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CHAPTER

15 NANOTECHNOLOGICAL APPLICATIONS FOR THE CONTROL OF PULMONARY INFECTIONS

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1 INTRODUCTION

Microbes, including viruses, bacteria and fungi, are the causal agents of pulmonary infections.[1–4] Infections of nose, sinuses, and throat are included in upper tract infections. Whereas infections of trachea, lungs and bronchial tubes are considered as lower tract infections.[5] Generally, upper tract infections are mild in nature; however, severe illness and high mortality rate are reported in lower tract infections.[6] It is estimated that about 4.2 million deaths occurs globally due to lower tract infections among all the age groups and about 1.8 million deaths have been reported in children. Children are more prone to lower tract viral infections.[3,7]

Usually the most common mode of transmission of the pulmonary infections is by contact of one person to another. Such infections are transmitted by direct or indirect contact. Individuals affected by cough and sneezing, transfer droplets consisting of microorganisms in a fraction of seconds through air or directly deposited into the mouth or nasal mucosa of another susceptible individual, for example, mouth droplet from people suffering from cough can be spread into another individual.[5] Indirect transmission involves the contact of susceptible individual with the contaminated instruments or the surface where organisms occur. Microorganisms can reside on the hand of the infected person and can be transferred, for example, by the shaking of hands. The needles and gloves of an infected person can also transmit infection to another person[5].

There are various types of pulmonary infections, such as: pneumonia, tuberculosis, pulmonary aspergillosis and nontuberculous mycobacterial infections. Pulmonary infections are commonly reported from developing and developed countries.[4,8–10] Although there are many microbiological testing methods available for the diagnosis of such infections and there are various antimicrobial treatment therapies for the management of pulmonary infections, sometimes the curing rate of these infections is reported to be low due to certain limitations. Microbiological testing methods are believed to be slow and insensitive, whereas, the uncontrolled and over use of antibiotics create the major problem of antibiotic resistance.[11,12] Recently, the ability of common pathogens to acquire resistance to widely used antimicrobial therapies has been increased.[13] The authors further suggested that the number of pathogens that exhibit resistance to one or multiple drugs (MDR) have been increasing gradually.

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Currently, the problem of antimicrobial resistance in both Gram-negative and Gram-positive bacteria and other pathogens causing pulmonary infections has become a major threat. Karchmer[14] reported that antimicrobial resistance is particularly prevalent among the most common pathogens associated with community-acquired respiratory tract infections, which includes *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis,* and *Streptococcus pyogenes.*[15] Hence, the morbidity and mortality associated with the pulmonary infection pose a growing challenge to clinical practitioners.[16] Considering the huge scope and applications of nanotechnology in biomedicine, it has been proven that nanotechnology will play a crucial role for the management of problems associated with antibiotic resistance including multiple drug resistance. Therefore, these life-threatening challenges including pulmonary infections can now be overcome with the help of nanotechnology.[12,17]

The aim of the present chapter is to discuss the global status of various pulmonary infections and the strategies for their management. Here, we have described treatment therapies available for pulmonary infections and their limitations. Given that multidrug resistance is a major challenge, novel and effective alternative treatment therapies need to be discovered. In addition, we have also discussed the role of nanotechnology for the management of pulmonary infections with a special focus on different types of nanomaterials.

2 SOME IMPORTANT PULMONARY INFECTIONS

2.1 PNEUMONIA

Pneumonia is an inflammatory disease, which affects lung air sacs (known as alveoli). This disease is mostly caused by viruses, bacteria, or fungi. Worldwide more than 450 million people suffer from pneumonia and four million people die from pneumonia annually. Common symptoms of pneumonia includes- persistent cold, fever with shaking hands, chest pain, and difficulty in breathing. Other severe sign and symbols of pneumonia are vomiting, unconsciousness, convulsions.[1] Bacteria are supposed to be the most common source of pneumonia. *Streptococcus pneumoniae* is responsible for more than 50% of the infections, *Haemophilus influenza* causes 20% of the infections. *Mycoplasma pneumoniae* also causes infection in 3% of the population and some other bacterium like *Stenotrophomonas maltophilia* also reported to cause pneumonia.[18] Certain viruses like coronaviruses, influenza virus, adenovirus, and respiratory syncytial virus causes pneumonia.[19] Fungal pneumonia is very rare. It is mostly observed in immunocompromised patients. Common fungi which cause pneumonia are *Cryptococcus neoformans, Pneumocystis jirovecii,* and *Coccidioides immitis.*[2,20]

