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Advanced Hybrid Nano-Particles Peptides for Targeted Treatment of Pulmonary Fibrosis

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ABSTRACT:
The development of advanced hybrid nano-particles peptides for targeted treatment of pulmonary fibrosis represents a significant advancement in the field of respiratory medicine. This abstract aims to provide a concise overview of the research and its implications. Pulmonary fibrosis is a chronic and progressive lung disease characterized by fibrosis, inflammation, and damage to the lung architecture. The etiology of pulmonary fibrosis, particularly idiopathic pulmonary fibrosis (IPF), remains largely unknown. Recent research has focused on the potential of nanoparticle-based drug delivery systems for the treatment of pulmonary fibrosis. Various types of nanomaterials, including lipid-polymer hybrid nanoparticles, have shown promising therapeutic effects in both in vitro and in vivo studies. These nanocarriers offer targeted delivery of peptides and drugs to the lungs, potentially improving the efficacy and reducing the systemic side effects of treatment. The review of recent advances in nanoparticle applications for respiratory disorders highlights the potential of nanomedicine in overcoming the limitations of conventional drugs and its promising applications in the treatment of pulmonary diseases. The emerging delivery approaches for targeted pulmonary fibrosis, including the development of various drug delivery systems, provide valuable insights into the ongoing efforts to address the unmet medical needs in the management of this challenging condition. This review underscores the potential of advanced hybrid nano-particles peptides as a targeted treatment modality for pulmonary fibrosis, offering new hope for improved therapeutic outcomes.

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INTRODUCTION

Pulmonary fibrosis is a chronic and progressive lung disorder characterized by the excessive deposition of fibrous tissue in the lungs, leading to impaired respiratory function. The condition is associated with a variety of causes, including environmental exposures, genetic factors, and autoimmune diseases [1]. The hallmark of pulmonary fibrosis is the irreversible scarring of lung tissue, ultimately resulting in compromised gas exchange and respiratory failure. Understanding the complex pathogenesis of pulmonary fibrosis is crucial for developing effective treatment strategies[2]. Current therapeutic options for pulmonary fibrosis are limited, primarily focusing on alleviating symptoms and slowing disease progression rather than providing a definitive cure[3]. Commonly employed treatments include anti-inflammatory drugs, immunosuppressants, and antifibrotic agents, yet their efficacy is often modest, and they may be associated with significant side effects. Furthermore, these treatments do not specifically target the underlying molecular mechanisms driving fibrosis, emphasizing the need for innovative and targeted therapeutic approaches[4]. The emergence of nanotechnology and peptide-based therapies offers a promising avenue for revolutionizing the treatment of pulmonary fibrosis. Advanced hybrid nano-particles, combining the benefits of nanomaterials and peptides, present a novel and targeted approach to address the shortcomings of current treatments. Nano-particles can enhance drug delivery to specific lung regions, improving bioavailability and reducing systemic side effects. Peptides, on the other hand, provide a unique advantage by targeting specific molecular pathways involved in fibrosis progression[5]. The synergy between nano-particles and peptides holds the potential to achieve precise and effective therapeutic outcomes in the context of pulmonary fibrosis. This review explores the rationale behind integrating these innovative approaches and their potential to transform the landscape of pulmonary fibrosis treatment[6].

NANO-PARTICLES IN PULMONARY FIBROSIS TREATMENT

Overview of Nano-Particle Technology

Nano-particles, with their diminutive size and unique physicochemical properties, have garnered significant attention in the field of drug delivery, particularly in the context of pulmonary fibrosis treatment. The development of nano-particle technology involves the precise engineering of materials at the nanoscale to exploit their advantageous characteristics[7]. Nano-particles can be composed of various materials such as lipids, polymers, and metals, and their design can be tailored for specific therapeutic applications. The size of nano-particles, typically ranging from 1 to 100 nanometers, allows for enhanced interaction with biological systems. This size range is advantageous for drug delivery purposes, as it facilitates deep penetration into tissues and enables efficient transport across biological barriers[8,3]. The ability to manipulate the surface properties of nano-particles further enhances their biocompatibility and interaction with target cells. Nano-particles serve as carriers for therapeutic payloads, protecting them from degradation and clearance mechanisms in the

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body. This protection ensures the stability of drugs during transit to the target site, increasing their bioavailability and efficacy[9]. The design of nano-particles can be optimized to achieve controlled drug release, allowing for sustained therapeutic effects over an extended period. Additionally, the small size of nano-particles enables them to navigate through intricate biological structures, reaching specific cellular and subcellular locations with precision[10].

Previous Applications in Respiratory Medicine

The application of nano-particles in respiratory medicine has demonstrated their versatility and potential for addressing challenges associated with traditional drug delivery methods. Inhalable nano-particles, in particular, have shown promise in delivering drugs directly to the lungs, a critical aspect in the treatment of respiratory diseases[11,2]. This targeted approach minimizes systemic exposure, reducing the risk of side effects and optimizing therapeutic outcomes. In asthma management, nano-particles have been utilized to deliver bronchodilators and anti-inflammatory drugs directly to the airways, providing rapid relief and improving patient compliance[12]. For chronic obstructive pulmonary disease (COPD), nano-particle formulations have been employed to enhance the bioavailability of drugs and reduce dosing frequency, improving overall treatment efficacy. Furthermore, in lung cancer therapy, nano-particles have facilitated the targeted delivery of chemotherapeutic agents, minimizing damage to healthy tissues and mitigating systemic toxicity[5]. These successful applications underscore the adaptability of nano-particle technology in respiratory medicine and set the stage for exploring its potential in the treatment of pulmonary fibrosis. By leveraging the lessons learned from previous applications, researchers can harness the advantages of nano-particles to develop targeted and efficient therapeutic interventions for this challenging lung condition[13].

