Nanoparticle-based Treatment for Respiratory Disorder

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Abstract

Every year, the increase in respiratory problem instances around the world impacts the well-being and standard of life of millions of individuals. Since chronic respiratory diseases (CRDs) are the leading cause of hospitalizations and deaths, sophisticated treatments that allow for the regulated delivery of medications to specific target sites are required. To address this demand, a variety of nanoparticles (NPs) has been studied, including carbon-based, dendrimers, polymeric, liposome, and quantum dots. The use of NPs as drug delivery vehicles can improve the efficacy of commercial drugs due to their advantages in targeted effects, prolonged drug release, and patient compliance. The use of nanotechnology as drug delivery systems to treat respiratory tract diseases, such as asthma, lung cancer, lung infections, and chronic respiratory disorders (CRDs), is covered in this chapter.

Keywords: Nanoparticles, Respiratory, Disorder, Chronic, Polymers

Cite this Article as: Qasim S, Kousar J, Rizwan R, Anis S, Saheen A, Arshad M, Fatima K, Kazmi SAA, Tahir I and Munir A, 2025. Nanoparticles based treatment for respiratory disorder. In: Nisa ZU, Altaf S, Zahra A and Saeed K (eds), Nanobiotech in Holistic Health: Innovations for Integrated Well-being. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 45-50. https://doi.org/10.47278/book.HH/2025.303

A Publication of Unique Scientific Publishers | Chapter No: 25-007 | Received: 16-Feb-2025
Revised: 16-Apr-2025
Accepted: 15-May-2025

Introduction

In 2016, respiratory disorders led various impairment and at least 9 million deaths globally reported by World Health Organization (WHO). A little over 15% of the fatalities were caused by these illnesses (Horváth et al., 2017). The most common respiratory conditions are common cold, bronchitis, pneumonia, TB, pharyngitis, laryngitis, and lower respiratory infections, and obstructive lung illnesses such as lung cancer, asthma, and the chronic obstructive pulmonary disorder (COPD). Air pollution and hereditary characteristics and bacterial and viral infections are the primary causes of the respiratory illnesses. Airborne illnesses and the infections could easily infect the lower respiratory airways, affecting them and result in acute respiratory infections (Thorlund et al., 2020). Severe respiratory infections can be the caused on by the newly discovered COVID-19 corona virus, as well as avian influenza A (H7N9) and severe acute respiratory syndrome corona virus (SARS-CoV). Genetic problems and air pollution are t causes of chronic respiratory diseases and such as lung cancer, cystic fibrosis (CF), asthma, COPD, and hay fever. Healing and restoring the respiratory system's functions is the primary treatment objective in the order to enhance patients' standrad of life (Thorlund et al., 2020). The primary objectives of the respiratory diseases treatment are to the reduce the number of deaths and the casualties, improve standard of life and lessen drug adverse effect, and provide an appropriate therapy for symptom relief.

The need for the new treatments that can be get past issues like drug resistance and poor drug efficacy and side effects and expense might make using medications based on nanotechnology are the more acceptable. The development of the nanomedicine and the nanotechnology in recent years has been created opportunities for treatment of respiratory disorders. The surface to volume ratio of nanoparticles (NPs) is extremely highly due to their nanoscale size (Yazdi et al., 2021). With the right designs this characteristic makes it possible to attach numerous ligand to the surface enhances the chances that are multiple covalent connections will be form, and can be used simultaneously in the targeted treatment (Ghorani-Azam et al., 2022). Additional the features of nanoparticles include the enhanced chemico-biological stability the potential to the bind to hydrophilic and hydrophobic medications, and the ability to be administered by injection or inhalation (Deng et al., 2021), depending solely on the reagents' chemical structure and the nano-carrier's physicochemical properties. One of the widely utilized medicine delivery methods for both respiratory and non-respiratory conditions is aerosol delivery (Bianco et al., 2021). Because they are functionalized for targeted distribution, have greater biocompatibility, and have fewer side effects, nanosystems may be more effective than traditional medications (Mousavi-Kouhi et al., 2021). Various kinds of nanoparticles, such as inorganic and organic ones, were accessible for biological applications; these should be discussed in further detail in order to build new nano-systems for particular uses. In order to provide fresh concepts for more practical future drugs, the NPs utilized to treat respiratory conditions were discussed in this chapter.