2.2 TUBERCULOSIS

Tuberculosis (TB) is caused by the *Mycobacterium tuberculosis*. These bacteria usually infect the lungs but may also affect other parts, such as liver and kidney. When TB is observed outside of the lungs it is known as extra-pulmonary TB. Immunocompromised patients are more susceptible to this infection. The mode of transmission of disease is air. When a TB patient speaks, coughs, or sneezes, TB bacteria may be spread and infect nearby individuals. Even if a person is infected with *M. tuberculosis*, it may be in inactive form and is only activated in patients with lower immunity or who is in a later stage of life.[21] Common signs of TB are persistent cough with sputum for more than 3 weeks, chest pain, loss of appetite, chill, fever, sweating at night, fatigueness and weight loss. Most patients do not show the

symptoms of TB but develop the disease at the later stage.[4,22] Not every individual become sick after this infection, they can have TB bacteria in the body but the body is able to fight against the bacteria. People with such an infection do not spread TB infection to others. This form of infection is known as Latent TB. TB bacteria are active when the immunity is lower, and in this case TB bacteria can be spread.[23]

2.3 PULMONARY ASPERGILLOSIS

Pulmonary aspergillosis is a fungal infection, which is mainly caused by *Aspergillus* species. This disease is characterized by the colonization of *Aspergillus* spores in the lungs. Aspergillosis is more commonly observed in people who are affected with TB or people with COPD. Mostly, aspergillosis is caused by *A. flavus, A. niger* and *A. terreus. A. fumigatus* is commonly found in patients suffering from invasive aspergillosis. There are three types of pulmonary infections: allergic bronchopulmonary aspergillosis (ABPA), chronic pulmonary aspergillosis (CPA), invasive pulmonary aspergillosis (IPA).[24,25] The common symptoms of aspergillosis are fever, cough, breathlessness and chest pain. ABPA infection is mainly characterized with asthmatic patients and with eosinophilia deficient patient. Generally, invasive aspergillosis is reported in immunocompromised patients with neutropenia and after organ transplantation.[26,27]

2.4 NONTUBERCULOUS MYCOBACTERIAL PULMONARY INFECTION

Nontuberculous mycobacterial (NTM) pulmonary infections are generally caused by mycobacteria other than *M. tuberculosis*. Most common causative agents of this disease are *M. kansasii, M. abscessus, M. fortuitum M. avium* and *M. intracellulare*. In the United States, the most predominant mycobacteria that are associated with pulmonary infections include *M. avium* complex, followed *by M. kansasii.*[28] More than 140 NTM species are reported. NTM pulmonary infections are noncontagious. They do not spread from individual to individual. However, these infections are transmitted by inhalation of mycobacteria. Symptoms of NTM pulmonary infections are chronic cough, sputum production, high fever and weight loss.[29] NTM pulmonary infections have been reported in immunocompromised patients, patients with lung transplantation, and those affected with cystic fibrosis (CF).[30]

