

to enhance absorption of peptide drugs administered nasally. This aspect of nasal drug delivery has been reviewed by several authors (35,67,68).

#### **4. PULMONARY DRUG DELIVERY**

Recently, the lung has emerged as a route of choice for both local and systemic drug delivery because of its extensive surface area, thin epithelial layer, and rich blood supply. Although the use of the lung as a route of drug delivery dates back to the early civilization, its potential for systemic drug delivery of therapeutic macromolecules has been studied over the past three decades. The lung has also attracted much attention as the target organ for gene delivery to treat conditions such as cystic fibrosis and lung cancer (69). Pulmonary delivery has several advantages over oral and parenteral delivery including avoidance of degradation of the drug in the gastrointestinal tract and circumvention of the first-pass effect. Further, the pulmonary route requires a lower dose to achieve the same therapeutic response compared to other routes of drug delivery. Drug administered to the lung may produce systemic fewer side effects and can provide rapid onset of action. Pulmonary drug delivery systems are needle-free non-invasive systems, and can be administered without assistance of trained healthcare professionals. Further, pulmonary delivery has improved therapeutic acceptance and causes less disruption in the patient's life style. One of the disadvantages of pulmonary route is that sophisticated delivery devices are required to ensure accurate dosing of a drug. As a result, pulmonary drug products are relatively expensive.

##### **4.1. Anatomy and Physiology of Respiratory Tract**

Anatomically, the human respiratory tract ranges from external nares to bronchioles and alveoli. However, pulmonary drug delivery targets the tracheobronchial region and gas exchange region of the lung. The tracheobronchial region begins at the larynx and includes the trachea and the ciliated bronchial airways down to the terminal bronchioles. The pulmonary gas exchange region consists of respiratory bronchioles, alveolar ducts, alveolar sacs, atria, and alveoli. Also, the respiratory tract is divided into upper and lower respiratory regions. The upper respiratory tract consists of the nose, nasal passages, mouth, eustachian tube, pharynx, esophagus, and larynx. The trachea and bronchia are sometimes classified as part of the upper respiratory tract. The lower respiratory tract consists of the gas exchange region (i.e., bronchioles and alveoli). The alveoli are surrounded by polyhedral structures, and the side of the alveoli that is exposed to atmosphere is surrounded by thin-walled epithelium. It is important to note that trachea is divided to form smaller bronchi that lead to lung lobes. Inside each lobe, the bronchus is further subdivided to form bronchioles (70).