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Targeted drug delivery to the lungs using mesoporous silica nanoparticles

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Abstract

Delivering drugs to tumour or defective cells effectively and efficiently while minimizing harmful side effects is one of the biggest issues facing the medical field. In order to address this issue, the pharmaceutical industry has developed a number of drug carriers that aid in getting the therapeutic medication or gene to the intended location. It has been discovered that mesoporous silica nanoparticles are biocompatible, chemically and thermally stable nanoparticles for this purpose the amount of research on MSNs has increased significantly in the last few years. Since 2001, when MCM-41 was first suggested as a drug carrier for a controlled delivery system, followed by SBA-15 and MCM-48. When changed, morphological features like pore size, pore volume, particle size, surface area, pH, and drug loading capacity have a significant impact on MSNs. Drug distribution to the intended place is elaborated by functionalizing MSNs with organic and inorganic groups. The most recent studies on MSN synthesis techniques and its uses in medical imaging, diagnostics, cellular uptake, target medication administration, cell tracing, and biosensing are also included in this review article.

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INTRODUCTION

Mesoporous nanoparticles have emerged as a promising avenue in the field of pulmonary treatment, offering a novel approach to address a wide range of respiratory ailments [1]. Respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), and lung cancer, represent a significant global health burden. Conventional pulmonary drug delivery methods, including inhalers and nebulizers, often

face limitations in terms of drug retention, targeting specific lung diseases. In this setting, mesoporous nanoparticles have become a game-changer. The highly organized porosity structure of these nanoscale materials allows for better medication bioavailability, controlled release, and effective drug encapsulation. The capacity of mesoporous nanoparticles to encapsulate a variety of therapeutic substances, such as tiny molecules, proteins, and nucleic acids, is one of its most important benefits. This adaptability is essential for creating customized treatment plans for a range of lung conditions. Additionally, the mesoporous structure enables fine-grained control over the release kinetics, guaranteeing that medications are released into the lungs at the appropriate rate and location.This property reduces adverse effects and improves the therapeutic efficacy of interventions.Additionally, to improve lung-specific medication delivery, mesoporous nanoparticles can be functionalized with targeting ligands like peptides or antibodies. By selectively binding to particular receptors or cell types in the respiratory system, these functionalized nanoparticles can enhance drug localization and lessen off-target effects [2]. This focused strategy has great promise for treating conditions like lung cancer, where exact medication administration is crucial.Mesoporous nanoparticles have the ability to carry drugs and can also be utilized for diagnostics. They can be loaded with imaging agents to enable real-time, non-invasive tracking of the course of a disease. This tool is especially helpful in the early diagnosis and evaluation of lung illnesses, facilitating prompt intervention and individualized care.Mesoporous nanoparticles' distinct structural features further add to their lower toxicity and biocompatibility. Controlled drug release is made possible by their adjustable pore size and surface characteristics, which also reduce harmful effects on healthy lung tissue. When it comes to chronic illnesses that need for ongoing care, this aspect is crucial.

Mesoporous nanoparticles have shown remarkable potential in preclinical and clinical studies. They have been utilized in the treatment of respiratory infections, lung cancer, and inflammatory lung conditions. By enhancing drug delivery efficiency, reducing side effects, and improving patient compliance, these nanoparticles are transforming the landscape of pulmonary therapeutics. Furthermore, mesoporous nanoparticles are paving the way for personalized medicine in pulmonary treatment. They allow for the development of patient-specific drug formulations, which consider individual differences in drug metabolism, disease severity, and lung physiology. This tailored approach holds great promise in optimizing treatment outcomes and minimizing adverse reactions [3]. While mesoporous nanoparticles have shown remarkable potential, challenges remain. Issues