3 EXISTING TREATMENTS FOR PULMONARY INFECTIONS

Different treatments are available for the management of pulmonary infections, but in case of some infections the duration of treatment may be very long, for example,TB. Macrolides drugs are commonly used in the management of various kinds of pulmonary infections and have received considerable attention because of their antiinflammatory and immunomodulatory actions, apart from the antibacterial efficacy. Min and Jang[31] studied the in vitro and in vivo efficacy of macrolides drugs (viz. azithromycin, clarithromycin, dirithromycin, erythromycin, roxithromycin, and telithromycin) against respiratory viral infections caused by rhinovirus, respiratory syncytial virus and influenza virus. The results showed significant antiviral activity against all the tested pulmonary viruses. Henry et al.[32] proposed the bacteriophage therapy for the treatment of pulmonary infections caused by antibiotic-resistant bacteria. They found that pulmonary infections caused by antibiotic-resistant *Pseudomonas aeruginosa* can be safely

managed by using various bacteriophages from the *Myoviridae* and Podoviridae family. In another similar study, Semler et al.[33] demonstrated the use of phage therapy for respiratory infections caused by antibiotic-resistant *Burkholderia cepacia*. The effectiveness of the therapy was studied by establishing the *B. cenocepacia* respiratory infections in mice using a nebulizer and a nose-only inhalation device, the mice were treated with different *B. cenocepacia*-specific phages delivered as either an aerosol or intraperitoneal injection. The results obtained after 2 days of treatment suggested that aerosol phage therapy appears to be an effective method. Whereas, the mice that received phage treatment by intraperitoneal injection did not show significant activity.

As mentioned previously, pneumonia is a pulmonary infection which affects the lungs. It is caused by various bacteria (eg, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Haemophilus influenzae* and *Mycoplasma pneumoniae*), viruses (eg, adenoviruses, rhinovirus, influenza virus, respiratory syncytial virus and parainfluenza virus) and fungi (eg, *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*, *Paracoccidioides brasiliensis*, *Sporothrix schenckii* and *Cryptococcus neoformans*). It is characterized primarily by inflammation of the alveoli in the lungs or by fluid filled alveoli (alveoli are microscopic sacs in the lungs that absorb oxygen). Generally, treatment of pneumonia depends on the type and severity of infections. Bacterial pneumonia is usually treated with different antibiotics (viz. azithromycin, erythromycin, doxycycline, gemifloxacin, levofloxacin, cephalexin, amoxicillin, vancomycin, etc.).[34] Efficient antifungals used for the management of fungal pneumonia include first, second and third-generation triazoles and echinocandins. In some cases Amphotericin B is less frequently used. However, viral pneumonia is treated with rest and plenty of fluids.[35]

TB is also one of the most life-threatening pulmonary infections and it is a major public health problem all over the world. According to a survey, India contributes about 26% of the global TB burden. Since ancient times, TB has been a leading cause of morbidity and mortality.[36] Over the last decade, scientists have made significant progress in treatment for TB. Regimens have been optimized and directly observed therapy short-course (DOTS) initiatives have been implemented.[37] Currently, chemotherapy used for TB commonly includes combination of first-line drugs, isoniazid, rifampin, pyrazinamide and ethambutol for about 6 months. If treatment fails because of drug resistance, then second-line drugs, such as, paraaminosalicylate, kanamycin, fluoroquinolones, capreomycin, ethionamide and cycloserine are recommended, although these drugs may have serious side effects.[38–41]

Aspergillosis in one of the most important diseases among the pulmonary infections caused by *Aspergillus* species. It is reported to be an emerging cause of life-threatening infections in immunocompromised patients having infections, such as, prolonged neutropenia, advanced HIV infection, inherited immunodeficiency and in patients who have undergone allogeneic hematopoietic stem cell transplantation (HSCT) and/or lung transplantation. Three different forms of aspergillosis have been reported so far. These include invasive aspergillosis, chronic (and saprophytic) aspergillosis and allergic forms of aspergillosis. Generally, voriconazole is superior to deoxycholate amphotericin B (D-AMB) and, hence, recommended in primary treatment for invasive aspergillosis in most patients. Apart from these, some of the FDA-approved compounds, such as, lipid formulations of amphotericin B (AMB lipid complex [ABLC], L-AMB, and AMB colloidal dispersion [ABCD]), caspofungin and antifungal triazoles (ie, itraconazole, voriconazole and posaconazole) are also recommended. Similarly, in chronic aspergillosis, the regular doses of itraconazole and voriconazole are usually prescribed by the physician. Whereas, the treatment for allergic forms of aspergillosis includes combination of corticosteroids and itraconazole.[42]

