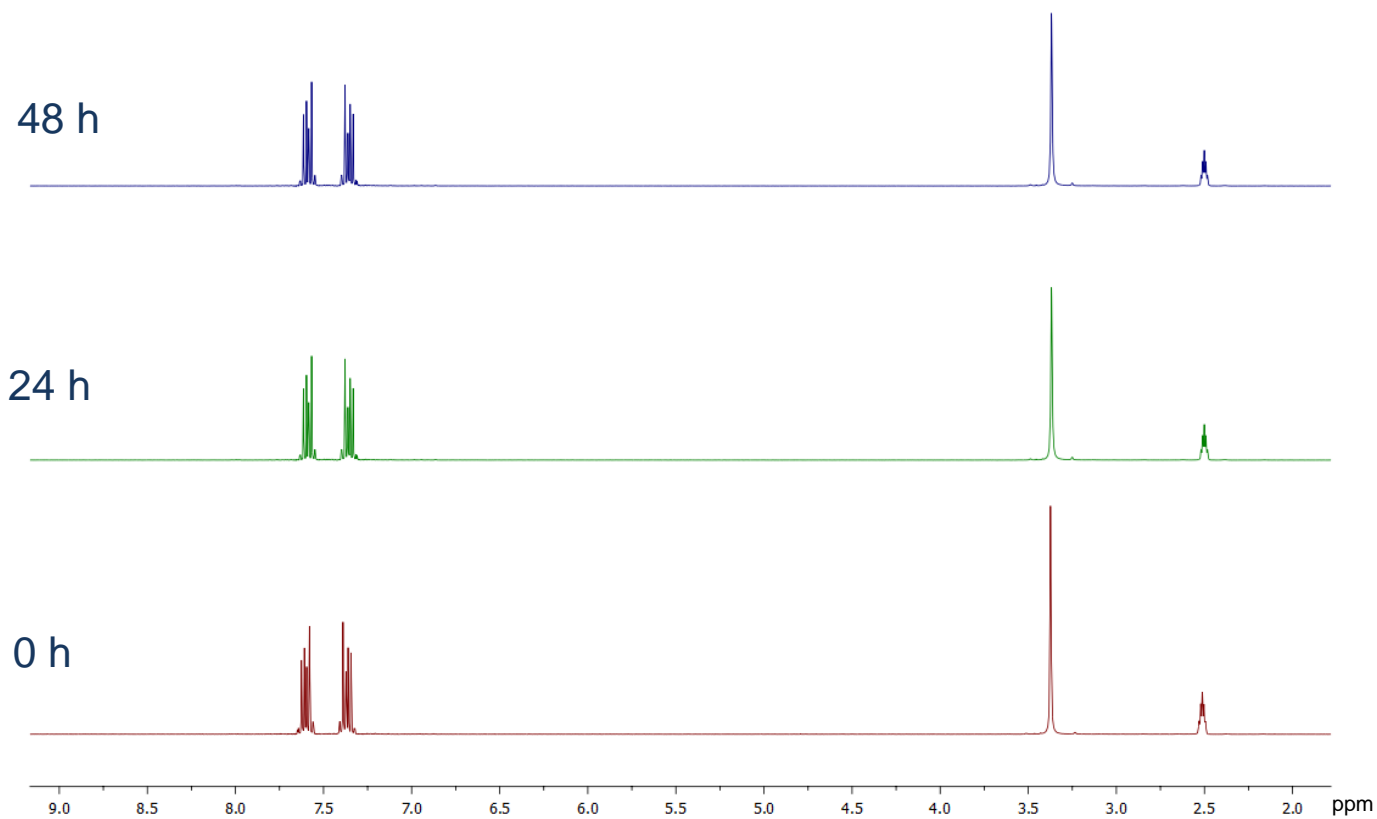
Structural characterization

- Spectroscopic (^1H and ^{13}C NMR, IR and UV-Vis), electrochemical (cyclic voltammetry) and crystallographic (single-crystal X-ray diffraction analysis) methods were applied for the characterization of the synthesized complex
- In the silver(I) complex, tia acts as a bridging ligand connecting two Ag(I) ions
- In the solid state, the complex has polynuclear structure, with tetrahedrally coordinated Ag(I) ion via two thianthrene sulfur atoms, one nitrate oxygen and one water oxygen atoms



