The 7th International Electronic Conference on Medicinal Chemistry (ECMC 2021)
01–30 NOVEMBER 2021 | ONLINE

Microbicidal plant-AgNP biocompounds with "smart" triiodides

Zehra Edis[1,2*], Samir Haj Bloukh[2,3], and Hamed Abu Sara[2,3]

[1] College of Pharmacy and Health Science, Department of Pharmaceutical Sciences, Ajman University, PO Box 346, Ajman, United Arab Emirates
[2] Center of Medical and Bio-allied Health Sciences Research, Ajman University, Ajman, United Arab Emirates
[3] College of Pharmacy and Health Science, Department of Clinical Sciences, Ajman University, PO Box 346, Ajman, United Arab Emirates; s.bloukh@ajman.ac.ae; h.abusara@ajman.ac.ae

***** Corresponding author: z.edis@ajman.ac.ae

جامعة عجمان
AJMAN UNIVERSITY

Microbicidal plant-AgNP biocompounds with “smart” triiodides

Graphical Abstract

Use one slide

جامعة عجمان
AJMAN UNIVERSITY

Abstract:
Multi-drug resistant ESKAPE pathogens are listed by WHO as threat to mankind. These microorganisms developed resistance mechanisms against some commonly used antimicrobials and drugs. New antimicrobials can be a combination of nanotechnology and plant constituents. Silver nanoparticles demonstrated already in many investigations unique antimicrobial properties during the last decade. Plants contain multiple biocompounds, which exert antimicrobial activities due to their synergistic actions. We investigated the antimicrobial activities of well-known *cinnamomum zeylanicum* (Cinn) with iodine (I_2), stabilized with polyvinypyrrolidone and compared the results with their trans-cinnamic acid (TCA) equivalents. The compounds were tested against five microbial strains by agar-well and disc-diffusion methods on discs and polyglycolic acid (PGA) sutures. The title compounds were characterized by different analytical methods and showed excellent to intermediate inhibition of the tested pathogenic strains. Our compounds can be seen as alternative disinfectants and coating agents on surgical sutures in the prevention of surgical site infections.

Keywords: Antimicrobial resistance; silver nanoparticles, cinnamomum zeylanicum

Introduction

Antimicrobial resistance is a danger to mankind according to the World Health Organization (WHO) [1]. Resistance occurred due to increase in uncontrolled, irrational antibiotic use, lack of incentives and research efforts for the development of new antibiotics [2]. ESKAPE pathogens like *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli* are multidrug resistant microorganisms are a cause of dangerous nosocomial infections [2].

Introduction

Morbidity and mortality caused by **infectious diseases** through microorganisms and **increased resistance towards antibiotics** is on the rise. The survival of the human race depends on development of new anti-bacterial compounds. Inorganic antimicrobial agents, like the elements **iodine, silver** and **copper** [4], and combinations of these elements [5,6] are important for drug development and biocidal applications [4-6].

Long term effectiveness and stability of the biocidal agent are important requirements. This can be achieved by using **polyiodide-structures** as a complex, molecular backbone, releasing the biocidal agent slowly and effectively over a long period of time due to halogen bonding [7].

Introduction

At the same time investigations of **polyiodides** result in stable compounds predestined for **long term release of iodine** in **controlled manner due to halogen bonding** [7,8].

The controlled release increases the activity of the drug by longer activity on the site and reduces side effects because less antimicrobial agent is needed [7].

Plant-synthesized nanomaterials are excellent alternatives to conventional drugs [7,9].

Nanomedicine can reduce the negative impact of resistant pathogens. Biosynthesized silver nanoparticles (AgNP) have good antimicrobial activity [7,9].

جامعة عجمان
AJMAN UNIVERSITY

Results and discussion

In this work, we investigated combinations of **hydrophobic *trans*-cinnamic acid (TCA)**, **natural *cinnamomum zeylanicum* bark extract (Cinn)** and **hydrophilic povidone iodine (PI)** to increase the antimicrobial effect of **AgNPs**.

Our hypothesis is to optimize antimicrobial activity of AgNPs by combining silver nanoparticles with the known microbicidal agents TCA, Cinn, and PI.

Reducing the AgNP content will decrease its hazards to human health and environment. The adverse effects related to PI and iodine can be minimized by this potent combination through controlled release of iodine [7].

جامعة عجمان
AJMAN UNIVERSITY

Results and discussion

We synthesized **AgNPs** with **trans-cinnamic acid (TCA)** and **povidone-iodine (PI)** with enhanced antimicrobial activity. Additionally, we prepared **AgNPs** with **natural cinnamon bark extract (Cinn)** with **PI** and **coated biodegradable Polyglycolic Acid (PGA) sutures** with the new materials separately.