Among the pulmonary infections, nontuberculous pulmonary infections caused by NTM are very common infections, which are increasingly recognized worldwide. About 150 different species of

NTM have been described. *M. avium* complex, *M. kansasii*, and *M. abscessus* are found to be most common NTM, which cause such infections. According to Davis et al.[43] existing therapy available for the treatment of nontuberculous mycobacterial pulmonary infection by *M. avium* showed very poor clinical response rates, drug toxicities, and side effects. They demonstrated that use of aerosolized amikacin as a standard oral therapy against nontuberculous mycobacterial pulmonary infection significantly improved treatment efficacy without producing systemic toxicity. Therefore, it was proposed that aerosolized delivery of amikacin is a promising adjunct to standard therapy for pulmonary nontuberculous mycobacterial infections. Moreover, extensive experimental trials are required to define its optimal role in the therapy of this disease.

In another study, Johnson and Odell[28] reviewed that the eradication of NTM infections is very difficult by the common treatment strategies. Moreover, it requires a prolonged course of therapy with a combination of drugs. However, there are numerous challenges regarding the treatment of NTM pulmonary infections, but few drugs which can manage these infections are available. Some macrolide drugs like azithromycin and clarithromycin are the efficient and important drugs in the therapy for MAC lung infections. In the case of a resistant strain, a combination therapy with rifampin or rifabutin, and ethambutol (triple therapy) with or without an intravenous aminoglycoside is recommended for about 18 months or more. Similarly, in the case of infection by *M. kansasii*, combination of isoniazid, rifampin and ethanbutol is mostly recommended for about 12 months. In addition, macrolides, such as, clarithromycin and the fourth generation fluoroquinolone moxifloxacin demonstrated very good in vitro activity against *M. kansasii* and may be an alternative to isoniazid. Whereas, lung infections due to *M. abscessus* are very difficult to treat successfully with drug therapy alone. Chemotherapy in conjunction with surgical resection is often recommended in those who can tolerate it. Overall, different kinds of medications and therapies are available for the management of pulmonary infections, but in case of some pulmonary infections existing treatments and therapies showed certain limitations, which are briefly discussed here.

4 LIMITATIONS AND SIDE EFFECTS OF THE TREATMENT OF PULMONARY INFECTIONS

There are a number of limitations for use of conventional strategies for diagnosis and treatments of patients with pulmonary infections. Consequently, unnecessary and prolonged exposure to antimicrobial agents adversely affect patient outcomes, while inappropriate and uncontrolled use of antibiotic therapy increases chance of antibiotic resistance. According to Murdoch,[12] the role of microbiological testing methods used for the diagnosis and management of lower respiratory tract infection continues to be debated. There are many limitations of microbiology laboratories to perform the conventional diagnostic tests for pulmonary infections. The culture based methods that are currently used are slow, insensitive, may not distinguish colonization from infection and may be influenced by previous antimicrobial used. On the other hand, serological tests are also slow and poorly sensitive. Therefore, many authoritative guidelines on the management of pulmonary infection, such as, community-acquired pneumonia in adults do not support routine comprehensive microbiological testing, except in certain situations or in patients with severe disease.[44,45]

Moreover, the uncontrolled and improper use of antibiotics as a treatment for pulmonary infections leads to the development of resistance towards those antibiotics. The problem of antibiotic resistance

was predominantly found in TB patients. Unfortunately, some causative agents of TB and many other pulmonary infections become resistant to multiple types of antibiotics. The loss of efficacy of antibiotics and the decrease in their ability to fight pulmonary infections in vulnerable patients is a matter of great concern.[21]

Nanotechnology is a multidisciplinary field that has recently emerged, and it looks as if it will be extremely helpful in the management of pulmonary infections. Nanotechnology based treatment methods and drug delivery strategies will help to deliver drug molecules at the specific site of infection.[46] The role of various nanomaterials in diagnosis and treatments of pulmonary infections is described here.