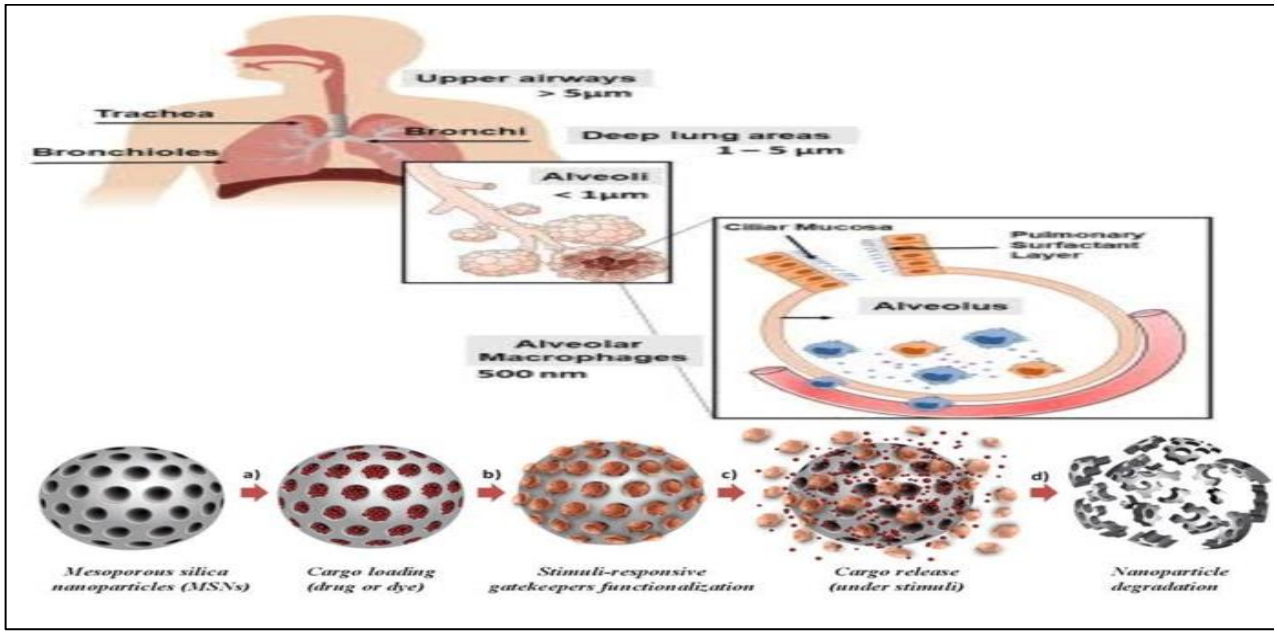

Figure 1 Graphical Presentations of Naoparticles in Targeted drug delivery to the lungs

related to large-scale production, regulatory approval, and long-term safety must be addressed. Moreover, further research is needed to fine-tune the nanoparticle design and optimize their use in specific pulmonary conditions.

In conclusion, mesoporous nanoparticles represent a breakthrough in pulmonary treatment. Their unique structural characteristics, drug delivery capabilities, and potential for personalized medicine are reshaping the way we approach respiratory diseases. With continued research and development, these nanoparticles have the potential to significantly improve the effectiveness of pulmonary therapies, offering new hope to patients with respiratory ailments and contributing to better overall healthcare outcomes [4].

Advantages and Disadvantages

Mesoporous nanoparticles hold promise in pulmonary treatment, but they also come with advantages and disadvantages that should be considered when evaluating their potential applications in this context. Here are some of the key advantages and disadvantages:

Advantages [5]

High Drug Loading Capacity: Mesoporous nanoparticles have a highly ordered porous structure with a large surface area, which allows for the efficient loading of a wide range of therapeutic agents, including small molecules, proteins, and nucleic acids. This property ensures that a significant amount of the drug can be delivered to the target site within the lungs.

Controlled Drug Release: The tunable pore size and surface properties of mesoporous nanoparticles enable precise control over drug release kinetics. This controlled release can lead to sustained therapeutic effects, reducing the need for frequent dosing and minimizing side effects.

