#### SHORT COMMUNICATION

# JOURNA S

## OPENOACCESS

### Boosting antimicrobial efficacy using polymeric nanoparticles

#### Rodrigo Cé

Biomedical Sciences Department, Centro Universitário Avantis - UNIAVAN, Brazil

#### ABSTRACT

Bacterial infections are a major threat in medicine, often causing significant morbidity and mortality. Despite the effectiveness of antibiotics, the rise of antibiotic-resistant strains presents a pressing challenge worsened by misuse. Antibiotics target essential cellular processes to combat microorganisms, including bacteria, fungi, and viruses. Nanoparticles offer promising alternatives with customizable properties for targeted therapy, employing unique antibacterial mechanisms. Carbon-based, metal-based, polymeric, and lipid-core nanocapsules show potential in inhibiting bacterial growth and curbing resistance. Lipid-core nanocapsules are versatile platforms for drug delivery, enhancing antibacterial activity and altering interactions with bacterial cells. In this study, we explore the efficacy of lipid-core nanocapsules in combating antibiotic resistance and improving patient outcomes, paving the way for advancements in modern medicine.

#### Introduction

In recent years, bacterial illnesses have emerged as a significant cause of fatalities and persistent infections. Although research has shown that the overuse of these medications has contributed to the formation of antibiotic-resistant forms of bacteria, antibiotics have long been the preferred treatment for bacterial illnesses due to their efficiency and accessibility [1,2]. Different classes and groupings of antibiotics have been created in an effort to address this problem. However, drug resistance is directly related to antibiotic misuse, which increases death rates and lengthens hospital admissions [3,4]. Microorganisms like bacteria, fungi, and viruses are eliminated by antimicrobial agents, which include antibiotics.

Currently, antibiotics' three primary targets are translation machinery, cell wall construction, and DNA replication. Bacteria may, however, acquire resistance to these treatments [5-7]. Since they can stop germ development and lessen symptoms, antibiotics are frequently used as the first line of defense in the treatment of infections [8].

Compared to conventional antimicrobial chemicals, using nanoparticles as antimicrobial agents provides a number of potential advantages. For instance, nanoparticles can be engineered to have particular characteristics that increase their efficacy in eradicating or preventing the growth of bacteria.

By adding ligands, which bind to receptors on the surface of microorganisms and improve the treatment's efficacy, nanoparticles can also be directed to particular cells or tissues [5,9,10]. The creation of nanoparticles with antibacterial capabilities can stop the development of antibiotic resistance. Pharmaceutical nanotechnology is a field that is quickly expanding. Nanoparticles are materials with at least one dimension between 1 and 100 nm [11,12]. They are efficient antibacterial delivery agents because of their high surface area-to-volume ratio [13]. Nanoparticles have distinctive properties, including form, size, charge, reactivity, and surface

#### **KEYWORDS**

Nanocapsules; Anti-bacterial agents; Bacterial infections; Drug resistance; Morbidity

#### **ARTICLE HISTORY**

Received 18 September 2023; Revised 15 November 2023; Accepted 10 December 2023

area to mass ratio, which can be applied in a variety of sectors, including medical science [10,13].

Researchers have investigated the potential of using nanoparticles to stop the growth of both Gram-positive and Gram-negative bacteria. Nanoparticles' antibacterial effects are related to non-oxidative processes, the development of oxidative stress, and the release of metal ions [14-16]. In addition, the penetration of the cell membrane, disruption of the cell membrane, and production of reactive oxygen species are frequently the causes of the impacts of nanoparticles on bacteria [3,5]. Nanoparticle-based therapies have the potential to improve bacterial growth inhibition and reduce resistance development [17]. There has been evidence of promising antibacterial action in a number of nanoscale systems, including carbon and metal, polymers, dendrimers, nanoemulsions, nanocomposites, liposomes, micelles, and polymeric nanocapsules [3,18-20]. Furthermore, lipid-core nanocapsules, a particular class of polymeric nanoparticles made of poly(e-caprolactone), sorbitan monostearate, medium-chain triglyceride, and polysorbate 80, have been researched as antibacterial agents to treat infections [20-22].