Advantages and Challenges in Pulmonary Fibrosis

The application of nano-particles in the treatment of pulmonary fibrosis holds several advantages that address the specific challenges associated with this complex disease. One of the primary advantages is the small size of nano-particles, which allows for effective penetration into fibrotic lung tissues[14]. In pulmonary fibrosis, aberrant deposition of extracellular matrix proteins occurs in specific regions of the lungs, leading to impaired respiratory function. Nano-particles, due to their size, can reach these targeted areas, ensuring that therapeutic agents are delivered precisely to the sites of fibrosis[15]. The protective role of nano-particles is particularly relevant in the context of pulmonary fibrosis, where the delicate lung environment can be hostile to therapeutic agents. Nano-particles shield drugs from enzymatic degradation and rapid clearance, maintaining their stability and enhancing their therapeutic efficacy[16]. This protective function is crucial for ensuring that the delivered drugs retain their bioactivity as they reach the fibrotic regions of the lungs. Controlled drug release is another significant advantage offered by nano-particles in

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pulmonary fibrosis treatment[17]. The sustained release of therapeutic agents from nano-carriers can provide a prolonged therapeutic effect, potentially reducing the frequency of administration and improving patient compliance. This controlled release is especially beneficial in managing the chronic and progressive nature of pulmonary fibrosis[7]. However, despite the promising advantages, the application of nano-particles in pulmonary fibrosis is not without challenges. Potential toxicity associated with certain nano-materials raises concerns about their safety for use in the delicate lung environment[3]. The immune response to nano-particles and the potential for long-term accumulation in tissues are areas of active investigation. Additionally, the complexity of fabricating biocompatible nano-particles that can effectively encapsulate and release therapeutic agents poses engineering challenges[18]. Addressing these challenges is imperative for the successful translation of nano-particle-based therapies from the laboratory to clinical settings. Researchers are exploring innovative strategies to enhance the biocompatibility of nano-materials, mitigate potential toxicity, and optimize their pharmacokinetics for safe and effective use in pulmonary fibrosis[19]. The relatively clear etiology and predisposing factors for PF are as follows: smoking, gastroesophageal reflux, genetic factors, some chemicals (e.g. organic or inorganic dust), some drugs (e.g. amiodarone and bleomycin), viral infections and some immune disorders (e.g. lupus erythematosus and scleroderma) shown in figure 1[20,3].

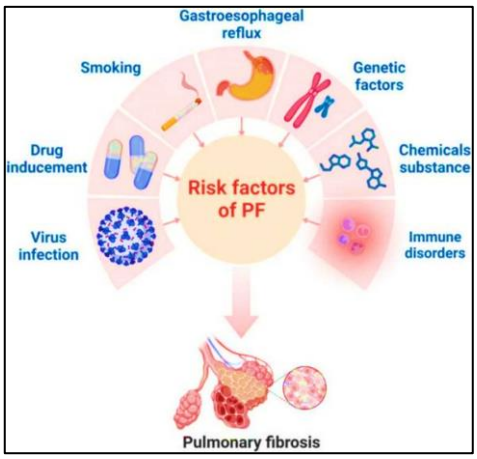

Figure 1: Etiology and predisposing factors leading to pulmonary fibrosis.

PEPTIDES IN PULMONARY FIBROSIS TREATMENT

Role of Peptides in Targeted Therapies

Peptides play a pivotal role in the field of targeted therapies, offering unique advantages that make them attractive candidates for the treatment of pulmonary fibrosis[21]. Peptides are short chains of amino acids, and their diverse structures and functions allow for precise modulation of specific molecular pathways involved in fibrosis progression[22]. In the context of targeted therapies, peptides can be designed to interact selectively with key cellular receptors, signaling molecules, or extracellular matrix components implicated in the fibrotic process. The specificity of peptides in targeting distinct molecular entities is particularly advantageous in pulmonary fibrosis, where the pathogenesis involves intricate cellular and molecular interactions[23]. By honing in on specific targets, peptides can interfere with the activation of fibroblasts, the deposition of collagen, and the inflammatory responses that

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contribute to fibrosis[24]. The ability to tailor peptides for selective targeting enhances the precision of therapeutic interventions, minimizing off-target effects and maximizing therapeutic efficacy[25]. Moreover, peptides can be engineered to exhibit favorable pharmacokinetic properties, enabling their efficient delivery to the lungs and facilitating interaction with target cells. The versatile nature of peptides allows for modifications to enhance stability, half-life, and bioavailability, ensuring their functionality in the challenging pulmonary microenvironment[26].