Respiratory Disorders

Chronic Respiratory Diseases (CRDs)

Numerous hospital stays, countless costs, and, in the most severe situations, fatalities are all caused by CRDs, which also lower many patients' quality of life. The most well-known CRDs include lung cancer, cystic fibrosis, asthma, allergic rhinitis, and chronic obstructive pulmonary disease (COPD) (Sleurs et al., 2019). The most prevalent non-communicable disease (CRD), asthma affects over 300 million people worldwide (Papi et al., 2018a). Its symptoms, which include coughing, chest tightness, and shortness of breath, call for long-term treatment and, in certain situations, endless periods (Strzempek et al., 2019). With upper respiratory system infections, pollen exposure, and air pollution, the intensity of symptoms might fluctuate over time and result in respiratory failure (Lambrecht et al., 2019). When an overactive immune response is triggered by exposure to airborne environmental allergens, asthma with allergies is the most common type of asthma. Bronchodilators and anti-inflammatory medications are inhaled as part of the treatment to lessen airway blockage and inflammation. Traditional therapies, however, primarily address asthma symptoms rather than the underlying cause of the condition. Under this method, the patient must take medication for the duration of their lives (Givens et al., 2018).

Another severe form of CRD, COPD, affects around 64 million people, accounts for 10% of deaths in the over-40 age group, and is the third leading cause of mortality globally (Barnes et al., 2018). Toxic particle exposure, like that seen in smoking, is the main cause of risk for COPD (Papi et al., 2018a). The conditions that make up COPD include emphysema and chronic bronchitis, however most individuals have both phenotypes.Chronic exposure to the compounds in cigarette smoke triggers reactive oxygen species (ROS), which leads to apoptosis and inflammatory-oxidative stress. Consequently, alveolar gap widening causes lung tissue to deteriorate, leading to emphysema.

About 70 000 people worldwide suffer with cystic fibrosis (CF), a hereditary condition caused by a malfunction in a protein that transports substances called the cystic fibrosis transmembrane (CFTR) (Stephenson et al., 2017). The secretion of chloride ions into exocrine glands is controlled by the CFTR protein. The absence of chloride ions impairs the mucociliary clearance and damages the airway mucosa by making gland secretion more viscous. Chronic pulmonary infections are thus characterized by the persistent colonization of bacteria and fungi, particularly *Pseudomonas aeruginosa* and *Candida spp.*, in the endobronchial region (Schwarz et al., 2018).

Acute Respiratory Infections (ARIs)

The primary cause of death for children under five is acute respiratory syndromes (ARIs), also referred to as ARSs. ARIs are among the world's leading causes of death, accounting for approximately 4 million deaths per year (FoIR et al., 2017). A common cold, pneumonia, laryngitis, bronchitis, pneumonia, and tuberculosis are illnesses caused by lower respiratory tract infections, which are mostly caused by viruses and bacteria. With the advent of new virus-related illnesses like the novel corona virus, COVID-19, the severity of ARIs rises annually. According to reports since the middle of the 1960s, there are seven reported human corona viruses that cause 15% of cases of the common cold (Yang et al., 2020).

The severe acute respiratory syndrome corona virus (SARS-CoV), the Middle East respiratory syndrome corona virus COVID-19 are the corona viruses that cause the greatest number of deaths in the human population. Initially identified in Saudi Arabia in 2012, MERS-CoV caused around 2494 cases and 858 fatalities across 27 nations. China was the first place where SARS-CoV and SARS-CoV-2 were isolated. In 32 different countries, SARS-CoV caused 8422 cases and approximately 919 fatalities in 2002 and 2003. Since its discovery in December 2019, the most current coronavirus-driven ARI, COVID-19, has attacked 54 075 995 individuals and killed 1 313 919 people in nearly every nation on Earth (as of November 16, 2020) (Dashboard et al., 2020). The lower respiratory tract is primarily impacted by COVID-19, and early symptoms in afflicted patients include fever, exhaustion, dry cough, and dyspnea. Additionally, the condition compromises important organs like the heart, liver, kidneys, and gastrointestinal tract, which results in a number of organ issues (Chauhan et al., 2020).

The avian influenza A (H7N9) viruses, which initially surfaced in China in 2013 and have since resurfaced every year as winter–spring epidemic waves, are another important source of ARIs.33 The H7N9 virus infected a significant number of people worldwide during 2016 and 2017, leading to 54 481 000 illnesses and 145 000 fatalities (Chavez et al., 2021). According to certain research, bacterial pneumonia, another significant ARI, was much more common during viral pandemics (Golda et al., 2011). The symptoms of pneumonia, which can be brought on by bacteria or viruses, include chills, fever, chest pain, coughing, sputum production, and dyspnea. Many hospital admissions among people 65 years of age or older are due to pneumonia, which is referred to be the "special enemy of old age (Metlay et al., 1997). Due to the negative toxic effects of small molecule antibiotics (like vancomycin) and their poor efficacy against strains of pneumonia that are resistant to multiple drugs, there is potential for improvement in the present treatments (Kim et al., 2018).

