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Antimicrobial copper complexes with polymeric pentaiodide chains

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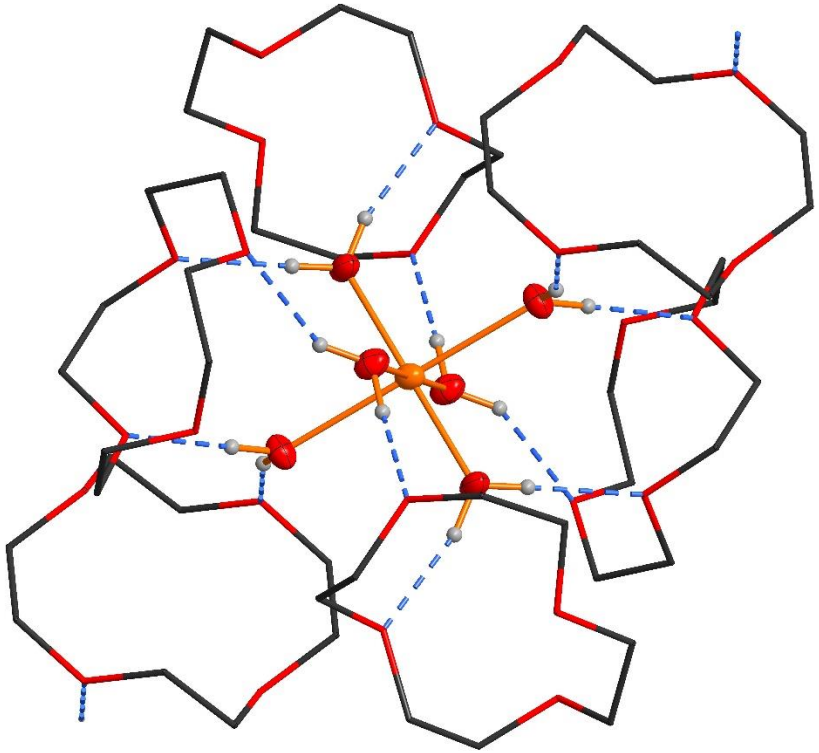
Antimicrobial copper complexes with polymeric pentaiodide chains

Graphical Abstract



Abstract:
Polyiodides are interesting compounds with unique structures depending on the surrounding molecules. A vast number of polyiodide structures exist already in literature. These compounds are stabilized by counterions or complexation and lead from basic structures to extended three-dimensional networks of polyiodides. Iodine is known as a microbicide since centuries throughout many cultures. We prepared a copper-12-crown-4-hexahydrate complexed pentaiodide with polymeric structure and investigated its structure and antimicrobial properties against nine microbial reference strains. The compound $[Cu(H_2O)_6(12\text{-crown-}4)_5]I_6 \times 2I_2$ showed excellent antifungal and intermediate antibacterial properties in comparison to common antibiotics. The structure of the chain-type pentaiodide is remarkable and can be described as triiodide ions connected to two iodine molecules.

Keywords: Antimicrobial; Polyiodides; Complexes; Pentaiodides; crystal structure

Introduction

Mankind faces dangerously rising levels of **antimicrobial resistance** by the so-called **ESKAPE pathogens** (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter* spp. and *Escherichia coli*) [1,2]. Conventional drugs and antimicrobials lose their efficiency against such emerging multi-drug resistant microorganisms [2–5]. Pathogens can be acquired in hospital settings through nosocomial infections and lead to delayed recovery, treatment failures, increasing health care costs, morbidity, and mortality [5,6].

In the current **COVID-19 pandemic**, nosocomial infections originating from emergency rooms and health care settings have negatively impacted the treatment of immunocompromised, severely ill patients with comorbidities.

Antimicrobial polymeric coatings can reduce the burden of infections through contaminated fomites in all indoor and outdoor settings [8–13]**. Inclusion of known antimicrobial agents like iodine and copper into polymeric coating materials can mitigate antimicrobial resistance** [13–16].

Introduction

We showed in our previous investigations the antimicrobial activities of **"smart" triiodides.**

The complex **$[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$** contains **copper and iodine** as inorganic biocides and is expected to show inhibitory action on pathogens.