Existing Peptide-based Approaches

The application of peptides in pulmonary fibrosis treatment has gained traction, with several existing approaches showcasing the potential of peptide-based therapies. One notable example is the inhibition of transforming growth factor-beta (TGF-β), a central player in the fibrotic cascade[27]. TGF-β promotes fibroblast activation and collagen deposition, contributing to the progression of pulmonary fibrosis. Peptides designed to interfere with TGF-β signaling pathways have demonstrated efficacy in preclinical studies, attenuating fibrosis and improving lung function. Integrins, cell surface receptors involved in cell-matrix interactions, have also emerged as viable targets for peptide-based interventions in pulmonary fibrosis[28]. Peptides mimicking specific integrin-binding motifs can disrupt fibroblast adhesion and migration, impeding the formation of fibrotic lesions. These integrin-targeting peptides have shown promise in preclinical models, highlighting their potential for further development as therapeutic agents[29]. Furthermore, antimicrobial peptides, initially investigated for their role in immune defense, have exhibited unexpected anti-fibrotic properties[30]. These peptides can modulate immune responses and attenuate inflammation, key processes in the pathogenesis of pulmonary fibrosis. As a result, antimicrobial peptides are being explored for their potential dual role in combating infection and mitigating fibrosis in lung diseases[21]. While these existing peptide-based approaches show encouraging results in experimental settings, their translation to clinical applications necessitates further investigation. Challenges such as stability, bioavailability, and targeted delivery must be addressed to optimize the therapeutic potential of these peptides in the complex milieu of the lungs[28].

Potential of Peptides in Pulmonary Fibrosis Treatment

The potential of peptides in pulmonary fibrosis treatment extends beyond existing approaches, offering a rich avenue for innovative therapeutic strategies. One promising aspect lies in the development of peptides that target specific cell types involved in fibrogenesis[31]. By selectively modulating the behavior of fibroblasts, myofibroblasts, and immune cells, peptides can disrupt the intricate cellular interactions driving fibrosis, ultimately halting or reversing disease progression[32,8]. The extracellular matrix (ECM) represents another promising target for peptide-based interventions in pulmonary fibrosis. Peptides designed to interact with and modify ECM components can influence the

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balance between matrix deposition and degradation. These peptides may prevent excessive collagen accumulation and promote the resolution of fibrosis by enhancing the activity of matrix metalloproteinases or inhibiting tissue inhibitors of metalloproteinases[9]. In addition to their direct anti-fibrotic effects, peptides can be engineered to possess immunomodulatory properties. Given the inflammatory component of pulmonary fibrosis, peptides that regulate immune responses can attenuate inflammation and contribute to the overall therapeutic efficacy. Targeting specific immune cell subsets or modulating cytokine signaling pathways through peptide-based interventions may offer a novel and complementary approach to current treatment strategies[15]. The combination of peptides with nano-particle technology further amplifies their potential in pulmonary fibrosis treatment. Nano-particles can serve as carriers for peptide delivery, enhancing their stability, bioavailability, and targeted delivery to fibrotic lung tissues. The synergy between peptides and nano-particles creates a multifaceted approach that addresses the complexity of pulmonary fibrosis at both the molecular and delivery levels[33]. As research in peptide-based therapies for pulmonary fibrosis progresses, a thorough understanding of the disease's heterogeneity and the identification of patient-specific biomarkers will be crucial for tailoring peptide interventions to individual needs. Additionally, addressing challenges such as potential immunogenicity, off-target effects, and optimizing dosing regimens will be essential for advancing peptide-based therapies from bench to bedside[4].

INTEGRATION OF NANO-PARTICLES AND PEPTIDES

Synergistic Benefits of Hybrid Nano-Particles Peptides

The integration of nano-particles and peptides represents a groundbreaking approach in the treatment of pulmonary fibrosis, offering synergistic benefits that capitalize on the strengths of both technologies[34]. Combining nano-particles and peptides in a hybrid formulation creates a versatile and powerful platform for targeted drug delivery and precise modulation of molecular pathways involved in fibrosis. The synergy between nano-particles and peptides is evident in their complementary attributes[35]. Nano-particles, with their small size and unique delivery capabilities, facilitate the transport of therapeutic peptides to the specific regions within the lungs affected by fibrosis. The nano-sized carriers protect peptides from enzymatic degradation and enhance their stability during transit, ensuring that the therapeutic cargo reaches its destination with maximum bioavailability. Furthermore, peptides contribute their molecular specificity to the hybrid formulation[12,6]. Designed to target key cellular receptors or signaling molecules implicated in fibrosis, peptides ensure that the therapeutic payload is delivered precisely to the sites of action. This targeted approach minimizes off-target effects and enhances the therapeutic efficacy of the treatment, a crucial factor in the complex pathophysiology of pulmonary fibrosis. The hybrid nature of nano-particles and peptides also addresses challenges associated with each technology individually[9]. For instance, potential toxicity

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or immunogenicity concerns related to certain nano-materials can be mitigated by encapsulating therapeutic peptides within biocompatible nano-carriers. This collaboration between nano-particles and peptides thus creates a harmonious and efficient system that overcomes individual limitations, providing a holistic solution for the targeted treatment of pulmonary fibrosis[36,8].