Tb is an ARI associated for the death of more individuals than any other microbiological pathogen, with roughly 1.5 million deaths recorded in 2018 (Okram & Singh, 2024). TB is a poverty-related disease, impacting the most disadvantaged and marginalized groups, therefore its elimination at a worldwide level is still not feasible. Night sweats, high temperatures, weight loss, coughing, and chest pain are the main signs of this illness (Sulis et al., 2014).

Asthma

Over thirty million individuals worldwide suffer from asthma, the most prevalent no communicable disease (Papi et al., 2018b). Coughing, chest tightness, and shortness of breath are among of its symptoms, which call for ongoing treatment—sometimes for an indeterminate amount of time (Strzempek et al., 2019). When upper respiratory system infections, pollen exposure, and air pollution are paired with symptoms that fluctuate in intensity over time, respiratory failure may result (Lambrecht et al., 2019).

Reversible airway blockage, bronchial hyper responsiveness, and persistent airway inflammation are the hallmarks of asthma, an inflammatory lung disease. An inflammatory reaction brought on by prolonged exposure to irritants damages lung tissue and narrows the tiny airways. Nanoparticles' anti-inflammatory properties have already been demonstrated in a number of inflammatory conditions (Yang et al., 2019). By making it easier for the medication to reach the target area and enhancing its deposition in the lungs, nanoparticles enhance the therapeutic impact (Yang et al., 2019).

Lung Infections (caused by Parasites, Fungus, Bacteria and Viruses)

A number of major lung infections can be fatal, including viral lung infections, pneumonia, and tuberculosis.Lung infections affect the majority of air sacs and, to a lesser extent, the airways that carry air to the lungs. Although a range of therapies and diagnostics have been employed to treat lung infections, therapy has become more challenging due to the rise of bacteria that are resistant to drugs and the negative consequences they cause once they enter the lung environment (Muhammad et al., 2022). More than ever, there is a need for innovative approaches to regulate bacterial activity. The application of nano material science can be a potential method in this area, and the growing body of knowledge in the synthesis of nanomaterials should be viewed as a worldwide approach.

Lung Cancer

Lung cancer is the most prevalent kind of cancer worldwide, and nanomaterials are crucial to cancer treatment. Uncontrolled cell development in lung tissues is the hallmark of lung cancer, which continues to be a significant and unsettling cause of death and widespread illness (Figure 1) Regenerative medicine and nano therapy have advanced in treating lung diseases and lung biology (Sanaei et al., 2022).

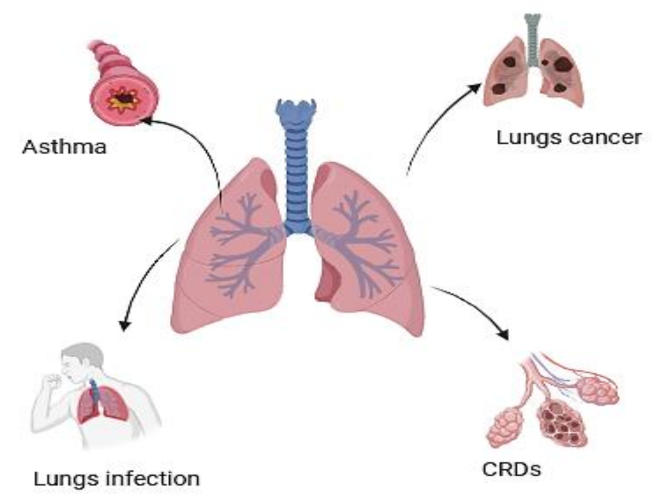

Fig. 1: Respiratory disorder illustration (Retrieved from BioRender)

Limitations for Treating Respiratory Diseases

The standard of life is significantly reduced by the negative impacts of the lack of creative tactics for fighting CRDs and ARIs, particularly for senior patients. The use of nanotechnology may help to partially solve the primary challenges commonly encountered in the treatment of respiratory diseases (such as multidrug-resistant strains, a lack of creative ideas, early detection challenges, failure therapy trials, side effects, and high cost) (Rodrigues et al., 2019). By using nanostructures, nanotechnology breaks down the boundaries between materials science, biology, and physics. Materials with particle sizes ranging from 1 to 100 nm are referred to as nanomaterials. Because of their huge surface area, these materials have special qualities. Accordingly, nanomaterials have been extensively researched in nanomedicine science for their potential use as drug delivery systems, biosensors, micro fluidics, and fillers for tissue engineering (Patra et al., 2018). Because of their direct targeting impact, ability to increase treatment efficacy, and ability to decrease side effects, NPs (nanoparticles) are more effective than some conventional approaches. This can lead to a sensitive decrease in toxicity and negative effects (Lombardo et al., 2019).