The ORTEP drawing of $[\text{Ag}(\text{NO}_3)(\text{H}_2\text{O})(\text{tia})]_n$ complex

^1H NMR Stability



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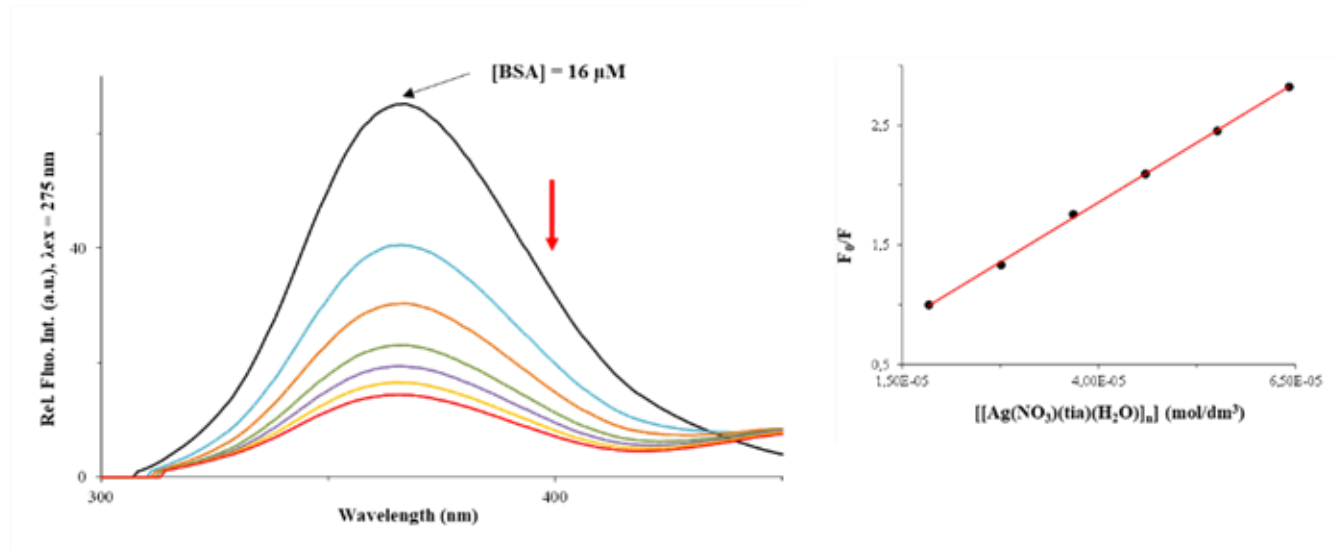
Antimicrobial susceptibility testing

Antimicrobial activity of silver(I) complex and the corresponding thianthrene ligand expressed as MIC ($\mu\text{g}/\text{mL}$) in comparison to their cytotoxicity against healthy human fibroblasts MRC-5 (IC_{50} , $\mu\text{g}/\text{mL}$)

Tested organisms	$[\text{Ag}(\text{NO}_3)(\text{tia})(\text{H}_2\text{O})]_n$	thianthrene
<i>C. albicans</i> ATCC 10231	7.81	> 200
<i>C. parapsilosis</i> ATCC 22019	3.91	> 200
<i>S. aureus</i> ATCC 25923	3.91	> 250
<i>L. monocytogenes</i> NCTC 11994	15.62	> 250
<i>E. coli</i> NCTC9001	15.62	> 250
MRC-5 cells	4.25	> 100