Design and Fabrication of Advanced Hybrid Nano-Particles

The design and fabrication of advanced hybrid nano-particles for pulmonary fibrosis treatment involve a meticulous process to optimize the properties of both nano-materials and therapeutic peptides[37]. The choice of nano-material is a critical aspect of hybrid nano-particle design. Biocompatible materials, such as lipids, polymers, or metals with proven safety profiles, are often selected to form the nano-carriers[38]. These materials provide structural integrity to the particles, ensuring stability during storage and transit. Additionally, they allow for surface modifications to enhance biocompatibility, reduce immunogenicity, and improve the overall pharmacokinetics of the hybrid nano-particles. Controlling the size and morphology of the nano-particles is essential for optimizing drug delivery to fibrotic lung tissues[39]. The nano-size range, typically between 1 and 100 nanometers, enables efficient penetration into the intricate structures of the lungs[21,4]. Techniques such as nanoprecipitation, emulsion-based methods, or self-assembly processes are employed to achieve uniform and reproducible nano-particle sizes. These fabrication methods are tailored to the specific requirements of the therapeutic peptides and the desired release kinetics for optimal treatment outcomes[7]. Incorporating therapeutic peptides into the hybrid nano-particles requires careful consideration of peptide stability and bioactivity[40]. Peptides may be covalently attached to the surface of the nano-particles, encapsulated within the core, or conjugated to targeting ligands for enhanced specificity. The chosen strategy depends on the physicochemical properties of both the peptides and the nano-material, as well as the desired mode of action within the pulmonary fibrosis microenvironment[41].

Targeting Mechanisms for Enhanced Efficacy

The targeting mechanisms employed in advanced hybrid nano-particles play a pivotal role in enhancing their efficacy in the treatment of pulmonary fibrosis[4]. By incorporating specific targeting ligands, such as peptides with affinity for receptors overexpressed in fibrotic tissues, these nano-particles can achieve site-specific delivery, maximizing therapeutic impact while minimizing potential side effects[6]. One common targeting approach involves the use of peptides that recognize receptors on the surface of fibroblasts or inflammatory cells involved in the fibrotic process. These targeting peptides, when conjugated to the surface of nano-particles, guide the hybrid formulation to the sites of active fibrosis[32]. This targeted delivery not only improves the overall efficacy of the treatment but also reduces the dosage required, potentially minimizing the risk of systemic side effects. In

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addition to cell-specific targeting, the extracellular matrix (ECM) within fibrotic tissues can also be exploited for enhanced specificity. Peptides designed to interact with ECM components, such as collagen or fibronectin, can improve the retention and penetration of hybrid nano-particles within fibrotic lesions. This ECM-targeted approach ensures that therapeutic peptides are delivered precisely to the regions where their action is needed most, optimizing their anti-fibrotic effects[41,5,9]. The enhanced permeability and retention (EPR) effect, a characteristic of pathological tissues with leaky vasculature, further contributes to the targeted delivery of hybrid nano-particles. This phenomenon allows nano-particles to accumulate selectively in fibrotic areas, taking advantage of the altered vascular permeability associated with pulmonary fibrosis. Leveraging the EPR effect enhances the overall efficiency of hybrid nano-particles in reaching their intended targets within the lungs[42]. The integration of multiple targeting mechanisms creates a sophisticated and multifaceted approach for enhanced efficacy. By combining cell-specific, ECM-targeted, and EPR-based strategies, hybrid nano-particles can navigate the complex microenvironment of pulmonary fibrosis with precision[16]. These targeting mechanisms collectively contribute to the success of advanced hybrid nano-particles in improving the therapeutic outcomes for patients with pulmonary fibrosis[22].

CHALLENGES AND FUTURE PERSPECTIVES

Current Limitations and Hurdles

Despite the promise of advanced hybrid nano-particles and peptides in the targeted treatment of pulmonary fibrosis, several challenges and hurdles exist, hindering their seamless translation from bench to bedside[43]. One prominent challenge is the complexity of the pulmonary fibrosis microenvironment. The heterogeneity of fibrotic lesions, the presence of varying inflammatory mediators, and the dynamic nature of the disease pose hurdles in designing a one-size-fits-all therapeutic approach[44]. Tailoring hybrid nano-particles and peptides to accommodate this complexity requires a deep understanding of the disease's nuances and the identification of patient-specific factors that influence treatment responses[21]. Moreover, the potential immunogenicity of nano-materials and peptides raises concerns about the safety of these formulations. Immune responses triggered by the hybrid nano-particles could compromise their therapeutic efficacy and lead to adverse reactions. Balancing the need for effective treatment with minimizing immune responses is a critical consideration in overcoming this hurdle[29]. Issues related to scalability and cost-effectiveness also present challenges. The production of advanced hybrid nano-particles with consistent quality on a large scale requires robust and scalable manufacturing processes[12]. Additionally, the costs associated with the fabrication of these sophisticated formulations may impact their accessibility and widespread adoption[45].

Potential Side Effects and Safety Concerns

Ensuring the safety of advanced hybrid nano-particles and peptides is paramount in their

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clinical application for pulmonary fibrosis treatment[46]. While these innovative therapies offer targeted drug delivery and precision in molecular modulation, potential side effects and safety concerns must be thoroughly addressed. One notable concern is the potential for off-target effects, where the nano-particles or peptides may inadvertently interact with non-fibrotic tissues, leading to unintended consequences[47]. The design of targeting mechanisms and thorough preclinical testing are essential steps in mitigating this risk. Additionally, understanding the biodistribution and clearance profiles of hybrid nano-particles is crucial for predicting and minimizing off-target effects. The biocompatibility of nano-materials is a key determinant of their safety profile. Certain materials may trigger immune responses or exhibit toxicity, which can compromise the overall safety of the hybrid formulation. Rigorous evaluation of the selected nano-materials, including long-term studies assessing potential chronic effects, is imperative for ensuring the safety of these therapeutic approaches. Another safety concern is the potential for immunogenicity associated with therapeutic peptides[48]. Peptides, especially those derived from foreign sources, may elicit immune responses that impact their efficacy and safety. Designing peptides with low immunogenicity or employing strategies to modulate immune responses is essential for mitigating this potential risk. The long-term effects of repeated administration of hybrid nano-particles and peptides also warrant thorough investigation. Understanding the potential for cumulative toxicity and the development of adaptive immune responses is crucial for establishing the safety profile of these therapies over extended treatment durations[49].