Furthermore, drug delivery with NPs is typically non-invasive, offers simple and inexpensive production techniques, strong being biodegradable and long-term stability (Zhou et al., 2018). Drug loading into nanoparticles can occur through covalent bonding, adsorption, or encapsulation among the drug and the surfaces of the nanoparticles. The outermost layers of the particles are altered to guarantee precise targeting of the various body parts. Typically, oligosaccharides, polymers, proteins, peptides, and other compounds are employed for this purpose (Popielarski et al., 2005). Following inhalation, Brownian diffusion deposits the nanoparticles into various areas of the respiratory system. The region of the respiratory tract where the deposition will take place is determined by the dimension of the nanocarriers. The nose, pharynx, and larynx are the best upper airways for smaller nanoparticles (B1 nm). While particles with a dimension of about B20 nm will mostly deposit into the deeper alveolar areas of the lungs, those with a size of about B5 nm exhibit excellent deposit into the trachea and bronchial regions. The way the nanocarriers and cells interact in aerosolized drug delivery nanoparticles are a better non-invasive way to access the respiratory tract while treating respiratory disorders (Oberd et al., 2005).

Where the nanocarriers are deposited in the body determines how they communicate with cells in the respiratory tract. Receptor-mediated endocytosis is often responsible for the nanoparticles' intracellular uptake. According to this method, certain biomolecules (including protein molecules, glycoprotein's, which and glycolysis) precipitate on the surfaces of nanoparticles to produce a complex that macrophage receptors can recognize. Through pseudo pod extensions, these biomolecules attach to the receptors of macrophages, facilitating the uptake of nanoparticles. Depending on the parts involved in the particle production and the interaction of the membrane, the endosomal material may take distinct routes at this step. The endosome may occasionally change into acid vesicles and merge with lysosomes. These structures can use enzymatic and hydrolytic processes to break down the drug delivery capsule (Rothen-Rutishauser & Blank, 2009).

Nowadays, a wide range of NPs are being investigated as drug delivery methods for the treatment of respiratory illnesses. Nanocarriers are often classified as either organic or inorganic. Their compositions, sizes, forms, surface characteristics, and manufacturing processes can all affect their physicochemical and biologic qualities.

Treatment of Respiratory Disorders with Nanoparticles

Different respiratory conditions have been treated using a variety of nanoparticle medication kinds.

Carbon-based Nanoparticles

Carbon-based materials, such as a) new industrial carbon like carbon fibers, b) conventional industrial carbon like activated carbon, and c) novel carbon nanomaterials like graphene and carbon nanotubes, are crucial to the development of material science. While macro carbon material lacks an appropriate band gap, making it difficult to function as an effective fluorescent material, primary research and applications of carbon-based substances are widespread in transdisciplinary disciplines (Liu et al., 2020). Carbon nanotubes and carbon nanodiamond are robust, lightweight, extremely conductive, and multipurpose. These nanoparticles' drug delivery mechanisms may be functionalized to provide reliable diagnostic instruments (Chauhan et al., 2020). Although carbon nanotubes are inhaled, they pose health hazards, including inflammation and lung fibrosis (Maiti et al., 2019), thus they are not appropriate for treating respiratory conditions. In recent years, a variety of newly developed carbon-based nanomaterials have been modified and used extensively in pharmacology, medicine, and biology due to their significant features (Poulsen et al., 2018).

Dendrimers

Due to the tree-like branching structures, the word dendrimer was the taken from the Greek word Dendron, which meaning tree. Based on their physicochemical properties and dendronsarms that are originate from the central core of make up a dendrimer (Ambekar et al., 2020). Dendrimers are the widely utilized in the gene editing and pharmacology and drug delivery and antibiotics (Liu et al., 2023). These days a variety of the dendrimers including PAMAM, polyethylene glycol and polylysine, are the frequently employed as the nanocarriers to cure disorder (Yousefi et al., 2020). To circumvent dendrimers 'cationic toxicity, dendrimers-based nanocarriers must be functionalized with the biomolecules which is simple to do because dendrimers have large amino groups (Ambekar et al., 2020).