5 NANOTECHNOLOGY IN MEDICINE

Nanotechnology is an emerging field of science that deals with the study, synthesis and manipulation of materials at nanometer range (ie, in 1–100 nm) or the order of billionths (10^{-9}) of a meter.[47–51] Particles in the nanometer range have changed properties, such as, physicochemical properties, which are distinct from their bulk materials (the macroscopic or microscopic scale) and single atom or molecule (at the atomic scale).[48,52] Nanomaterials are referred to as engineered nanometer dimensions material, which have novel properties, such as, quantum effects and large surface area to volume ratio.[52] These materials are fabricated by a top-down approach, in which bulk materials or technologies are miniaturized, or a bottom-up approach, where assembly occurs atom by atom, from primary to larger, and towards more complex materials.[53] The synthesis of materials in the nanoscale results in magnetic, mechanical, chemical, and electronic effects that are not shown by the bulk materials. These nanoscale effects have been exploited practically in every field of technology, and include commercial applications in energy conversion, textiles, cosmetics, electronics, water purification, lubricants, computing and much more.[54,55] "Nanobiotechnology" is the study of the interaction between biological systems and nanomaterials,[56] and the related field of nanomedicine seeks to employ nanosized materials to diagnose, treat and prevent human diseases.[57–59] The changed physicochemical properties critically influenced the nature of interaction when these nanosized particles come into contact with the biological systems. Moreover, many biological processes, such as, immune recognition and passage across biological barriers are also governed by size considerations.[60] In this context, various applications of nanotechnology, such as, delivery of drug and nucleic acid-based therapeutics to particular disease site makes it a most promising technology of the era. According to Buxton[61] delivery of therapeutics by inhalation provides an opportunity for direct transport of drug to the lung epithelium of the respiratory tract.

5.1 APPLICATIONS OF DIFFERENT NANOPARTICLES FOR THE TREATMENT OF PULMONARY INFECTIONS

The multidisciplinary approach of nanotechnology plays a crucial role to find efficient solution over problems in various sectors. The application and innovation of nanotechnology in the field of medicine is known as "nanomedicine." This broad technology is capable to treat range of diseases. The use of nanoparticles in the field of medicine opens new possibilities and provides new methods for treatment of diseases. Various types of nanoparticles are used in medicine to treat diseases, such as, infectious diseases, viral, bacterial, respiratory tract diseases, and so on. The nanoparticles used for treatment

of diseases include: metal nanoparticles, liposomes, polymeric nanoparticles, dendrimers, nanocomplexes, nanorods, quantum dots, nanoemulsions, and so on.[62]

Currently, most recent studies in the field of nanomedicine changed the point of view of drug delivery therapy. Scientists are using nanoparticles as a carrier for drug delivery therapy.[63] In fact, much research has not been carried out concerning the use of nanoparticles in pulmonary diseases. However, in recent years scientists may develop promising nanocarriers for treatment of diseases that affect respiratory tract. Recent studies showed that nanoparticles in pulmonary infection treatment can influence immune system, can create oxidative stress, and can cause genotoxicity.[64]

Studies on nanoparticles for treatment of pulmonary infectious diseases is an emerging field of interest, not only for the treatment of respiratory tract conditions but also for systemic administration of drug delivery for treatment of pulmonary disease. A variety of metal and metal oxide nanoparticles, such as, silver, gold, copper, titanium oxides, and so on have been successfully exploited for pulmonary drug delivery.[65]

Globally, more than 1.5 million deaths are reported annually from respiratory infections, including at least 42% of lower respiratory infections and 24% of upper respiratory infections in developing countries like China, India, Iran, Oman, Philippines, Qatar, Republic of Korea, Saudi Arabia, Thailand, and the United Arab Emirates. The frequent use of antibiotics lead to antibiotic resistance, which enables antibiotic-resistant bacteria to survive despite treatment with existing antibacterial drugs.[66,67] The growing number of multidrug resistant strains has made it imperative the development of new antibiotics and novel approaches to deliver existing agents.