Strategies for Overcoming Challenges

Addressing the challenges associated with advanced hybrid nano-particles and peptides in pulmonary fibrosis treatment requires strategic and multidisciplinary approaches. One strategy involves refining the design and engineering of nano-particles to enhance their biocompatibility and reduce potential immunogenicity[50]. The careful selection of nano-materials with proven safety profiles, surface modifications to improve biocompatibility, and the incorporation of stealth coatings to evade immune recognition are avenues for overcoming challenges related to nano-particle safety[32]. In terms of peptides, computational design approaches and molecular optimization can be employed to minimize immunogenicity and enhance their stability. Peptide modifications, such as PEGylation (polyethylene glycol attachment), can extend their circulation time and improve overall biocompatibility, mitigating potential side effects[44]. The development of personalized and patient-specific therapeutic strategies is another promising avenue for overcoming challenges in pulmonary fibrosis treatment[51]. Utilizing advanced diagnostic tools, such as molecular profiling and imaging techniques, can enable a more precise understanding of individual disease characteristics. Tailoring hybrid nano-particles and peptides based on patient-specific factors may enhance treatment outcomes while minimizing adverse effects[52]. Collaboration between researchers, clinicians, and industry

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stakeholders is crucial for addressing scalability and cost-effectiveness challenges. Streamlining manufacturing processes, optimizing formulation techniques, and exploring novel materials or technologies for cost-efficient production can contribute to overcoming these hurdles[29]. Additionally, regulatory agencies play a pivotal role in facilitating the translation of these innovative therapies into the clinic, necessitating a collaborative effort to navigate the regulatory landscape[53,54].

Future Directions and Emerging Technologies

The future of advanced hybrid nano-particles and peptides in pulmonary fibrosis treatment holds exciting possibilities, with ongoing research and emerging technologies paving the way for novel therapeutic strategies[55]. One promising direction is the integration of advanced imaging techniques with targeted therapies. Real-time monitoring of the distribution and efficacy of hybrid nano-particles within the lungs can provide valuable insights into treatment responses[4]. Imaging technologies, such as positron emission tomography (PET) and magnetic resonance imaging (MRI), offer the potential to track the biodistribution of nano-particles and assess their therapeutic impact, enabling a more dynamic and personalized approach to treatment[56,57]. The utilization of artificial intelligence (AI) and machine learning in drug design and optimization is another emerging area[7]. These technologies can accelerate the identification of novel peptides, predict their interactions with nano-materials, and optimize their therapeutic properties[58]. Integrating AI-driven approaches into the development of hybrid nano-particles and peptides may expedite the discovery process and enhance the overall efficiency of therapeutic design[9]. Nanotechnology platforms incorporating stimuli-responsive materials represent an innovative approach for responsive and on-demand drug release[59]. Stimuli such as pH, temperature, or specific molecular triggers within the fibrotic microenvironment can be exploited to trigger the release of therapeutic peptides from nano-particles precisely when and where they are needed most[60]. This responsive drug delivery approach holds the potential to further enhance the efficacy and safety profile of advanced hybrid formulations[20]. Furthermore, exploring the potential of combination therapies involving hybrid nano-particles and peptides with other treatment modalities, such as gene therapy or cell-based therapies, is an intriguing avenue for future research[61]. Synergistic approaches that target multiple pathways implicated in pulmonary fibrosis may yield more comprehensive and potent therapeutic outcomes[62].

Conclusion

The exploration of advanced hybrid nano-particles and peptides for targeted treatment of pulmonary fibrosis has uncovered a promising convergence of nanotechnology and molecular precision. By synergistically integrating the advantages of nano-particles and peptides, this review emphasizes their potential to overcome the limitations of current therapeutic approaches. The targeted drug delivery capabilities of nano-particles, coupled with the molecular specificity of peptides, present a

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multifaceted platform for addressing the intricate pathophysiology of pulmonary fibrosis. The review underscores the progress made in previous applications of nano-particles in respiratory medicine and highlights existing peptide-based approaches, such as TGF-β inhibition and integrin targeting, as promising strategies. The integration of these technologies in advanced hybrid formulations signifies a sophisticated approach to circumvent challenges associated with individual technologies, promising precise and effective treatment outcomes. Implications for pulmonary fibrosis treatment include the potential for revolutionizing the standard of care, minimizing side effects through targeted delivery, and opening avenues for personalized medicine. However, further research and development efforts are imperative to optimize formulations, address safety concerns, initiate clinical translation, discover reliable biomarkers, and explore synergistic combination therapies. The call for continuous commitment to advancing these technologies reflects the collective effort needed to bring innovative therapies from the laboratory to the clinic, ultimately improving the prognosis and quality of life for individuals afflicted by pulmonary fibrosis.