Polymeric Nanoparticles

Solid colloidal particles that re known as the polymeric nanoparticles and they are ideally composed of the polymers that can be the obtained naturally or artificially (Yazdi et al., 2020). Polymeric micelles and the polymersomes are examples of the last three kinds of the polymeric nanoparticles: hydrogels and nanospheres and nanocapsules. In the order to the chemically or physically absorb a lot of the water or dissolved medications hydrogels polymeric materials with a large number of the linked hydrophilic groups have a three-dimensional network. Medicines and other substance that are inserted into a matrix of the polymers in nanosphere polymeric nanoparticles (NPs) whereas the therapeutic ingredients is contained inside a polymers capsule shell in nano capsule polymerics NPs. Polymeric nano particles are useful for the treating a variety of disorder because they deliver the medication to the precise locations and in a precise quantity (Sur et al., 2019).

Liposome

Liposomes (LPs) are the packets made of the concentric lipid bilayers also known as the lamellae that develop on their own when they specific lipids are hydrated in the water. Lipid bilayers are the used to create LPs which are resemble self-assembling colloidal polymeric nanoparticle. Lipids can be form spherical and oval shaped structures because of their hydrophilic and hydrophobic sides (Saraf et al., 2020). Solid lipid nanoparticles and micelles and phytosomes and nanoemulsions are the nanoparticles that resemble themselves as liposomes. More precisely liposomes are the ideal for encasing the hydrophilic medications due to their watery core. The phagosomal form of the hydrophobic medicines may also be the positioned between the bilayer of lipids of cell membrane (Kumar et al., 2020).

Lipid Nanocarriers

Liposomes may be most porous and safe nanocarriers that are in the body since lipids make up narrowly permeable cell membranes. Liposomes are basis for the majority of FDA-approved nanoparticles albeit they have significantly drawbacks. Continuous exposure to the aqueous solutions and the bodily fluids can be cause liposomes to oxidative degrade and the leak drugs (Thompson et al., 2017). Since solid lipid nanoparticles and the nanoemulsions cover a wider spectrum of the medications and are the less expensive drug delivery methods they might be better options than liposome (Roy et al., 2022). Due to their poor water solubility lipid-based nanocarriers may be able to the overcome the challenges of limited availability for the oral treatment. Because of the lipid nanoparticles (NPs) are the nanosized and lipid soluble, they are more pharmacokinetic and the biocompatible and less toxic and can be scaled up for the industrial manufacturing (Dumont et al., 2018).

Quantum Dots

A breakthrough in nanoscience quantum dots (QDs) is the semiconductor of inorganic crystals with varying quantities of electrons that inhabit specific and well-defined quantum states (Reshma et al., 2019). Both the organic and inorganic classifications apply to common QDs composed of carbon, graphene, phosphides, cd or zinc chalcogenides, and indium arsenide (Ruiyi et al., 2020).

Others

Researchers are favoring nanoscale materials with promising research and application opportunities for respiratory medication administration, and more and more nanoscale drug-carrying devices are being created for respiratory drug delivery. Bilosomes, also known as bile bodies, are vesicular structures derived from bile salts that are more stable and effective at encapsulating drugs than conventional liposomes (Zakaria et al., 2013).

To increase its bioavailability and solubility, resveratrol was loaded into PEGylated bilosomes. The results demonstrated that the nanoparticles suppressed the Mpro enzyme of the severe acute respiratory syndrome corona virus type 2, which may be used as a medication carrier to treat respiratory illnesses. Another new approach to the delivery of inhaled biologics is the use of nanosomes. Natural pure heavy-chain antibodies are extracted to create nanosomes, which are tiny therapeutic proteins (~15 kDa). Their brief half-life across the bloodstream made them a good fit for pulmonary administration. A nanosome called ALX-0171 is made for targeting respiratory syncytial virus (RSV)-specific proteins at sub-nanomolar concentrations. The results showed that when administered by dispersion in a rat model, both nostril and lungs RSV titers were significantly reduced (Detalle et al., 2016).

Conclusion

Acute and chronic respiratory conditions contribute significantly to the global health burden by lowering the quality of life and increasing mortality rates. Conventional therapy approaches are useful for controlling symptoms, but they have side effects, such as low bioavailability, expensive costs, and drug resistance. The high surface area volum to ratio, functionalization potential, and nanoscale size of NPs provide improved drug delivery capabilities. Nanoparticle-based medication delivery systems offer innovative approaches that have the potential to completely transform respiratory healthcare by removing hurdles associated with drug resistance and ineffective treatments. Nanomedicine has demonstrated exceptional promise in treating tuberculosis, Asthma, lung cancer, COPD, and viral infections. For example, inhalable nanoparticles make direct medication deposition into the lungs possible, which improves therapy results at lower dosages. But issues like long-term toxicity, obtaining regulatory permits, and mass production must be resolved. Future studies should focus on improving targeted treatments, guaranteeing biocompatibility, and perfecting nanocarrier compositions.

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