In the realm of pharmaceutical nanotechnology, research on the use of nanoparticles to fight diseases and avoid microbial drug resistance is expanding. Effective bacterial growth inhibition is made possible by the capacity of nanoparticles to engage with diverse bacterial cell components through a variety of factors, including van der Waals forces, electrostatic attraction, hydrophobic contacts, and receptor ligand interactions [23-26]. Nanoparticles have been demonstrated to cause oxidative stress, alterations in cell membrane permeability, enzymatic inhibition, and other processes, according to studies [27,28]. Non-oxidative processes, oxidative stress, and metal ion release are a few of these mechanisms [29-31].

<sup>\*</sup>Correspondence: Prof. Dr. Rodrigo Cé, Biomedical Sciences Department, Centro Universitário Avantis - UNIAVAN, Brazil, e-mail: rodrigoce@hotmail.com/ rodrigoce@uniavan.edu.br

<sup>© 2023</sup> The Author(s). Published by Reseapro Journals. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Gram-positive or Gram-negative bacteria may be more resistant to antibacterial nanoparticles than others [32]. Testing a bacteria's susceptibility to nanoparticles by bacterial plating is possible. A possible method for combating medication resistance is the creation of novel nanoparticles with antibacterial capabilities [33,34].

The non-volatile, chemically stable structure of polymeric nanoparticles as antibacterial agents binds to target surfaces while avoiding biological membranes like the skin [35]. Polycationic antimicrobials, such as quaternary ammonium compounds that act against both Gram-positive and Gram-negative bacteria, are very efficient because they have a high surface density of active groups [35,36].

Five clinical strains of *Staphylococcus aureus* that were resistant to a number of antibiotics, including ciprofloxacin, clindamycin, erythromycin, gentamicin, oxacillin, and penicillin G, were successfully inhibited from growing in a study by Cé et al. using lipid-core nanocapsules. Six strains of the filamentous *fungus Aspergillus fumigatus, Aspergillus flavus*, and *Aspergillus niger* were likewise unable to grow as a result of these combinations. In both sets of tests, dapsone's growth-inhibitory action was enhanced by its encapsulation in nanoparticles. Furthermore, the addition of chitosan to the formulations enhanced their ability to combat *Staphylococcus aureus*, whereas the antifungal effects of the drug's nanoencapsulation were more clearly felt [37].

Fusidic acid can be added to lipid-core nanocapsules to increase their in vitro antibacterial activity against strains of Staphylococcus aureus, Enterococcus faecalis, and Staphylococcus epidermidis, according to a different study by Cé et al. Additionally, measurements of mean diameter, polydispersity index, and zeta potential were used to assess how the nanocapsules interacted with bacteria. In this case, the stretching mode of the C double bond O (amide I), or stretching mode (C=O) of the COO group in S. aureus, the stretching mode of the COO group in E. faecalis, the stretching mode of the C-O-Cester bonds in S. aureus, and the stretching mode of the C double bond O (amide I) probably related to the formation of aggregates after exposure of the formulations to the bacteria were observed in infrared fusidic acid was enclosed in lipid-core nanocapsules, coated with or without chitosan, which altered the drug's biological behavior and enhanced its effectiveness in vitro against strains of S. aureus, E. faecalis, and S. epidermidis [20].

The production of polymeric nanocapsules for preventing microbial growth using self-assembly processes will probably remain a promising method in the future. These nanocapsules can be customized in terms of size and structure to maximize performance. They are made to encapsulate and deliver antimicrobial drugs to target bacteria. Self-assembly methods are anticipated to become more effective and scalable with technological advancements, enabling the manufacturing of more nanocapsules at a reduced cost.

#### Conclusions

Polymeric nanocapsules' capacity to specifically target microbial cells while preserving healthy cells is one of its main benefits. This is especially crucial in light of the growth in antimicrobial resistance, which has created a demand for more specialized treatments that work well. Since the antimicrobial drugs may be given directly to the site of infection in a regulated and sustained manner using nanocapsules, it may be able to lessen the likelihood that resistance would develop.

#### **Disclosure statement**

No potential conflict of interest was reported by the authors.