The study carried out by Zhang et al.[68] revealed that polyphosphoester- based silver nanoparticles enhance in vitro antibacterial activities against pathogens associated with CF and decreases the cytotoxicity of bronchial epithelial cells in human. They developed novel degradable polyphosphoester- based polymeric nanoparticles that are able to carry silver cations toward the treatment of lung infections associated with CF through formation of silver acetylides. Another study on liposomal antibacterial targeted pulmonary infection therapy revealed that after several cycles of treatment with liposome and antibacterial drug amikacin in patients showed continuous improvement in pulmonary function and significant reduction in bacterial density.[69] These type of studies suggest that efficacy of antibacterial drugs increases when administered in combination with nanoparticles.[60]

Bhardwaj and coworkers[70] used a mixture of chemotherapeutic agent-loaded vesicular system to overcome TB by developing ligand appended liposome with dry powder inhaler. According to Barash et al.[71] the categorization and detection of specific pattern of lung cancer can be possible using gold nanoparticles sensor with a device profiles unstable organic compounds. Broza et al.[72] reported the use of nanomaterials-based sensors for the identification of breath-print of early-stage lung cancer.

5.2 NANOTECHNOLOGY FOR PULMONARY DRUG DELIVERY

Pulmonary drug delivery has many advantages compared to unusual drug delivery strategies, especially rapid drug uptake, a large surface area for solute transport, and improved drug bioavailability, as well as its noninvasive nature.[73–76] Antimicrobial agents enter into the lung by means of systemic nanoparticles administration, which is determined and potentially harmful upon systemic exposure to the drugs. On the other hand, various nanoparticles exhibit privileged accumulation in the lung—other organs have also been tried. It was reported that intratracheally administered antibiotics loaded nanoparticles were able to enter through the alveolar-capillary barrier into the systemic circulation and collect in

extra-pulmonary organ containing spleen, liver, kidney, and bone.[77] Today, the drug dosage form and therapeutic efficiency is improved by "micronization" of drugs. The drug if micronized into microspheres with appropriate particle size can be administered directly to the lungs through the mechanical prevention of capillary bed in the lungs.[78,79]

Nanosuspensions may be an ideal approach to deliver drugs that show deprived solubility in pulmonary secretions.[80] In addition, due to the nanoparticulate nature and homogeneous size distribution of nanosuspensions, it is possible that in each aerosol droplet at least one drug nanoparticle is present leading to an even distribution of drug in lungs compared to the microparticulate form of the drug. In routine suspension aerosols, numerous droplets are free of drug and others are filled with the drug in high amounts, directing to irregular release and circulation of the drug within the lungs. Nanosuspensions could be utilized in all available types of nebulizer.[81]

Aggarwal et al.[80] studied antitubercular drugs, for example, pyrazinamide, isoniazid, and rifampicin were integrated into various formulations of solid lipid ranged from 1.1 to 2.1 μm and these formulations were nebulized to guinea pigs orally for direct pulmonary delivery. Likewise, conditions, such as, pulmonary aspergillosis can easily be targeted by applying appropriate drug candidates like amphotericin B, in the form of pulmonary nanosuspensions as a substitute of using stealth liposomes.[82] Numerous respiratory diseases have been treated by using the nanocarrier systems, which can be easily transferred through the airways.[83,84] A large number of pulmonary diseases that have been searched includes- CF and some other genetic disorders, COPD, tuberculosis, pediatric diseases, and cancer.[76,85–88]