References

1. Lederer DJ, Martinez FJ. Idiopathic pulmonary fibrosis. N Engl J Med. 2018;378:1811–23.
2. Ballester B, Milara J, Cortijo J. Idiopathic pulmonary fibrosis and lung cancer: mechanisms and molecular targets. Int J Mol Sci. 2019;20:593.
3. Deng Z, Fear MW, Choi YS, Wood FM, Allahham A, Mutsaers SE, Prêle CM. The extracellular matrix and mechanotransduction in pulmonary fibrosis. Int J Biochem Cell B. 2020;126:105802.
4. Martinez FJ, Collard HR, Pardo A, Raghu G, Richeldi L, Selman M, Swigris JJ, Taniguchi H, Wells AU. Idiopathic pulmonary fibrosis. Nat Rev Dis Primers. 2017;3:1–19.
5. Assad N, Sood A, Campen MJ, Zychowski KE. Metal-induced pulmonary fibrosis. Curr Environ Health Rep. 2018;5:486–98.
6. Sgalla G, Iovene B, Calvello M, Ori M, Varone F, Richeldi L. Idiopathic pulmonary fibrosis: pathogenesis and management. Respirs Res. 2018;19:1–18.
7. Vianello A, Guarnieri G, Braccioni F, Lococo S, Molena B, Cecchetto A, Giraudo C, De Marchi LB, Caminati M, Senna G. The pathogenesis, epidemiology and biomarkers of susceptibility of pulmonary fibrosis in COVID-19 survivors. Clin Chem Lab Med. 2022;60:307–16.
8. Zhang C, Wu Z, Li JW, Tan K, Yang W, Zhao H, Wang GQ. Discharge may not be the end of treatment: Pay attention to pulmonary fibrosis caused by severe COVID-19. J Med Virol. 2021;93:1378–86.
9. Ryan N, Meskell P. The experience of people with idiopathic pulmonary fibrosis living through the COVID-19 pandemic. J Adv Nurs. 2022;78(7):2232–44.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 3219-3234 | ISSN:2251-6727

10. Carvalho LV, da Silva SC, Fontes JL, Cardoso L, Salomar M, Duarte-Neto AN, Figueira C, Brito R, Mesquita B, de Freitas LA. COVID-19 beyond DAD: persisting microcirculation thrombosis, hidden infections, and early pulmonary fibrosis as remaining challenges of the disease. Hum Pathol Rep. 2022;27:300607.
11. Covvey JR, Mancl EE. Recent evidence for pharmacological treatment of idiopathic pulmonary fibrosis. Ann Pharmacother. 2014;48:1611–9.
12. Skibba M, Drelich A, Poellmann M, Hong S, Brasier AR. Nanoapproaches to modifying epigenetics of epithelial mesenchymal transition for treatment of pulmonary fibrosis. Front Pharmacol. 2020;11:607689.
13. Homma S, Bando M, Azuma A, Sakamoto S, Sugino K, Ishii Y, Izumi S, Inase N, Inoue Y, Ebina M. Japanese guideline for the treatment of idiopathic pulmonary fibrosis. Respir Investig. 2018;56:268–91.
14. Kato M, Sasaki S, Nakamura T, Kurokawa K, Yamada T, Ochi Y, Ihara H, Takahashi F, Takahashi K. Gastrointestinal adverse effects of nintedanib and the associated risk factors in patients with idiopathic pulmonary fibrosis. Sci Rep-UK. 2019;9:1–9.
15. Hanta I, Cilli A, Sevinc C. The effectiveness, safety, and tolerability of Pirfenidone in idiopathic pulmonary fibrosis: a retrospective study. Adv Ther. 2019;36:1126–31.
16. Ghumman M, Dhamecha D, Gonsalves A, Fortier L, Sorkhdini P, Zhou Y, Menon JU. Emerging drug delivery strategies for idiopathic pulmonary fibrosis treatment. Eur J Pharm Biopharm. 2021;164:1–12.
17. Galli JA, Pandya A, Vega-Olivo M, Dass C, Zhao H, Criner GJ. Pirfenidone and nintedanib for pulmonary fibrosis in clinical practice: tolerability and adverse drug reactions. Respirology. 2017;22:1171–8.
18. Mu W, Chu Q, Liu Y, Zhang N. A review on nano-based drug delivery system for cancer chemoimmunotherapy. Nano-Micro Lett. 2020;12:1–24.
19. Thubelihle Ndebele R, Yao Q, Shi Y-N, Zhai Y-Y, Xu H-L, Lu C-T, Zhao Y-Z. Progress in the application of nano-and micro-based drug delivery systems in pulmonary drug delivery. BIO Integr. 2022;13:71–83.
20. Zhou Z, et al. Rational design of cancer nanomedicine: nanoproperty integration and synchronization. Adv Mater. 2017;29:1606628.
21. Bai X, Zhao G, Chen Q, Li Z, Gao M, Ho W, Xu X, Zhang XQ. Inhaled siRNA nanoparticles targeting IL11 inhibit lung fibrosis and improve pulmonary function post-bleomycin challenge. Sci Adv. 2022;8:eabn7162.
22. Camelo A, Dunmore R, Sleeman MA, Clarke DL. The epithelium in idiopathic pulmonary fibrosis: breaking the barrier. Front Pharmacol. 2014;4:173.
23. Wang JM, Robertson SH, Wang Z, He M, Virgincar RS, Schrank GM, Smigla

RM, O'Riordan TG, Sundy J, Ebner L. Using hyperpolarized 129Xe MRI to quantify regional gas transfer in idiopathic pulmonary fibrosis. Thorax. 2018;73:21–8.