Targeted Drug Delivery: Mesoporous nanoparticles can be functionalized with targeting ligands, such as antibodies or peptides, to improve lung-specific drug delivery. This targeted approach enhances drug localization to specific lung regions or cells, increasing therapeutic efficacy while minimizing off-target effects.

Biocompatibility: In order to limit harm to healthy lung tissue during pulmonary treatment, these nanoparticles must be generally well-tolerated by the body and show reduced toxicity.

Personalized Medicine: The creation of medication compositions tailored to each patient is made possible by mesoporous nanoparticles. Treatment outcomes may be improved by adjusting treatment techniques to account for individual differences in medication metabolism, illness severity, and lung physiology.

Applications for Diagnostics: Mesoporous nanoparticles can be loaded with imaging agents to monitor the course of a disease and the effectiveness of treatment in real time in the lungs.

Decreased Side Effects: Since the medication is mostly administered to the lungs, where it is meant to act, the controlled release of the medicine and the targeted administration of mesoporous nanoparticles can lessen systemic side effects.

Disadvantages [6]

Complex Synthesis: The creation of mesoporous nanoparticles can be a challenging process that calls for certain tools and knowledge. Commercialization and large-scale production may face difficulties as a result.

Regulatory Obstacles: Because of worries about safety, effectiveness, and quality control, obtaining regulatory permission for the use of mesoporous nanoparticles in pulmonary treatment may be a drawn-out and difficult procedure.

Long-Term Safety Concerns: Although mesoporous nanoparticles are usually thought to be biocompatible, longer-term safety investigations are still required to assess any possible negative effects from repeated exposure, particularly when it comes to respiratory conditions that are chronic.

Size Control: It can be difficult to precisely regulate the size and dispersion of mesoporous nanoparticles, and changes in particle size may have an impact on the effectiveness of targeting and the rate at which drugs release.

Risk of Agglomeration: Mesoporous nanoparticles may be prone to clump together, which may impair how well they disperse in

formulations meant for inhalation and how well they work to transport drugs to the lungs.

Cost: The costlier manufacture of mesoporous nanoparticles than conventional medicinal formulations may affect the accessibility and affordability of these materials for patients.

Needs for study and Development: To optimize mesoporous nanoparticles for certain pulmonary disorders and to address any obstacles or restrictions that may occur during their development and application, further study is necessary.

Applications [7]

Mesoporous nanoparticles have been used in the treatment of lung diseases in a number of ways, providing creative approaches to a variety of respiratory ailments. They are effective tools for enhancing medication delivery, diagnostics, and therapeutic results in the field of respiratory medicine because of their special qualities. Mesoporous nanoparticles have been used in pulmonary treatment for the following noteworthy reasons:

Medication Delivery: The main use of mesoporous nanoparticles is to improve the transportation of medicinal substances to the lungs. They are effective at encapsulating a wide range of medications, such as bronchodilators, antibiotics, anti-inflammatory compounds, and anticancer medications. The systemic negative effects of this tailored drug administration can be reduced while therapeutic efficacy is increased.

Controlled and Sustained Drug Release: Mesoporous nanoparticles allow for the controlled and sustained release of medications, which is beneficial for pulmonary therapy. By lowering the frequency of dose and guaranteeing a constant medication concentration at the target region, it enables sustained therapeutic benefits. For people with chronic respiratory conditions like COPD and asthma, this is very helpful.

Targeted Therapy: Diseased lung tissues or cells can be the only target of functionalized mesoporous nanoparticles. The selectivity of the nanoparticles for particular cell types or receptors can be increased by attaching ligands, such as peptides or antibodies. By improving drug localization, this tailored strategy lessens off-target effects.

Treatment of Respiratory Infections: The potential use of mesoporous nanoparticles in the management of bacterial and viral respiratory infections has been investigated. Antimicrobial medicines can be carefully released at the site of infection to improve treatment efficacy and slow the emergence of antibiotic resistance.

Cancer Therapy: Mesoporous nanoparticles are utilized to deliver chemotherapeutic drugs directly to tumor cells while protecting healthy lung tissue in the context of treating lung cancer. This focused strategy increases the medications' anticancer benefits while reducing systemic toxicity.

