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Nanoparticle-Based Therapeutic Strategies in Respiratory Diseases: Current Approaches and Future Perspectives

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INTRODUCTION: Respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), lung cancer, tuberculosis, and acute respiratory distress syndrome (ARDS) remain major global health challenges, causing significant morbidity and mortality worldwide.^{1,2} Despite the availability of pharmacological treatments such as bronchodilators, corticosteroids, antibiotics, and chemotherapeutics, most conventional drug administration routes (oral or intravenous) are often associated with critical limitations. These systemic delivery methods lead to the widespread distribution of drugs throughout the body rather than targeted accumulation at the site of infection or inflammation. This lack of specificity reduces the drug concentration at the affected region while increasing off-target toxicity in healthy tissues.³ Furthermore, many orally administered drugs suffer degradation in the gastrointestinal tract or undergo first-pass metabolism in the liver, which significantly decreases the amount of active drug reaching the systemic circulation and ultimately the target lung tissues.⁴ Many therapeutic drugs also have short half-lives, necessitating frequent dosing to maintain therapeutic levels, reducing patient compliance in chronic or long-term treatments.⁵ Therefore, there is an urgent need for advanced drug delivery systems capable of improving pulmonary targeting, enhancing therapeutic efficacy, and minimizing systemic side effects.

Nanotechnology offers a promising and innovative alternative platform for addressing these challenges. Nanoparticles, ranging from 1-100 nm and employed as drug delivery systems, display unique physical, chemical, and biological properties compared to their macro-scale counterparts. As a transformative field in biomedical science, nanotechnology enables the design of novel nanoformulations to overcome the major limitations of conventional treatments. Nano-based drug delivery systems can enhance solubility, extend drug half-life, and achieve localized accumulation in the lungs by penetrating mucosal barriers.⁶ Different nanoparticle types, such as polymeric, lipid-based, and metallic nanoparticles, have been developed to optimize therapeutic efficiency and minimize side effects.⁷ Considering liposomes, polymeric nanoparticles, solid lipid nanoparticles, and inorganic nanoparticles as representative platforms for pulmonary applications a comparison of conventional and nanotechnology-based drug delivery systems is important (Figure 1).

Recent studies highlight the great potential of nanoparticle-based systems for respiratory diseases. For example, inhalable reactive oxygen species (ROS)-responsive nanoparticles were designed to release anti-inflammatory drugs only in regions with high oxidative stress, reducing inflammation and tissue damage in COPD and ARDS models.⁸ Similarly, glutathione (GSH)-triggered nanoparticles utilize redox-sensitive linkers to release antibiotics selectively in infection sites, improving bacterial clearance in pulmonary infections.⁹ Nanoliposomal formulations of salbutamol sulfate provide controlled bronchodilator release and prolonged lung retention in asthma therapy.¹⁰ Biodegradable poly(lactic acid) (PLA) nanoparticles enhance the stability and controlled release of anti-inflammatory agents,

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offering improved safety profiles.¹¹ Meanwhile, mannose-conjugated chitosan nanoparticles effectively target alveolar macrophages for the treatment of tuberculosis, improving drug accumulation and antimicrobial efficacy.¹² Collectively, these examples underscore that nanotechnology-based systems hold great promise for overcoming the intrinsic barriers of conventional therapies by achieving site-specific, sustained, and safer drug delivery in respiratory diseases.

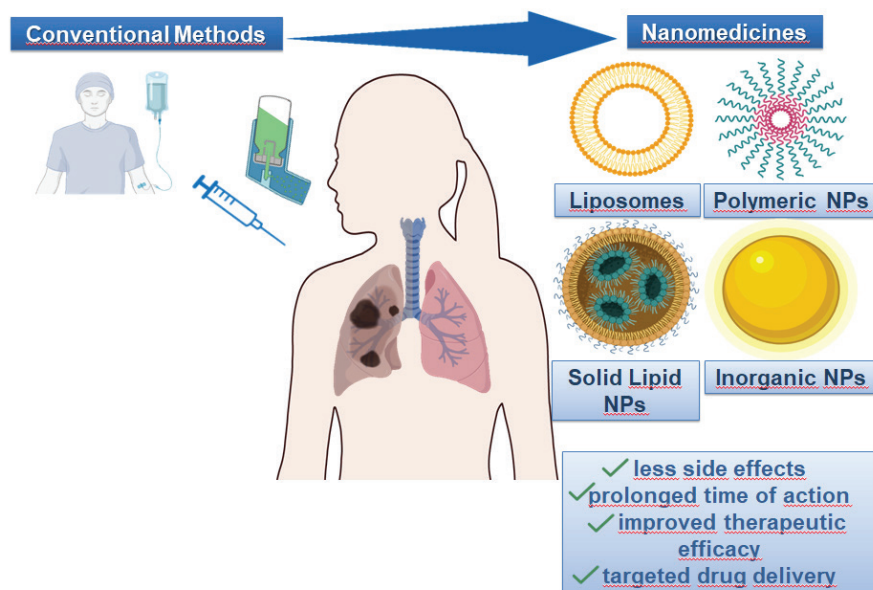


Figure 1. Schematic representation of conventional and nanotechnology-based drug delivery systems

CONCLUSION: Nanoparticle-based drug delivery systems provide a significant advancement in the treatment of respiratory diseases by overcoming the fundamental limitations of conventional therapies. Through their small size, tunable physicochemical properties, and ability to target specific lung regions, nanoparticles ensure improved bioavailability, controlled release, and reduced systemic toxicity. Studies on various nanocarriers —such as ROS-responsive and GSH-triggered nanoparticles, nanoliposomal salbutamol sulfate, PLA nanoparticles, and mannose-conjugated chitosan nanoparticles— have demonstrated promising outcomes in enhancing drug retention, reducing inflammation, and improving therapeutic efficacy in respiratory disorders. Despite these achievements, challenges such as mucus barrier penetration, long-term pulmonary toxicity, and large-scale reproducibility still remain. However, ongoing interdisciplinary research combining materials science, pharmacology, and pulmonary biology continues to improve the design, safety, and performance of nanoparticle systems. Collectively, these advancements indicate that nanotechnology can transform the current therapeutic landscape of respiratory medicine, making treatments more effective, safer, and more patient-centered.

Future Perspectives

The future of nanoparticle-based pulmonary therapies lies in the development of next-generation smart and personalized nanomedicines. **Stimuli-responsive nanoparticles** capable of detecting disease-specific microenvironments, such as pH shifts, oxidative stress, or enzymatic activity, will enable localized and on-demand drug release, minimizing off-target effects. **Personalized nanomedicine** approaches will allow the design of patient-specific formulations that combine multiple therapeutic agents, offering synergistic efficacy for complex respiratory

disorders. **Hybrid nanoplatforms** that integrate metallic nanoparticles (e.g., silver, gold) with natural bioactive compounds such as phycocyanin are expected to exhibit both therapeutic and diagnostic potential, enhancing the scope of precision medicine. Furthermore, advancements in inhalation device technology, aerosol engineering, and biocompatible excipient development will further support the translation of nanoparticle-based formulations from laboratory research to clinical application. As large-scale production, regulatory harmonization, and long-term safety validation advance, nanoparticle-based systems are expected to become a cornerstone of future respiratory therapies, offering precision, safety, and efficacy beyond the limitations of current treatments.

KEYWORDS: Nano-delivery systems, respiratory diseases, nanoparticles

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