24. Fulaz S, Vitale S, Quinn L, Casey E. Nanoparticle–biofilm interactions: the role of the EPS matrix. Trends Microbiol. 2019;27:915–26.
25. Liu Q, Zhang X, Xue J, Chai J, Qin L, Guan J, Zhang X, Mao S. Exploring the intrinsic micro−/nanoparticle size on their in vivo fate after lung delivery. J Controll Release. 2022;347:435–48.
26. Praphawatvet T, Peters JI, Williams RO III. Inhaled nanoparticles—an updated review. Int J Pharmaceut. 2020;587:119671.
27. Zhao J, Qin L, Song R, Su J, Yuan Y, Zhang X, Mao S. Elucidating inhaled liposome surface charge on its interaction with biological barriers in the lung. Eur J Pharm Biopharma. 2022;172:101–11.
28. Fischer D, Li Y, Ahlemeyer B, Krieglstein J, Kissel T. In vitro cytotoxicity testing of polycations: influence of polymer structure on cell viability and hemolysis. Biomaterials. 2003;24:1121–31.
29. Bhatt P, Kumar V, Subramaniyan V, Nagarajan K, Sekar M, Chinni SV, et al. Plasma modification techniques for natural polymer-based drug delivery systems. Pharmaceutics [Internet]. 2023;15(8):2066. Available from: http://dx.doi.org/10.3390/pharmaceutics15082066
30. Malik MK, Kumar V, Singh J, Bhatt P, Dixit R, Kumar S. Phosphorylation of alkali extracted mandua starch by STPP/STMP for improving digestion resistibility. ACS Omega [Internet]. 2023;8(13):11750–67. Available from: http://dx.doi.org/10.1021/acsomega.2c05783
31. Sharma SK, Singh S. Antimicrobial herbal soap formulation. J Pharm Res Int [Internet]. 2020;82–8. Available from: http://dx.doi.org/10.9734/jpri/2020/v32i3630995
32. Kaurav M, Kanoujia J, Gupta M, Goyal P, Pant S, Rai S, et al. In-depth analysis of the chemical composition, pharmacological effects, pharmacokinetics, and patent history of mangiferin. Phytomed Plus [Internet]. 2023;3(2):100445. Available from: http://dx.doi.org/10.1016/j.phyplu.2023.100445
33. Goyal C, Bhatt P, Rawat S, Kumar Sharma V, Rani Ahuja M. Estimation of shelf-life of Balachaturbhadrika syrup containing different sweetening agents. Res J Pharm Technol [Internet]. 2022;5078–83. Available from: http://dx.doi.org/10.52711/0974-360x.2022.00853
34. Ahamed S, Bhatt P, Sultanuddin SJ, Walia R, Haque MA, InayathAhamed SB. An Intelligent IoT enabled Health Care Surveillance using Machine Learning. In: 2022 International Conference on Advances in Computing, Communication and Applied Informatics (ACCAI). IEEE; 2022.
35. Bhatt P, Kumar A, Shukla R. Nanorobots recent and future advances

in cancer or dentistry therapy- A review. Am J PharmTech Res [Internet]. 2019;9(3):321–31. Available from: http://dx.doi.org/10.46624/ajptr.2019.v9.i3.027

36. Bhatt P, Kumar V, Rastogi H, Malik MK, Dixit R, Garg S, et al. Functional and tableting properties of alkali-isolated and phosphorylated barnyard millet (Echinochloa esculenta) starch. ACS Omega [Internet]. 2023;8(33):30294–305. Available from: http://dx.doi.org/10.1021/acsomega.3c03158
37. Lee HY, Mohammed KA, Nasreen N. Nanoparticle-based targeted gene therapy for lung cancer. Am J Cancer Res. 2016;6:1118–1134. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4948865/
38. Villate-Beitia I, Zarate J, Puras G, Pedraz JL. Gene delivery to the lungs: pulmonary gene therapy for cystic fibrosis. Drug Dev Ind Pharm. 2017;43:1071–1081. Available from: https://pubmed.ncbi.nlm.nih.gov/28112559/
39. Yan Z, McCray PB, Jr, Engelhardt JF. Advances in gene therapy for cystic fibrosis lung disease. Hum Mol Genet. 2019;28:R88–R94. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6448807/
40. Fernández Fernández E, Santos-Carballal B, de Santi C, Ramsey JM, MacLoughlin R, Cryan SA, et al. Biopolymer-based nanoparticles for cystic fibrosis lung gene therapy studies. Materials (Basel) 2018;11:122. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6337449/
41. Hardee CL, Arévalo-Soliz LM, Hornstein BD, Zechiedrich L. Advances in non-viral DNA vectors for gene therapy. Genes (Basel) 2017;8:65. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5448233/
42. Chidambaram M, Manavalan R, Kathiresan K. Nanotherapeutics to overcome conventional cancer chemotherapy limitations. J Pharm Pharm Sci. 2011;14:67–77. Available from: https://pubmed.ncbi.nlm.nih.gov/21388910/
43. Sun S, Wang Y, Zhou R, Deng Z, Han Y, Han X, et al. Targeting and regulating of an oncogene via nanovector delivery of MicroRNA using patient-derived xenografts. Theranostics. 2017;7:677–693. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5302015/
44. Wang Y, Sun S, Zhang Z, Shi D. Nanomaterials for cancer precision medicine. Adv Mater. 2018;30:e1705660. Available from: https://pubmed.ncbi.nlm.nih.gov/29569784/
45. Wang J, Li J, Yu J, Zhang H, Zhang B. Large hollow cavity luminous nanoparticles with near-infrared persistent luminescence and tunable sizes for tumor afterglow imaging and

chemo-/photodynamic therapies. ACS Nano. 2018;12:4246–4258. Available from: https://pubmed.ncbi.nlm.nih.gov/29688057/