Protein binding studies

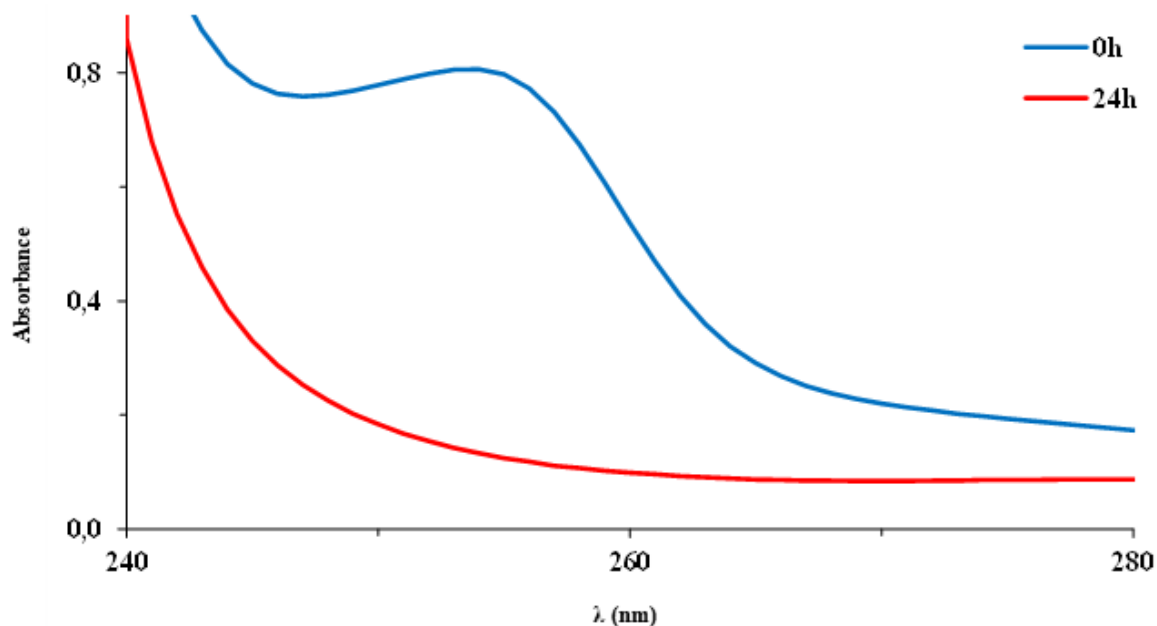
$[[\text{Ag}(\text{NO}_3)(\text{tia})(\text{H}_2\text{O})]_n] = 0 - 65 \mu\text{M}$, Phosphate buffer saline (pH = 7.4)



	$K_{sv} (\text{M}^{-1})$	Hypochromism (%)	$K_q (\text{M}^{-1}\text{s}^{-1})$	$K_A (\text{M}^{-1})$	n
$[\text{Ag}(\text{NO}_3)(\text{tia})(\text{H}_2\text{O})]_n$	$(1.56 \pm 0.01) \cdot 10^5$	78.03	$1.56 \cdot 10^{13}$	$3.05 \cdot 10^6$	1.41