We tested our compound against a total of **10 microbial strains** in comparison to five common antibiotics.
The inhibitory effect of our complex polymeric compound on *C. albicans* WDCM 00054 Vitroids showcased its antifungal activity.

$[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$ exhibits **excellent activity** against reference strains of microorganisms compared to selected antibiotics.

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Results and discussion

The methods used for the characterization of our novel polymeric complex compound **$[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$** confirmed its composition and structure.
The results are in accordance to previous studies [27–31].

The complex consists of **sandwiched copper-hexahydrates within polymeric pentaiodide-chains.**

A recent database check revealed that the interesting topology of this chain-type polyiodide is new.

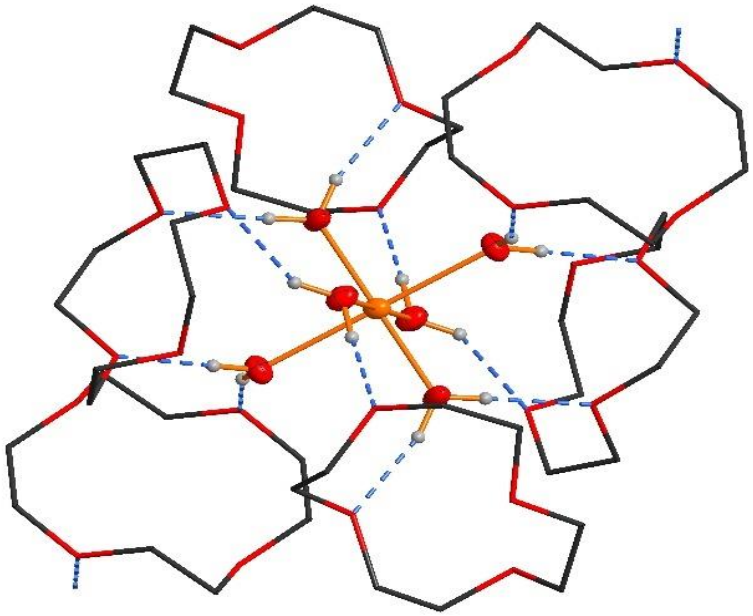
Results and discussion

Table 1. Crystal data, data collection and refinement of $[Cu(H_2O)_6(12\text{-crown-}4)_5]I_6 \times 2I_2$.

Item	Parameter
Formula	$C_{40}H_{92}CuI_{10}O_{26}$
Mr	1160.84
Linear absorption factor	μ = 4.64 mm^{-1}
Crystal system, space group	Triclinic, P-1
a	10.7289 (4) Å
b	12.3645 (5) Å
c	15.1570 (7) Å
α	113.470 (4)°
β	99.187 (4)°
γ	92.543 (3)°
Temp.	100 K
Volume, Z	V = 1807.70 (14) $Å^3$, Z = 1
Diffractometer	Xcalibur
Radiation	Mo Kα, λ = 0.71073 Å
Measured reflections	17,571
Independent reflections	7846
Reflections with $I > 2\sigma(I)$	5930
Rint; Completeness	0.042; 99.3%
Refined parameters	371
$R[F^2 > 2\sigma(F^2)]$	0.042
$wR(F^2)$; GooF	0.081, 1.05
ρ_{max}; ρ_{min}	0.86 e $Å^{-3}$; −0.87 e $Å^{-3}$