46. Yang W, Shi X, Shi Y, Yao D, Chen S, Zhou X, et al. Beyond the roles in biomimetic chemistry: an insight into the intrinsic catalytic activity of an enzyme for tumor-selective phototheranostics. ACS Nano. 2018;12:12169–12180. Available from: https://pubmed.ncbi.nlm.nih.gov/30444696/
47. Liu XL, Chen S, Zhang H, Zhou J, Fan HM, Liang XJ. Magnetic nanomaterials for advanced regenerative medicine: the promise and challenges. Adv Mater. 2019;31:e1804922. Available from: https://pubmed.ncbi.nlm.nih.gov/30802844/
48. Zhang B, Yan W, Zhu Y, Yang W, Le W, Chen B, et al. Nanomaterials in neural-stem-cell-mediated regenerative medicine: imaging and treatment of neurological diseases. Adv Mater. 2018;30:e1705694. Available from: https://pubmed.ncbi.nlm.nih.gov/29527897/
49. Pöttler M, Cicha I, Unterweger H, Janko C, Friedrich RP, Alexiou C. Nanoparticles for regenerative medicine. Nanomedicine (Lond) 2019;14:1929–1933. Available from: https://pubmed.ncbi.nlm.nih.gov/31352888/
50. Wang K, Wen S, He L, Li A, Li Y, Dong H, et al. "Minimalist" nanovaccine constituted from near whole antigen for cancer immunotherapy. ACS Nano. 2018;12:6398–6409. Available from: https://pubmed.ncbi.nlm.nih.gov/29929311/
51. Wang J, Li P, Yu Y, Fu Y, Jiang H, Lu M, et al. Pulmonary surfactant-biomimetic nanoparticles potentiate heterosubtypic influenza immunity. Science. 2020;367:eaau0810. Available from: https://pubmed.ncbi.nlm.nih.gov/32001665/
52. Gutjahr A, Phelip C, Coolen AL, Monge C, Boisgard AS, Paul S, et al. Biodegradable polymeric nanoparticles-based vaccine adjuvants for lymph nodes targeting. Vaccines (Basel) 2016;4:1–16. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6466355/
53. Shen C, Li J, Zhang Y, Li Y, Shen G, Zhu J, et al. Polyethylenimine-based micro/nanoparticles as vaccine adjuvants. Int J Nanomedicine. 2017;12:5443–5460. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5538158/
54. Kwon EJ, Skalak M, Bertucci A, Braun G, Ricci F, Ruoslahti E, et al. Porous silicon nanoparticle delivery of tandem peptide anti-infectives for the treatment of Pseudomonas aeruginosa lung infections. Adv Mater. 2017;29:1–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29164787/
55. Ho DK, Nichols BLB, Edgar KJ, Murgia X, Loretz B, Lehr CM.

Challenges and strategies in drug delivery systems for treatment of pulmonary infections. Eur J Pharm Biopharm. 2019;144:110–124. Available from: https://pubmed.ncbi.nlm.nih.gov/31546097/

56. Moreno-Sastre M, Pastor M, Salomon CJ, Esquisabel A, Pedraz JL. Pulmonary drug delivery: a review on nanocarriers for antibacterial chemotherapy. J Antimicrob Chemother. 2015;70:2945–2955. Available from: https://pubmed.ncbi.nlm.nih.gov/26231247/
57. Wagner AM, Knipe JM, Orive G, Peppas NA. Quantum dots in biomedical applications. Acta Biomater. 2019;94:44–63. Available from: https://pubmed.ncbi.nlm.nih.gov/30878612/
58. Liu J, Lécuyer T, Seguin J, Mignet N, Scherman D, Viana B, et al. Imaging and therapeutic applications of persistent luminescence nanomaterials. Adv Drug Deliv Rev. 2019;138:193–210. Available from: https://pubmed.ncbi.nlm.nih.gov/30223019/
59. Yang L, Feuchtinger A, Möller W, Ding Y, Kutschke D, Möller G, et al. Three-dimensional quantitative co-mapping of pulmonary morphology and nanoparticle distribution with cellular resolution in nondissected murine lungs. ACS Nano. 2019;13:1029–1041. Available from: https://pubmed.ncbi.nlm.nih.gov/30645154/
60. Horiguchi M, Kojima H, Sakai H, Kubo H, Yamashita C. Pulmonary administration of integrin-nanoparticles regenerates collapsed alveoli. J Control Release. 2014;187:167–174. Available from: https://pubmed.ncbi.nlm.nih.gov/24727019/
61. Naderi N, Karponis D, Mosahebi A, Seifalian AM. Nanoparticles in wound healing; from hope to promise, from promise to routine. Front Biosci (Landmark Ed) 2018;23:1038–1059. Available from: https://pubmed.ncbi.nlm.nih.gov/29772595/
62. Lim YH, Tiemann KM, Hunstad DA, Elsabahy M, Wooley KL. Polymeric nanoparticles in development for treatment of pulmonary infectious diseases. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2016;8:842–871. Available from: https://pubmed.ncbi.nlm.nih.gov/26853809/