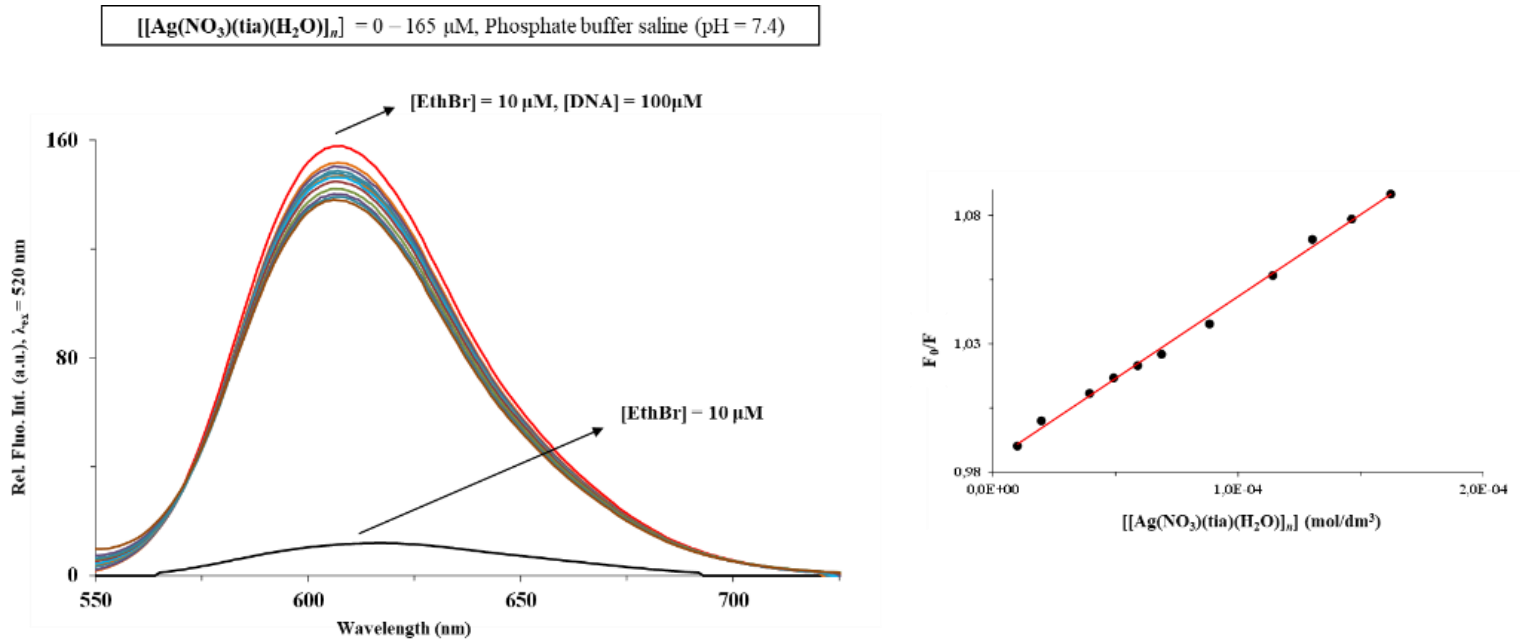
Fluorescence emission spectra of BSA in the presence of an increasing concentration of $[\text{Ag}(\text{NO}_3)(\text{H}_2\text{O})(\text{tia})]_n$ complex alongside with the values of the binding constants. Arrow shows the intensity changes upon increased amount of the complex. Inserted graph: Stern-Volmer plots of F_0/F vs [complex]

Partition coefficient (logP)



- Octanol–water partition coefficient (logP), which is a measure of lipophilicity, for $[\text{Ag}(\text{NO}_3)(\text{H}_2\text{O})(\text{tia})]_n$ complex, is found to be 0.72, indicating its hydrophobic properties
- This value is in accordance with logP values of new pharmacophores in the Comprehensive Medicinal Chemistry database being in range from -0.4 to 5.6

DNA binding study



The emission spectra of EthBr-DNA system in the absence and presence of the investigated complex including the plot of $\log(F_0 - F)/F$ versus $\log[\text{complex}]$

- From the K_{sv} value of $6.49 \cdot 10^2 \text{ M}^{-1}$, it can be concluded that the presently investigated complex binds to DNA through the electrostatic mode