Mucolytic drugs: In diseases like cystic fibrosis and chronic bronchitis, mucolytic drugs help break down mucus and enhance airway clearance. These agents can be delivered using mesoporous nanoparticles. This software can lessen the chance of exacerbations and help with symptom management.

Gene and RNA Therapy: RNA-based medicines and genetic material can be delivered using mesoporous nanoparticles. This is important for the treatment of genetic lung illnesses and other conditions where underlying problems need to be addressed by genetic alterations.

Imaging and Diagnostics: For diagnostic reasons, mesoporous nanoparticles can be loaded with contrast agents or imaging dyes. They allow for the non-invasive monitoring of lung diseases, such as the evaluation of respiratory function or the advancement of lung malignancies, when inhaled.

Personalized medicine: Mesoporous nanoparticles' adjustable properties enable the creation of medication compositions that are unique to each patient. Individual variations in lung physiology, medication metabolism, and disease severity are taken into account when customizing therapies, which may enhance therapeutic results and patient compliance.

Research and Studies in Biology: Mesoporous nanoparticles can be used to create *in vitro* lung models for drug testing as well as to investigate the biology of the lung. They can act as platforms for examining how cells react to various chemicals,

which advances our knowledge of lung disorders. Despite the many benefits mesoporous nanoparticles provide for treating lung conditions, issues with their production, regulatory approval, and long-term safety must be resolved. To optimize these nanoparticles for certain lung illnesses and to maximize their potential in enhancing respiratory health and patient quality of life, further research and development are required.

Methodology

From the creation and synthesis of the nanoparticles to their use in the delivery of therapeutic drugs to the lungs, there are several steps in the process of employing mesoporous nanoparticles in pulmonary treatment. An outline of the main techniques for using mesoporous nanoparticles in lung therapy is provided below:

Nanoparticle Production

Choice of Materials:

Select materials that are suitable for the intended medication or therapeutic agent and biocompatible for the mesoporous nanoparticles.

Controlled Synthesis:

Usually with the use of a template or sol-gel chemistry, create nanoparticles with precise dimensions, shapes, and pore structures. Optimizing medication loading and release requires control over these parameters.

Surface Alteration:

Functionalization: To enable targeted medication administration or enhance compatibility with the respiratory system, modify the surface of the nanoparticle by adding particular ligands, such as peptides or antibodies.

Medication Encapsulation [8]

Choice of Therapeutic Agent: Based on the particular ailment being treated, select the right medication or therapeutic agent.

Formulate a loading protocol that will allow the medication to be incorporated into the mesoporous nanoparticles with a high loading efficiency.

Characterization:

Physicochemical Analysis: Conduct a thorough characterization of the mesoporous nanoparticles, including size, surface area, pore size, and drug loading capacity. Techniques such as transmission electron microscopy (TEM), scanning electron microscopy (SEM), X-ray diffraction (XRD), and nitrogen adsorption-desorption isotherms can be employed.

***In vitro* Release Studies:** Evaluate the release kinetics of the drug from the nanoparticles to ensure controlled and sustained drug release.

In vitro Testing [9]

Cell Culture Studies: Assess the cytotoxicity and biocompatibility of the mesoporous nanoparticles in relevant lung cell lines to ensure their safety.

Efficacy Studies: Conduct *in vitro* studies to determine the therapeutic efficacy of the drug-loaded nanoparticles in relevant disease models.

In vivo Animal Studies:

Animal Model Selection: Choose an appropriate animal model that closely mimics the human lung physiology and the disease being treated.

Nanoparticle Administration: Administer the drug-loaded mesoporous nanoparticles via inhalation, intratracheal instillation, or other appropriate routes to test their effectiveness and safety *In vivo*.

Pharmacokinetics and Biodistribution: Study the nanoparticles' behavior in the lungs, drug release kinetics, and systemic biodistribution to assess their efficacy and potential side effects.