We used ***trans*-cinnamic acid for the chemical reduction** and **natural cinnamon bark extract for the biological reduction (green synthesis)** of silver nitrate to **AgNPs**.

TCA and *cinnamomum zeylanicum* bark extracts (Cinn) act also as **reducing, capping, and stabilizing agents** [7].

PI is a stabilizing agent and reservoir for triiodide anions releasing free molecular iodine for biocidal action [7].

Results and discussion

TCA, Cinn, and PI as stabilizing agents prevent agglomeration of silver, resulting in smaller AgNPs and better microbial growth control.

This **hybrid antimicrobial agent/biocide/drug delivery system** can be an advantage to prevent SSI and biofilm formation:

TCA-AgNP, TCA-AgNP-PI,

Cinn-AgNP and Cinn-AgNP-PI

Results and discussion

TCA-AgNP, TCA-AgNP-PI,
Cinn-AgNP and Cinn-AgNP-PI
and their dip-coated PGA sutures were tested against **10 reference strains of microorganisms** and compared to four common antibiotics (chloramphenicol, cefotaxime, gentamycin, and nystatin) by **zone inhibition with disc- and agar-well-diffusion methods.**

TCA-AgNP-PI and Cinn-AgNP-PI are broad spectrum microbicidal agents and can be used to coat sutures to prevent the development of Surgical Site Infections (SSI).

Results and discussion

Our compounds exhibited **microbicidal action**.

The **Gram-negative pathogens** *P. aeruginosa*, *E. coli*, *K. pneumoniae*, and the **Gram-positve** *S. aureus* were inhibited by TCA-AgNP-PI and its dip-coated PGA suture stronger than Cinn-AgNP-PI.

The size of the nanoparticles :

Capping agent used	Particle size mean (nm)
TCA-AgNP	61.3 ± 11.2
TCA-AgNP-PI	57.2 ± 10.4
Cinn-AgNP	88.1 ± 20.6
Cinn-AgNP-PI	51.5 ± 7.8

Conclusions

TCA-AgNP-PI has stronger antimicrobial activity against the studied pathogens than **Cinn-AgNP-PI**.

We confirmed the composition of TCA-AgNP-PI and Cinn-AgNP-PI by DLS, UV-Vis, FT-IR, Raman, XRD and microstructural analysis by SEM/EDS.

Smart materials based on synergistic antimicrobial action are interesting alternatives against resistant microorganisms.

Acknowledgements

- **Ajman University**
- Center of Medical and Bio-allied Health Sciences Research, Ajman University
- **Deanship of Graduate Studies and Research**, AU, Ajman, United Arab Emirates
- **Artist "@art_by_amie_"** for providing us with digital art images as graphical abstracts for our publications
- All our colleagues

جامعة عجمان
AJMAN UNIVERSITY

References

1. Shrivastava, S.; Shrivastava, P.; Ramasamy, J. World health organization releases global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. J. Med. Soc. 2018, 32, 76-77. doi:10.4103/jms.jms_25_17.
2. Chokshi, A.; Sifri, Z.; Cennimo, D.; Horng, H. Global Contributors to Antibiotic Resistance. J. Glob. Infect. Dis. 2019, 11, 36–42. doi:10.4103/jgid.jgid_110_18.
3. Mulani, M.S.; Kamble, E.E.; Kumkar, S.N.; Tawre, M.S.; Pardesi, K.R. Emerging Strategies to Combat ESKAPE Pathogens in the Era of Antimicrobial Resistance: A Review. Front. Microbiol. 2019, 10, 539-563. doi: 10.3389/fmicb.2019.00539.
4. S. L. Warnes, V. Caves and C. W. Keevil, Environ. Microbiol., 14, 2012, 1730.
5. J. Singh and P. Singh, Bioinorg. Chem. Appl., 2012, 2012, 104549.
6. R. Starosta, K. Stokowa, M. Florek, J. Król, A. Chwiłkowska, J. Kulbacka, J. Saczko, J. Skała and M. Jeżowska-Bojczuk, J. Inorg. Biochem., 105, 2011, 1102.
7. **Edis, Z.*; Haj Bloukh, S.; Ibrahim, M.R.; Abu Sara, H. "Smart" antimicrobial nanocomplexes with potential to decrease surgical site infections (SSI). Pharmaceutics 2020, 12(4), 361. 10.3390/pharmaceutics12040361 https://doi.org/10.3390/pharmaceutics12040361**
8. **Zehra Edis[1,*], Samir Haj Bloukh[1], Hamed Abu Sara[1], Hanusha Bhakhoa[2], Lydia Rhyman[2,3] and Ponnadurai Ramasami[2,3,*],** "Smart" triiodide compounds: Does halogen bonding influence antimicrobial activities? Pathogens **2019**, 8, 182-202.https://doi.org/10.3390/pathogens8040182
9. **May Reda, Akram Ashames*, Zehra Edis, Samir Bloukh, Richie Bhandare and Hamed Abu Sara,** Green Synthesis of Potent Antimicrobial Silver Nanoparticles Using Different Plant Extracts and Their Mixtures, Processes **2019**, 7, 510; doi:10.3390/pr7080510