The pharmacodynamics and pharmacokinetics of a drug are exceedingly reliant on its physical and chemical features, which are influenced by the type of formulation used to deliver it. Through scaling down size of compounds, Nano-Drug Delivery System (NDDS) can transform and improve the performance of many drugs to an extent not reachable by conservative formulations.[89] For example, NDDS can be capitalized to encapsulate drugs and thereby (1) protect them from degradation, (2) target the drugs to particular cells/tissues/organs, releasing them in a restricted behavior as a response to a precise stimulus, (3) increase their solubility, (4) enhance their epithelial absorption and increase their blood circulation time, and (5) enhance their uptake by cells.[90–92] Moreover, combined NDDS can concurrently detect and treat a disease by encompassing both imaging and therapeutic compounds, which are termed as theranostics.[93] Nanomedicine could play a key role in the near future to achieve the highly desired modified medicine.[94] Over the last few decades, the usefulness of the design and development of NDDS to overcome a variety of biopharmaceutical drawbacks in the diagnosis, prevention, vaccination, and disease treatment has been intensively explored by a large number of research groups globally, leading to an enormous number of scientific articles available in international journals. Moreover, it has generated a generous rational property platform. Nevertheless, and despite the fact that nanomedicine began as a discipline almost half a century ago, only a few NDDS have found their way to the market.[94,95] This experience could be explained by the lack of economic profitability, consumer mistrust and the lack of assurance because of poor information or education, unproductive regulation of novel and generic products, and feeble patent protection.[96]

The respiratory system and the skin are together directly in contact with the environment, which represents a possible entrance door for the therapeutic compounds into the body. Due to the increasing frequency of pulmonary diseases with high mortality and morbidity, the pulmonary drug delivery is emerging as a noninvasive and smart approach for the treatment of a variety of pathogenic disorders.[97]

Therefore, intravenous and oral routes for disease management are acquiring an ever growing interest for systemic administration of therapeutic agents due to their various advantages.[74]

Currently, researchers have made enormous strides in the progress of pulmonary delivery technologies, both in terms of inhaler design and progresses in nanoscale carrier engineering. At present there are three main different classes of devices for pulmonary drug delivery: metered dose inhalers, nebulizers, and dry powder inhalers. These inhalers are based on diverse delivery mechanisms, and entail different types of drug formulations. Furthermore, the development of novel biologically active compounds like proteins and nucleic acids require the design of innovative delivery technologies.[98]

Bioavailability of administered drug is a major problem in pulmonary infections. Therefore, researchers have developed considerable interest in pulmonary drug delivery and also focused on enhancement of bioavailability of therapeutic biomolecules having high molecular weight.[99–100] Among the various carriers used as drug delivery systems for pulmonary infections, nanocarriers have been found to be most promising due to their significant advantages like prolonged drug release and cell-specific targeted drug delivery.[84,98]

6 CONCLUSIONS

Pulmonary infections caused by bacteria, fungi, and viruses are increasing and reemerging due to improper use of antibiotics and changing environmental conditions. The conventional methods of diagnosis and treatment of pulmonary infections have limitations. The cultural and serological methods used for identification are slow, tedious, may not distinguish colonization from infection, and may be influenced by previous antimicrobials used for the treatment. In this context, PCR methods have been useful up to a certain extent for rapid identification of the causal organism. Nano-PCR and nanobiosensors may play important role in diagnosis of pulmonary infections. The long-term treatment of pulmonary infections by antibiotics and their inappropriate use has resulted in the multidrug resistance problem. This problem is mainly evidenced by tuberculosis, which has become a global problem; therefore, there is a need to develop alternative strategies for the treatment of tuberculosis. The use of nanotechnology in diagnosis of pulmonary infections and also for delivery of drugs would be of paramount importance. Nanoparticles, particularly biodegradable nanoparticles, can be used for this purpose. The activity of the nanoparticles can also be enhanced by their use in combination with existing antibiotics. Finally, nanotechnology will provide a viable alternative for the development of a long-term strategy to tackle the problems of diagnosis and drug delivery in pulmonary infections.

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