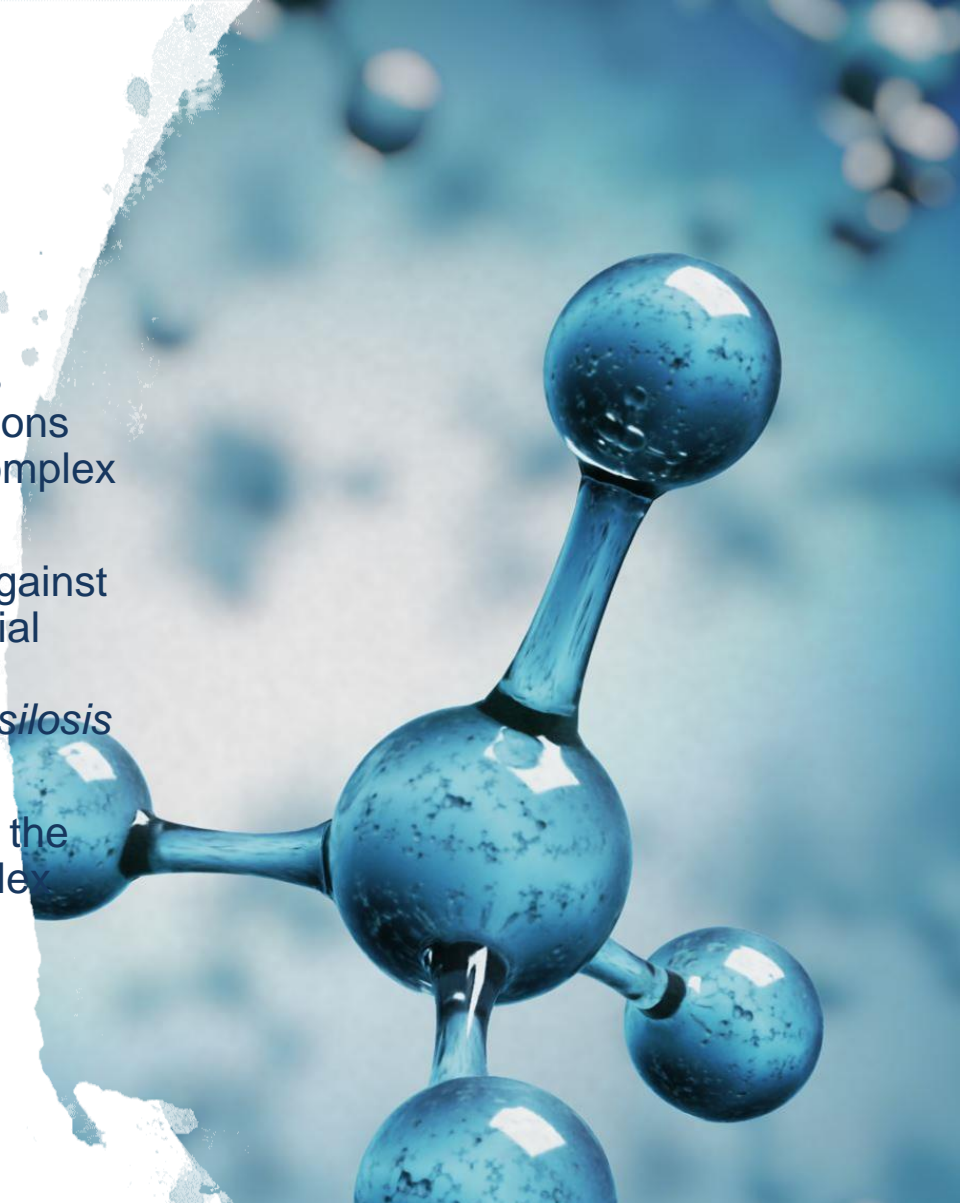
Conclusions

- Sulfur-containing ligand, thianthrene (tia), is effective bridging ligand between two Ag(I) ions forming polynuclear $[Ag(NO_3)(H_2O)(tia)]_n$ complex
- This complex shows considerable activity against two different *Candida* spp. and three bacterial species, being the most active toward *Staphylococcus aureus* and *Candida parapsilosis*
- BSA could transport the silver(I) complex to the infected cells, and inside the cell, this complex could exert its antimicrobial activity through interaction with DNA

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