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RESEARCH

Mannosylated nanostructured lipid carriers of thiabendazole against *Pseudomonas aeruginosa* lung biofilm infection: in vitro and in vivo characterization, with relevance to cystic fibrosis

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Abstract

This study aimed to develop mannosylated nanostructured lipid carriers loaded with Thiabendazole for intravenous delivery to prevent lung biofilm formation. Mannosylated NLCs combine the targeting capabilities of mannose-functionalized carriers with the favorable physicochemical properties of NLCs. Mannose-coated NLCs (MCT-NLCs), prepared via microemulsification using Glyceryl monostearate, olive oil, and Geraniol, had an approximate size of 240 nm, a zeta potential of about − 32.5 mV, an entrapment efficiency of 96%, and released about 84% of the drug within 24 h. Microscopy showed spherical particles under 250 nm, supported by thermal and diffraction analyses. TEM and IR spectra confirmed surface mannose. In vitro, they demonstrated sustained drug release compared to free drug. After IV administration, these NLCs reduced bacterial counts and minimized lung tissue damage in rats infected with *Pseudomonas aeruginosa* over seven days, demonstrating improved initial in vivo results, though they did not eradicate the infection. This study did not evaluate the formulation's safety, as it is a repurposed work. In vivo, the NLCs significantly lowered bacterial load and inflammation in a rat model of inhaled *Pseudomonas aeruginosa* biofilms relevant to cystic fibrosis over seven days, indicating potential to reduce bacterial contamination and tissue damage, although their targeting mechanism and ability to cure were not confirmed.

Keywords Mannosylated · Thiabendazole · Antibiofilm · Microemulsification

Introduction

Cystic fibrosis (CF), an autosomal recessive, life-threatening genetic disorder affecting about 70,000 people worldwide, with nearly 1000 new diagnoses each year, results from mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The disease occurs when an individual inherits two harmful CFTR variants, of which over 2000 have been identified to date. CFTR regulates mucus viscosity by encoding a membrane protein that channels bicarbonate and chloride across the exocrine epithelium of various organs (Ledger et al. 2024). As a result, CF presents with pulmonary symptoms such as chronic and progressive obstructive lung disease, sinusitis, and bronchiectasis. *Pseudomonas aeruginosa* (*P. aeruginosa*) is the most common respiratory pathogen in cystic fibrosis (Reyne et al. 2023; Vani et al. 2023). Because it causes frequent acute pulmonary exacerbations, it is the primary cause of morbidity and mortality related to gradual pulmonary deterioration (Kurt et al. 2025). Evidence suggests that bacteria proliferate in environments conducive to biofilm formation (e.g., highly viscous sputum, acidic pH, and anaerobiosis) at the site of infection, further complicating antibiotic effectiveness and delivery during long-term treatment. A wide range of virulence factors, most of which are positively regulated by quorum sensing (QS), must be expressed in concert for *P. aeruginosa* to cause disease. QS regulates genes for biofilm formation, secreted virulence factors, immune-modulatory and proinflammatory chemicals, and about 10% of the *P. aeruginosa* genome. Currently, the available treatments on the market are high-dose ciprofloxacin, parenteral

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