#### References

- 1. Hsueh PR. New Delhi metallo- $\beta$ -lactamase-1 (NDM-1): an emerging threat among Enterobacteriaceae. J Formos Med Assoc. 2010;109(10):685-687.
- Kohanski MA, Dwyer DJ, Collins JJ. How antibiotics kill bacteria: from targets to networks. Nat Rev Microbiol. 2010;8(6):423-435.
- Mubeen B, Ansar AN, Rasool R, Ullah I, Imam SS, Alshehri S, et al. Nanotechnology as a Novel Approach in Combating Microbes Providing an Alternative to Antibiotics. Antibiotics (Basel). 2021;10(12):1473.
- Pelgrift RY, Friedman AJ. Nanotechnology as a therapeutic tool to combat microbial resistance. Adv Drug Deliv Rev. 2013;65(13-14):1803-1815.
- 5. Wang LL, Hu C, Shao LQ. The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int J Nanomedicine. 2017;12:1227-1249.
- 6. Poole K. Mechanisms of bacterial biocide and antibiotic resistance. J Appl Microbiol. 2002;92:55-64.
- 7. Jayaraman R. Antibiotic resistance: an overview of mechanisms and a paradigm shift. Curr Sci India. 2009;96(11):1475-1484.
- Ewald PW. Evolutionary biology and the treatment of signs and symptoms of infectious disease. J Theor Biol. 1980;86(1):169-176.
- 9. Gao W, Thamphiwatana S, Angsantikul P, Zhang L. Nanoparticle approaches against bacterial infections. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2014;6(6):532-547.
- Seil JT, Webster TJ. Antimicrobial applications of nanotechnology: methods and literature. Int J Nanomedicine. 2012;7:2767-2781.
- 11. Khan I, Saeed K, Khan I. Nanoparticles: Properties, applications and toxicities. Arab J Chem. 2019;12(7):908-931.
- Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol. 2018;9:1050-1074.
- Ingle AP, Duran N, Rai M. Bioactivity, mechanism of action, and cytotoxicity of copper-based nanoparticles: a review. Appl Microbiol Biotechnol. 2014;98:1001-1009.
- 14. Leung YH, Ng AM, Xu X, Shen Z, Gethings LA, Wong MT, et al. Mechanisms of antibacterial activity of MgO: non-ROS mediated toxicity of MgO nanoparticles towards Escherichia coli Small. 2014;10(6):1171-1183.
- 15. Gurunathan S, Han JW, Dayem AA, Eppakayala V, Kim JH. Oxidative stress-mediated antibacterial activity of graphene oxide and reduced graphene oxide in Pseudomonas aeruginosa. Int J Nanomedicine. 2012;7:5901-5914.
- 16. Nagy A, Harrison A, Sabbani S, Munson RS Jr, Dutta PK, Waldman WJ. Silver nanoparticles embedded in zeolite membranes: release of silver ions and mechanism of antibacterial action. Int J Nanomedicine. 2011;6:1833-1852.
- Sobhani Z, Samani SM, Montaseri H, Khezri E. Nanoparticles of chitosan loaded ciprofloxacin: fabrication and antimicrobial activity. Adv Pharmaceut Bull. 2017;7(3):427.
- Sharmin S, Rahaman MM, Sarkar C, Atolani O, Islam MT, Adeyemi OS. Nanoparticles as antimicrobial and antiviral agents: A literature-based perspective study. Heliyon. 2021;7(3):E06456.
- Staroń A, Długosz O. Antimicrobial properties of nanoparticles in the context of advantages and potential risks of their use. J Environ Sci Health A. 2021;56(6):680-693.
- 20. Cé R, Pacheco BZ, Ciocheta TM, Barbosa FS, de CS Alves A, Dallemole DR, et al. Antibacterial activity against Gram-positive bacteria using fusidic acid-loaded lipid-core nanocapsules. Reactive and Functional Polymers. 2021;162:104876.
- 21. Jäger E, Venturini CG, Poletto FS, Colomé LM, Pohlmann JP, Bernardi A, et al. Sustained release from lipid-core nanocapsules by

varying the core viscosity and the particle surface area. J Biomed Nanotechnol. 2009;5(1):130-140.

