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Nanoparticle Approaches Against Bacterial Infections

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Abstract:

A number of nanoparticle-based drug delivery systems have been approved for clinical use to treat a variety of infectious diseases, and many other antimicrobial nanoparticle formulations are currently under various stages of pre-clinical and clinical tests. Three studies were included in this report to support the effectiveness of nanoparticle-based drug delivery. The first study demonstrated the approach to selectively deliver antimicrobials to the sites of bacterial infections by utilizing bacterial toxins to activate drug release from gold nanoparticle-stabilized phospholipid liposomes. While the second and third study showed the effectiveness of PH-sensitive drug release from liposomes in different sites.

Introduction:

Over the last few decades, the application of nanotechnology, particularly the use of nanoparticles for drug delivery, has generated significant impact in medicine. Various nanoparticle delivery platforms, especially liposomes, polymeric nanoparticles, dendrimers, and inorganic nanoparticles, have received significant attention. Drug molecules loaded into nano-carriers through physical encapsulation, adsorption, or chemical conjugation exhibit an improved pharmacokinetic profile and therapeutic index when compared to their free drug counterparts. Other advantages of nanoparticle delivery systems, including improved drug solubility, prolonged systemic circulation, sustained and controlled release, precise drug targeting, and concurrent delivery of multiple drugs, have also been validated in various studies. [1]

Discussion:

To begin with three of many studies regarding the use of nanoparticle-based drug are included in this report

- **Bacterial toxin-triggered drug release from gold nanoparticle-stabilized liposomes for the treatment of bacterial infection.** [1]

The binding of modified gold nanoparticles to the surface of liposomes can effectively prevent them from fusing with one another and from undesirable payload release in regular storage or physiological environments. In till these protected liposomes come in contact with bacteria that secrete toxins, the toxins will insert into the liposome membranes and form pores, through which the encapsulated therapeutic agents are released. The released drugs subsequently impose antimicrobial effects on the toxin-secreting bacteria. Using methicillin-resistant Staphylococcus aureus as a model bacterium and vancomycin as a model anti-MRSA antibiotic, the study showed that the synthesized gold nanoparticle-stabilized liposomes can completely release the encapsulated vancomycin within 24 h in the presence of MRSA bacteria and lead to inhibition of MRSA growth as effective as an equal amount of vancomycin-loaded liposomes (without nanoparticle stabilizers) and free vancomycin. This bacterial toxin enabled drug release from nanoparticle-stabilized liposomes provides a new, safe, and effective approach for the treatment of bacterial infections.

- **Nanoparticle-Stabilized Liposomes for pH-Responsive Gastric Drug Delivery** [2]

By adsorbing small chitosan-modified gold nanoparticles onto the outer surface of negatively charged phospholipid liposomes, making the modified liposomes at gastric pH have excellent stability with limited fusion ability and negligible cargo releases. But when the stabilized liposomes are present in an environment with neutral pH, the gold stabilizers detach from the liposomes, resulting in free liposomes that can actively fuse with bacterial membranes. Using

H. pylori as a model bacterium and doxycycline as a model antibiotic, the study showed such pH-responsive fusion activity and drug release profile of the nanoparticle-stabilized liposomes. Particularly, at neutral pH the gold nanoparticles detach, and thus the doxycycline-loaded liposomes rapidly fuse with bacteria and cause superior bactericidal efficacy as compared to the free doxycycline counterpart. the results suggest that the reported liposome system holds a substantial potential for gastric drug delivery; it remains inactive (stable) in the stomach lumen but actively interacts with bacteria once it reaches the mucus layer of the stomach where the bacteria may reside.

❖ **Nanoparticle Stabilized Liposomes for Acne Therapy** [3]

The nanoparticle-stabilized liposomes have numerous advantages over free drug molecules as an acne treatment alternative. Carboxyl-functionalized gold nanoparticles (AuC) were attached to the surface of liposomes (AuC-liposomes) loaded with doxycycline. Both fluorescent and antimicrobial studies demonstrated that based on electrostatic interaction, negatively charged AuC attached to the liposome's positively charged surface and stabilized liposomes in a neutral pH environment (pH = 7.4). We know the main cause of acne is Propionibacterium acnes. Upon entering the skin's acidic environment (pH = 4), AuC detached from the liposome's surface and liposomes could fuse with P. acnes residing in the pores. Furthermore, toxicity studies showed that AuC-liposomes did not induce any significant toxicity, while two of the leading over-the-counter therapies, benzoyl peroxide and salicylic acid, generated substantial skin irritation.

Conclusion:

To conclude nanoparticle-stabilized liposomes have become an emerging drug delivery platform for treatment of various bacterial infections, because of their effectiveness, and their advantages comparted to the free drug as the studies have shown.

Reference:

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