Therapeutic Monitoring:

Assessment of Lung Function: Evaluate the impact of the treatment on lung function, such as measuring changes in airway resistance or lung capacity.

Histological Analysis: Conduct histological examinations to assess changes in lung tissue and the presence of any side effects or adverse reactions.

Optimization: Based on the results from and *in vivo* studies, refine the formulation, drug release kinetics, and targeting strategies to improve therapeutic outcomes and minimize side effects.

Table 1 Nanoparticle-based therapy Drugs and Treatment

S. No	Drug	Treatment
1	Budesidone	Inhalable mesoporous silica nanoparticles for sustained pulmonary drug delivery [11]
2	Indomethacin	Mesoporous silica coated gold nanoparticles for synergistic thermochemotherapy of asthma [12]
3	Doxorubicin	Hollow mesoporous organosilica nanoparticles for efficient drug delivery and photothermal therapy [13]
4	Montelukast	Mesoporous carbon nanoparticles as a carrier for sustained pulmonary drug release in asthma treatment [14]
5	Dexamethasone	Mesoporous silica coated gold nanoparticles for combined therapy of chronic obstructive pulmonary disease [15]
6	Rifampin	Rifampin Loaded Mesoporous Silica Nanoparticles as a Potential System for Pulmonary Drug Delivery [16]
7	Curcumin	Curcumin Release from Hollow Mesoporous Silica Nanoparticles for PM2.5-Induced Acute Lung Injury Treatment [17]
8	Pirfenidone	Pirfenidone Target to Fibroblast Activation Protein for Pulmonary Fibrosis Therapy [18]
9	Cobalt protoporphyrin	Cobalt protoporphyrin-induced nano-self-assembly for CT imaging, magnetic-guidance, and antioxidative protection of stem cells in pulmonary fibrosis treatment [19]
10	Doxorubicin	Doxorubicin loaded large-pore mesoporous hydroxyapatite coated superparamagnetic Fe3O4 nanoparticles for cancer treatment [20]
11	Salvianolic acid B-loaded polydopamine	modified hollow mesoporous organic silica nanoparticles for treatment of breast cancer metastasis via suppressing cancer-associated fibroblasts [21]
12	Doxorubicin	doxorubicin-loaded N-isopropylacrylamide-co-methacrylic acid coated mesoporous silica nanoparticles used anthraquinone anticancer drug for treatment of human malignancies. [22]
13	Clarithromycin	Amine Functionalized Mesoporous Silica Nanoparticles enhance the efficacy against Gram positive and Gram negative bacterial samples. [23]
14	glucose-6-phosphate isomerase	mesoporous silica nanocarriers in the treatment of rheumatoid arthritis.n[24]
15	amoxicillin molecule	treatment for covid-19 implementing functionalized mesoporous SBA-15 with aminopropyl groups [25]

Regulatory Considerations: Address regulatory and safety requirements for clinical translation, including the development of standardized protocols, quality control, and adherence to regulatory guidelines for drug delivery systems.

Clinical Trials: If the mesoporous nanoparticles show promising results in preclinical studies, proceed to clinical trials to evaluate their safety and efficacy in human patients.

Scale-up and Production: Develop scalable processes for the large-scale production of mesoporous nanoparticles for clinical use, ensuring consistency and quality control.

Commercialization: Work on the commercialization of the nanoparticle-based therapy, which may involve collaborations with pharmaceutical companies, regulatory approval, and market access strategies.