Results and discussion

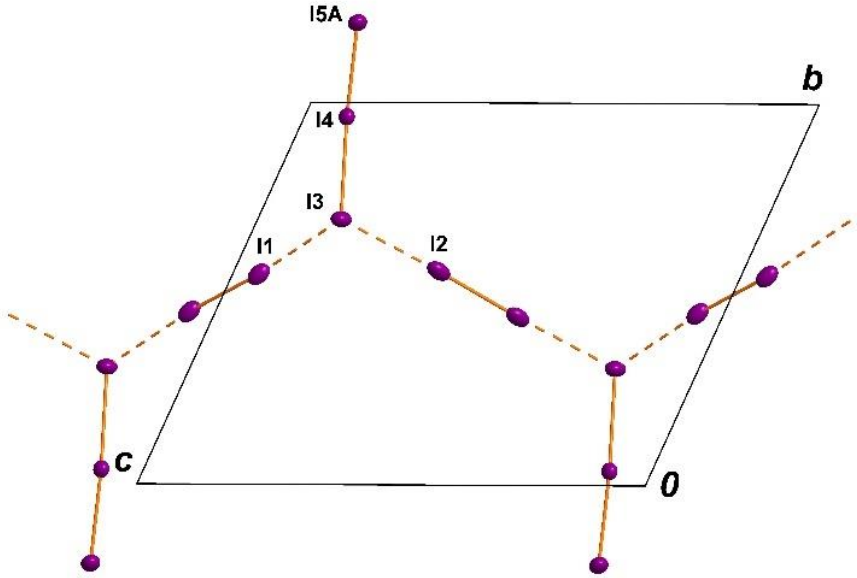
The **asymmetric unit** of the title crystal structure **$[Cu(H_2O)_6(12\text{-crown-}4)_5]I_6 \times 2I_2$** contains one half of a hexaaquacopper(II) complex, 2.5 12-crown-4 molecules, two halves of an iodine molecule and one triiodide anion :



Results and discussion

The anionic part of the title structure is a chain-type polymer consisting of **triiodide anions and iodine molecules**. **Each triiodide anion forms two halogen bonds to neighboring iodine molecules by one iodine atom (I3).**

The bond lengths within the formal **triiodide anion (I3–I4–I5) are very asymmetric** (I3–I4 = 3.0563(5) Å, I4–I5A = 2.8014(10) Å) [25,26].



Results and discussion

Table 2. Antimicrobial testing of antibiotics (A), $[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$ by agar well (AW), and disc dilution studies (1,2,3). ZOI (mm) against microbial strains by diffusion assay.

Strain	Antibiotic	A	AW [+]	1 [+]	2 [+]	3 [+]
S. pneumoniae ATCC 49619	G	18	20	19	0	0
S. aureus ATCC 25923	G	28	23	35	14	0
S. pyogenes ATCC 19615	C	25	20	21	0	0
E. faecalis ATCC 29212	CTX	25	19	18	0	0
B. subtilis WDCM 00003	S	20	21	33	11	0
P. mirabilis ATCC 29906	G	25	0	15	0	0
P. aeruginosa WDCM 00026	CTX	21	16	12	0	0
E. coli WDCM 00013	A	20	15	25	8	0
K. pneumoniae WDCM 00097	CTX	17	NA	24	7	0
C. albicans WDCM 00054	NY	16	51	53	14	0

[+] Agar well (AW) diffusion studies (20 mg crystals of $[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$ in 6 mm diameter well) and disc diffusion studies (6 mm disc impregnated with 2 mL of 50 µg/mL (1), 2 mL of 25 µg/mL (2) and 2 mL of 12.5 µg/mL (3) of $[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$). A Amikacin (30 µg/disc). G Gentamicin (30 µg/disc). CTX (Cefotaxime) (30 µg/disc). NY (Nystatin) (100 IU). C Chloramphenicol (10 µg/disc). Streptomycin (10 µg/disc). Grey shaded area represents Gram-negative bacteria. 0 = Resistant. No statistically significant differences ($p > 0.05$) between row-based values through Pearson correlation.

Results and discussion

The **morphology and form of aggregation of the microorganisms** is a strong indicator for the inibitory action of our polymeric complex compound.
The susceptibility of **cocci** is **highest in *S. aureus*, followed by *S. pyogenes*, then *S. pneumonia* and finally *E. faecalis*.** These microorganisms appear in form of clusters, chains, pairs and single, in pairs or chains, respectively.
Staphylococci are more inhibited by $[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$ than streptococci.
Non-motile species are more susceptible to our compound than motile strains with flaggellae.

Results and discussion

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Non-motile species are more susceptible to our compound than motile strains with flaggellae.

Conclusions

$[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$ has excellent antifungal properties against *C. albicans WDCM 00054* and inhibits strongly the studied bacterial strains.

These results suggest the **use of hexaaquacopper(II) complexes with polymeric-pentaiodide chains as antimicrobial coating** agents against resistant pathogens causing nosocomial infections.

