

## NEXT-GENERATION DRUG DELIVERY: EXPLORING THE POTENTIAL OF BACTERIAL GHOSTS

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### ABSTRACT

The emergence of bacterial ghosts (BGs) as drug carriers represents a promising advancement in the field of nanomedicine. Bacterial ghosts are hollow, non-viable bacterial cells that retain their structural integrity and possess unique properties, making them suitable for drug delivery applications. This review highlights the mechanisms of bacterial ghost formation, their physicochemical properties, drug loading and release mechanisms, potential therapeutic applications, advantages over conventional carriers, and the challenges faced in their development. The review concludes with future perspectives on the integration of bacterial ghosts into innovative drug delivery systems.

### 1. INTRODUCTION

The quest for effective and targeted drug delivery systems has intensified in recent years, driven by the limitations of traditional methods. Conventional drug delivery systems often suffer from issues such as low bioavailability, rapid clearance, and off-target effects.

Bacterial ghosts, produced through the lysis of Gram-negative bacteria, offer a novel approach to drug delivery, combining the advantages of biological and synthetic carriers. Their unique characteristics—such as biocompatibility, biodegradability, and tunable surface properties—position them as promising candidates for next-generation drug delivery systems (Görlach et al., 2020; Shakya et al., 2021).



*Figure 1: Bacterial ghost as a novel vaccine designing method. Source: PreScouter. (2015). [Bacterial Ghost as a Novel Vaccine Designing Method].*

## 2. Mechanism of Formation

Bacterial ghosts are created through a controlled process that involves the lysis of bacterial cells, typically via methods such as

- **Chemical Lysis:** Utilization of detergents (e.g., Triton X-100) or specific enzymes (e.g., lysozyme) to disrupt the cell membrane (Jiang et al., 2018).
- **Genetic Engineering:** Induction of cell lysis through the expression of lysis genes, such as the phiX174 gene, which codes for a lysis protein that facilitates the release of ghost structures (Kaur et al., 2020).

The resulting hollow structures maintain the outer membrane and inner space of the bacteria, providing a scaffold for drug loading and delivery (Harris et al., 2017).

## 3. Properties of Bacterial Ghosts

### 3.1 Biocompatibility and Biodegradability

Bacterial ghosts are composed of natural materials, making them biocompatible and biodegradable. Their non-toxic nature allows for safe administration *in vivo*, minimizing adverse effects. Studies have shown that BGs can elicit minimal immune responses, further supporting their potential in therapeutic applications (Rein et al., 2022).

### 3.2 Structural Integrity

The preserved structural features of bacterial ghosts facilitate the encapsulation of therapeutic agents while protecting them from degradation. The outer membrane provides a protective barrier, enhancing stability during storage and transit (Liu et al., 2019).

### 3.3 Surface Modifications

Bacterial ghosts can be engineered to display specific ligands or antibodies on their surface, enabling targeted drug delivery to specific tissues or cells. This feature enhances their potential in cancer therapy and vaccine delivery (Shakya et al., 2021).

## 4. Drug Loading and Release Mechanisms

### 4.1 Loading Techniques

Bacterial ghosts can incorporate a variety of therapeutic agents through several techniques

- **Passive Loading:** Drugs diffuse into the ghost's interior, relying on concentration gradients. This method is simple but may have limitations in efficiency (Jiang et al., 2018).
- **Active Loading:** Techniques such as electroporation, sonication, or chemical methods can facilitate a higher drug uptake by creating temporary pores in the bacterial ghost membrane (Görlach et al., 2020).

### 4.2 Release Kinetics

Drug release from bacterial ghosts can be controlled by modifying the composition and structure of the ghosts. Release profiles can be designed for sustained or targeted release, depending on therapeutic needs. Studies have demonstrated that release can occur through diffusion, erosion, or a combination of both mechanisms (Liu et al., 2019).

## 5. Therapeutic Applications

### 5.1 Antimicrobial Delivery

Bacterial ghosts have been explored for delivering antibiotics, particularly in treating infections caused by resistant bacteria. Their inherent properties can enhance the efficacy of antimicrobial agents. For instance, BGs can encapsulate and deliver ciprofloxacin effectively against *Staphylococcus aureus* infections (Kaur et al., 2020).

### 5.2 Cancer Therapy

Bacterial ghosts can be engineered to deliver chemotherapeutic agents specifically to tumor cells, minimizing damage to surrounding healthy tissues. Targeted delivery is achieved

through surface modifications, such as attaching antibodies that recognize tumor markers. For example, BGs loaded with doxorubicin showed enhanced cytotoxic effects against breast cancer cells (Harris et al., 2017).

### 5.3 Vaccine Development

Bacterial ghosts can serve as adjuvants or delivery vehicles for vaccines, enhancing immune responses. Their ability to present antigens in a manner similar to live bacteria stimulates robust immune reactions without the risks associated with live pathogens. Research has demonstrated that BGs can effectively deliver bacterial or viral antigens, promoting a strong immunogenic response (Shakya et al., 2021).

## 6. Advantages Over Conventional Carriers

Bacterial ghosts offer several advantages compared to traditional drug delivery systems, such as liposomes and polymeric nanoparticles

- **Biocompatibility:** Reduced immunogenicity compared to synthetic carriers, leading to fewer side effects (Rein et al., 2022).
- **Natural Degradation:** Bacterial ghosts are broken down in vivo, eliminating long-term accumulation and toxicity concerns (Liu et al., 2019).
- **Cost-Effectiveness:** Production processes can be optimized for cost-efficiency, leveraging bacterial fermentation techniques (Görlach et al., 2020).

## 7. Challenges and Limitations

Despite their potential, several challenges hinder the widespread application of bacterial ghosts in drug delivery

- **Production Scalability:** Developing methods for large-scale production that maintain quality and reproducibility remains a challenge (Kaur et al., 2020).
- **Stability:** Ensuring the stability of bacterial ghosts during storage and transportation is crucial for clinical applications (Harris et al., 2017).
- **Regulatory Hurdles:** Navigating the regulatory landscape for approval can be complex due to the novelty of bacterial ghost technology (Rein et al., 2022).

## 8. Future Perspectives

The future of bacterial ghosts in drug delivery is promising, with several avenues for research and development.

- **Genetic Engineering:** Advances in synthetic biology can lead to more sophisticated bacterial ghost designs with enhanced functionalities, such as the ability to respond to environmental stimuli (Shakya et al., 2021).
- **Combination Therapies:** Exploring the use of bacterial ghosts in combination with other drug delivery systems may provide synergistic effects, enhancing therapeutic outcomes (Jiang et al., 2018).
- **Clinical Trials:** Conducting rigorous clinical studies will be essential to validate the safety and efficacy of bacterial ghosts as drug carriers (Görlach et al., 2020).

## 9. CONCLUSION

Bacterial ghosts represent a novel and versatile platform for drug delivery, offering unique advantages that address the limitations of traditional systems. As research continues to uncover their full potential, bacterial ghosts could significantly impact the field of pharmacotherapy, paving the way for more effective and targeted treatment options.

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