References

pharmaceutics

MDPI

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]

1 Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, Ajman University, Ajman PO Box 346, UAE; may.ibrahim@ajman.ac.ae

2 Department of Clinical Sciences, College of Pharmacy and Health Sciences, Ajman University, Ajman PO Box 346, UAE; s.bloukh@ajman.ac.ae (S.H.B.); h.abusara@ajman.ac.ae (H.A.S.)

* Correspondence: z.edis@ajman.ac.ae

Received: 10 March 2020; Accepted: 13 April 2020; Published: 15 April 2020

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

References

biomimetics

MDPI

Article

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

Zehra Edis [1,*] and Samir Haj Bloukh [2]

[1] Department of Pharmaceutical Sciences, College of Pharmacy and Health Science, Ajman University, Ajman P.O. Box 346, UAE

[2] Department of Clinical Sciences, College of Pharmacy and Health Science, Ajman University, Ajman PO Box 346, UAE; s.bloukh@ajman.ac.ae

* Correspondence: z.edis@ajman.ac.ae

Received: 27 August 2020; Accepted: 11 September 2020; Published: 17 September 2020

check for updates

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

International Journal of
Environmental Research and Public Health

MDPI

Article

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

Samir Haj Bloukh [1], Zehra Edis [2,*], Annis A. Shaikh [3] and Habib M. Pathan [3]

1 College of Pharmacy and Health Science, Department of Clinical Sciences, Ajman University, PO Box 346 Ajman, UAE; s.bloukh@ajman.ac.ae
2 College of Pharmacy and Health Science, Department of Pharmaceutical Sciences, Ajman University, PO Box 346 Ajman, UAE
3 Advanced Physics Laboratory, Department of Physics, Savitribai Phule Pune University, Pune 411007, India; annisshaikh786@gmail.com (A.A.S.); pathan@physics.unipune.ac.in (H.M.P.)
* Correspondence: z.edis@ajman.ac.ae; Tel.: +971-56-694-7751

Received: 9 July 2020; Accepted: 28 July 2020; Published: 4 August 2020

check for updates

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

pathogens

MDPI

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,*]

1 College of Pharmacy and Health Science, Ajman University, Ajman P.O. Box 346, UAE; s.bloukh@ajman.ac.ae (S.H.B.); h.abusara@ajman.ac.ae (H.A.S.)
2 Computational Chemistry Group, Department of Chemistry, Faculty of Science, University of Mauritius, Réduit 80837, Mauritius; hbhakhoa@gmail.com (H.B.); lyd.rhyman@gmail.com (L.R.)
3 Department of Chemical Sciences, University of Johannesburg, Doornfontein, Johannesburg 2028, South Africa
* Correspondence: z.edis@ajman.ac.ae (Z.E.); p.ramasami@uom.ac.mu (P.R.)

Received: 3 September 2019; Accepted: 8 October 2019; Published: 10 October 2019

check for updates

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

processes

MDPI

Article

Green Synthesis of Potent Antimicrobial Silver Nanoparticles Using Different Plant Extracts and Their Mixtures

May Reda [1], Akram Ashames [1,*], Zehra Edis [1], Samir Bloukh [2], Richie Bhandare [1] and Hamed Abu Sara [2]

[1] Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, Ajman University, P.O. Box 346, Ajman, UAE

[2] Department of Clinical Sciences, College of Pharmacy and Health Sciences, Ajman University, P.O. Box 346, Ajman, UAE

* Correspondence: a.ashames@ajman.ac.ae

Received: 21 June 2019; Accepted: 2 August 2019; Published: 4 August 2019

check for updates

Abstract: Nano-sized metals have been introduced as a promising solution for microbial resistance to antimicrobial agents. Silver nanoparticles (AgNPs) have been proven to possess good antimicrobial activity. Green synthesis of AgNPs has been reported as safe, low cost and ecofriendly. This methodology uses extracts originating from different plants to reduce silver ions from $AgNO_3$ into nano-sized particles. In this study, extracts of several plants including ginger, garlic, capsicum and their mixtures were successfully used to produce AgNPs. Numerous spectroscopic, light scattering