We confirmed the composition and structure by X-ray crystallography, UV-Vis, FT-IR, Raman, XRD and microstructural analysis by SEM/EDS. All analytical results are in agreement with each other and previous studies of related compounds.

Conclusions

The title compound **$[Cu(12\text{-crown-}4)_5(H_2O)_6]I_6 \times 2I_2$** reveals an interesting **structure**, which consists of

- **three different conformers of 12-crown-4-molecules and**
- **new polymeric pentaiodide chains**

The unique topology of the polymeric polyiodide chains facilitate the **antimicrobial activity against pathogens by controlled iodine release from its polymeric I_2-I_3^--I_2 chain structure.**

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- SVKM'S Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, India
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Article

A Look Behind the Scenes at COVID-19: National Strategies of Infection Control and Their Impact on Mortality

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Abstract: (1) Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began spreading across the globe in December and, as of 9 July 2020, had inflicted more than 550,000 deaths. Public health measures implemented to control the outbreak caused socio-economic havoc in many countries. The pandemic highlighted the quality of health care systems, responses of policymakers in harmony with the population, and socio-economic resilience factors. We suggest that different national strategies had an impact on mortality and case count. (2) Methods: We collected fatality data for 17 countries until 2 June 2020 from public data and associated these with implemented containment measures. (3) Results: The outcomes present the effectiveness of control mechanisms in mitigating the virus for selected countries and the UAE as a special case. Pre-existing conditions defined

References

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Article

Facile Synthesis of Antimicrobial Aloe Vera-"Smart" Triiodide-PVP Biomaterials

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Abstract: Antibiotic resistance is an eminent threat for the survival of mankind. Nosocomial infections caused by multidrug resistant microorganisms are a reason for morbidity and mortality worldwide. Plant-based antimicrobial agents are based on synergistic mechanisms which prevent resistance and have been used for centuries against ailments. We suggest the use of cost-effective, eco-friendly *Aloe Vera Barbadensis* Miller (AV)-iodine biomaterials as a new generation of antimicrobial agents. In a facile, one-pot synthesis, we encapsulated fresh AV gel with polyvinylpyrrolidone (PVP) as a stabilizing agent and incorporated iodine moieties in the form of iodine (I_2) and sodium iodide (NaI) into the polymer matrix. Ultraviolet-visible spectroscopy (UV-Vis), Fourier transform infrared spectroscopy

References

pathogens

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Article

"Smart" Triiodide Compounds: Does Halogen Bonding Influence Antimicrobial Activities?

Zehra Edis [1,*], Samir Haj Bloukh [1], Hamed Abu Sara [1], Hanusha Bhakhoa [2], Lydia Rhyman [2,3] and Ponnadurai Ramasami [2,3,*]

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Abstract: Antimicrobial agents containing symmetrical triiodides complexes with halogen bonding may release free iodine molecules in a controlled manner. This happens due to interactions with the plasma membrane of microorganisms which lead to changes in the structure of the triiodide anion. To verify this hypothesis, the triiodide complex $[Na(12\text{-crown-}4)_2]I_3$ was prepared by an optimized one-pot synthesis and tested against 18 clinical isolates, 10 reference strains of pathogens and five antibiotics. The antimicrobial activities of this symmetrical triiodide complex were determined by zone of inhibition plate studies through disc- and agar-well-diffusion methods. The triiodide complex proved to be a broad spectrum microbicidal agent. The biological activities were related to the calculated partition coefficient (octanol/water). The microstructural analysis of SEM and

References

pharmaceutics

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Article

"Smart" Antimicrobial Nanocomplexes with Potential to Decrease Surgical Site Infections (SSI)

Zehra Edis [1,*], Samir Haj Bloukh [2], May Reda Ibrahim [1] and Hamed Abu Sara [2]

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check for updates

Abstract: The emergence of resistant pathogens is a burden on mankind and threatens the existence of our species. Natural and plant-derived antimicrobial agents need to be developed in the race against antibiotic resistance. Nanotechnology is a promising approach with a variety of products. Biosynthesized silver nanoparticles (AgNP) have good antimicrobial activity. We prepared AgNPs with *trans*-cinnamic acid (TCA) and povidone–iodine (PI) with increased antimicrobial