Table 1 Nanoparticle-based therapy Drugs and Treatment (Continued)

S. No	Drug	Treatment
16	Bleomycin Hydrolase	Mannose-Modified Hierarchically Porous UiO-66 for Preventing Bleomycin-Induced Pulmonary Fibrosis [26]
17	Tacrolimus	encapsulated mesoporous silica nanoparticles embedded hydrogel for the treatment of atopic dermatitis [27]
18	Polypyrrole	Polypyrrole-Coated Mesoporous TiO2 Nanocomposites for Photothermal, Sonodynamic, and Chemotherapeutic Treatments and Dual-Modal Ultrasound/Photoacoustic Imaging of Tumors [28]
19	Bismuth Sulfide	Actively Targeted Deep Tissue Imaging and Photothermal-Chemo Therapy of Breast Cancer by Antibody-Functionalized Drug-Loaded X-Ray-Responsive Bismuth Sulfide@Mesoporous Silica Core–Shell Nanoparticles [29]
20	Bovine serum albumin	Bovine serum albumin-based and dual-responsive targeted hollow mesoporous silica nanoparticles for breast cancer therapy [30]
21	Quercetin	Quercetin-Loaded Mesoporous Silica Nanoparticles on Myocardial Ischemia-Reperfusion Injury in Rats and Its Mechanism [31]
22	Alginate/Chitosan	Effect of pH-Responsive Alginate/Chitosan Multilayers Coating on Delivery Efficiency, Cellular Uptake and Biodistribution of Mesoporous Silica Nanoparticles Based Nanocarriers [32]
23	Endosomolytic	Endosomolytic and Tumor-Penetrating Mesoporous Silica Nanoparticles for siRNA/miRNA Combination Cancer Therapy [33]
24	silsesquioxane	Mesoporous silica nanoparticles with organo-bridged silsesquioxane framework as innovative platforms for bioimaging and therapeutic agent delivery [34]
25	triamcinolone acetonide	Physicochemical characterization and *in vivo* evaluation of triamcinolone acetonide-loaded hydroxyapatite nanocomposites for treatment of rheumatoid arthritis [35]
26	Oligonucleotide	An emerging focus area for drug delivery in chronic inflammatory respiratory diseases [36]
27	Lactoferrin	Synthesis of lactoferrin mesoporous silica nanoparticles for pemetrexed/ellagic acid synergistic breast cancer therapy [37]
28	Polyethyleneimine	Polyethyleneimine Coating Enhances the Cellular Uptake of Mesoporous Silica Nanoparticles and Allows Safe Delivery of siRNA and DNA Constructs [38]
29	Apigenin	Apigenin Attenuates Mesoporous Silica Nanoparticles-Induced Nephrotoxicity by Activating FOXO3a [39]
30	polymyxin B-hyaluronic acid/ poly (lactic-co-glycolic acid)	Mucus-permeable polymyxin B-hyaluronic acid/ poly (lactic-co-glycolic acid) nanoparticle platform for the nebulized treatment of lung infections [40]

It's essential to recognize that the specific methodology for mesoporous nanoparticles in pulmonary treatment may vary based on the disease being targeted, the therapeutic agent being used, and the desired treatment outcome. Rigorous preclinical and clinical evaluation is crucial to ensure the safety and effectiveness of these nanoparticles in practical applications. Ongoing research and development are essential for optimizing and expanding the use of mesoporous nanoparticles in pulmonary treatments [10].

CONCLUSION

To sum up, this review brought to light a number of fascinating advancements made by scientists

working on mesoporous silica-based nanoparticles. Since the development of this innovative medicine delivery method, there has been a greater potential and motivation for the scientists to pursue it. These particles can pass through cells despite having a variety of shapes and sizes, even smaller than those of eukaryotic cells. Because there is no premature release, it is also a great substitute for traditional oral delivery methods. With long-term treatments, it may be possible to more effectively regulate the kinetic release of the drug by altering environmental cues. MSNs are a promising class of nanocarriers designed to carry extremely hazardous medications, such as chemotherapeutic treatments, that have the unique ability to selectively kill tumour cells. MSNs have drug release that is stimulus responsive, which maximises the benefits of anti cancer medications while reducing their negative effects.

Mesoporous silica material can be modified morphologically to create a variety of material shapes. Different pore architectures and particle sizes ranging from hundreds of microns to millilitres are produced by varying the pH and stirring rate. Mesitylene is the most effective pore expander for MSNs that doesn't change the size of the particles.

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