

TB, an infectious disease commenced by the infection of bacterium *Mycobacterium tuberculosis*, which affects the lungs and other pulmonary organs. This disease is known to spread from sick person through the expulsion of bacteria in the air because of cough or sneeze [28]. The person infected by *M. tuberculosis* shows symptoms such as cough with sputum and blood (in few cases), chest pains, fatigue, fever, weight loss, sneezing, and night sweats. The people who do cigarette smoking and have compromised immune systems, diabetes mellitus, HIV are at higher risk to develop TB [29]. In 2018, TB has been accorded for 10 million people globally of all age groups. The development of multidrug resistant (MDR) from rifampicin has also become the global concern, as the cases of MDR-TB is increasing exponentially [30]. The high burden of TB is accounted by countries such as Bangladesh, China, India, Indonesia, Nigeria, Pakistan, Philippines, and South Africa [31].

Lung cancer, a malignant lung tumor disease caused by smoking and is responsible for the growth of unregulated of genetically altered cells going repeated division [32–35]. In 2012, 8.2 million deaths have been accorded for this disease as estimated by GLOBOCAN. It generally occurs by smoking which causes mutation in protective genes and damages the DNA. This alteration and damages accumulate with time, which is the reason that people who start or quit smoking also suffer from this deadly disease [36]. Other than smoking, there are other risk factors associated with lung cancer such as asbestos, passive inhaling of biomass fuel, diesel exhaust, passive inhalation of tobacco, and other environmental factors [37, 38]. The clinical symptom of this disease involves chest pain, fatigue, hoarseness, persistent cough, loss of appetite, excessive weight loss, and shortness of breath [39]. As per the consensus of WHO, lung cancer holds the 2nd position for mortality globally and moreover, the 70% of death because of lung cancer occurs in low- and middle-income countries such as Australia, Belgium, Denmark, France, Hungary, India, Ireland, Netherlands, New Zealand, Norway, and the United States [40, 41].

2.2. Anatomy and Physiology of the Lungs

Lungs are a pair of air-filled spongy organs that performs the function of gaseous exchange and delivers the oxygen to every cell. It comprises a total of five lobes, where three are in the right lung and two are in the left lung [42]. The lung interior contains smaller air-passages, alveoli, bronchi, blood vessels, and lymph tissues. The bronchi portion of the lung is further subdivided into primary (1 degree) and secondary (2 degree) bronchi as well as bronchioles and at last the alveoli. Moreover,

the lung contains more than 0.3 billion alveoli [43]. Additionally, all the alveolus is covered with respiratory capillaries, which form a complex network containing around 0.28 trillion capillaries, facilitating the large surface area of about 70 m² [44]. Primarily the alveolar gas-exchange takes place at the lining comprising alveolar epithelium, endothelium, and interstitial cell layers. Also, among the alveolar epithelium and capillaries, single endothelial layer is also present. The distance among the capillaries and alveoli is very less approximately 0.5 μm, this acute thinness owes to the blood-gas interface, where exchange of gas take place by diffusion [45]. These alveoli are covered with alveolar fluid as well as mucus, which are primarily made up of surface proteins and phospholipids. The phospholipid surfactant layer of alveoli allows the proper functioning of gaseous exchange and reduces the surface tension in the alveoli [45]. Moreover, these distant respiratory passages are maintained intact by connective tissue, which are bounded by several types of cells such as fibroblasts, lymph vessels, macrophages, and nerves cells. This aid as an ideal site for drug administration as it has access to both lymphatic and pulmonary system [46].

3. METHODS

3.1. Mechanism of Drug Administration

Over the past few decades, the systemic absorption of different types of drugs after pulmonary applications have been tested on animals and humans [47]. Through the pulmonary pathway, the therapeutic agent can be administered in our body through two ways, that is, intranasal and inhalative administration. The intranasal administration has anatomical constrain like narrow lumen of airway [48]. Whereas oral inhalative administration has been found to better than intranasal administration, as it allows the administration of small particles and reduces the loss of therapeutic drug before reaching the target site [49]. Moreover, oral inhalative administration is further categorized as intratracheal inhalation and intratracheal instillation. Most common method is “intratracheal instillation” in which minute amount of therapeutic solution is delivered by special syringe into the lungs. As it allows the quantitative and fast delivery of drug to the lungs [50]. Additionally the confined drug deposition is attained that also on relatively limited absorption area. Hence, this makes this process easy and nonexpensive but drug distribution in this case is nonuniform [51]. During preclinical assessment on animals, intratracheal instillation method was used to determine the absorption capacity