- 22. Venturini CG, Jäger E, Oliveira CP, Bernardi A, Battastini AM, Guterres SS, et al. Formulation of lipid core nanocapsules. Colloids Surf A Physicochem Eng Asp. 2011;375(1-3):200-208.
- 23. Armentano I, Arciola CR, Fortunati E, Ferrari D, Mattioli S, Amoroso CF, et al. The interaction of bacteria with engineered nanostructured polymeric materials: a review. Scientific World J. 2014;2014:410423.
- 24. Li H, Chen Q, Zhao J, Urmila K. Enhancing the antimicrobial activity of natural extraction using the synthetic ultrasmall metal nanoparticles. Sci Rep. 2015;5:11033.
- 25. Luan B, Huynh T, Zhou R. Complete wetting of graphene by biological lipids. Nanoscale. 2016;8(10):5750-5754.
- 26. Gao W, Thamphiwatana S, Angsantikul P, Zhang L. Nanoparticle approaches against bacterial infections. Wires Nanomed Nanobi. 2014;6(6):532-547.
- 27. Xu Y, Wei MT, Ou Yang HD, Walker SG, Wang HZ, Gordon CR, et al. Exposure to TiO2 nanoparticles increases Staphylococcus aureus infection of HeLa cells. J Nanobiotechnology. 2016;14:34.
- 28. Yang W, Shen C, Ji Q, An H, Wang J, Liu Q, et al. Food storage material silver nanoparticles interfere with DNA replication fidelity and bind with DNA. Nanotechnology. 2009;20(8):085102.
- 29. Leung YH, Ng AM, Xu X, Shen Z, Gethings LA, Wong MT, et al. Mechanisms of antibacterial activity of MgO: non-ROS mediated toxicity of MgO nanoparticles towards Escherichia coli. Small. 2014;10(6):1171-1183.
- 30. Gurunathan S, Han JW, Dayem AA, Eppakayala V, Kim JH. Oxidative stress-mediated antibacterial activity of graphene oxide

and reduced graphene oxide in Pseudomonas aeruginosa. Int J Nanomedicine. 2012;7:5901-5914.

- 31. Zakharova OV, Godymchuk AY, Gusev AA, Gulchenko SI, Vasyukova IA, Kuznetsov DV. Considerable variation of antibacterial activity of Cu nanoparticles suspensions depending on the storage time, dispersive medium, and particle sizes. Biomed Res Int. 2015;2015:412530.
- 32. Mubeen B, Ansar AN, Rasool R, Ullah I, Imam SS, Alshehri S, et al. Nanotechnology as a Novel Approach in Combating Microbes Providing an Alternative to Antibiotics. Antibiotics (Basel). 2021;10(12):1473.
- 33. Beyth N, Houri-Haddad Y, Domb A, Khan W, Hazan R. Alternative antimicrobial approach: nano-antimicrobial materials. Evid Based Complement Alternat Med. 2015;2015:246012.
- 34. Pelgrift RY, Friedman AJ. Nanotechnology as a therapeutic tool to combat microbial resistance. Adv Drug Deliv Rev. 2013;65(13-14):1803-1815.
- 35. Zaltsman N, Kesler-Shvero D, Weiss EI, Beyth N. Synthesis variants of quaternary ammonium polyethyleneimine nanoparticles and their antibacterial efficacy in dental materials. J Appl Biomater Funct Mater. 2016:205-211.
- 36. Kesler Shvero D, Abramovitz I, Zaltsman N, Perez Davidi M, Weiss EI, Beyth N. Towards antibacterial endodontic sealers using quaternary ammonium nanoparticles. Int Endod J. 2013;46(8):747-754.
- 37. Cé R, Marchi JG, Bergamo VZ, Fuentefria AM, Lavayen V, Guterres SS, et al. Chitosan-coated dapsone-loaded lipid-core nanocapsules: Growth inhibition of clinical isolates, multidrug-resistant Staphylococcus aureus and Aspergillus ssp. Colloids Surf A Physicochem Eng Asp. 2016;511:153-161.

40