



**FIG. 2** The respiratory tract and its intrinsic barriers for successful drug delivery to the lungs by inhalation. The respiratory tract, which includes the nasal mucosa, hypopharynx, and large and small airway structures, provides a large mucosal surface for drug absorption. It is mainly composed of two epithelial cell types, airway and alveolar epithelium but with different characteristics such as diameters from 3 to 5 mm and from 66  $\mu\text{m}$  depth of bronchi to 250  $\mu\text{m}$  diameter to 100–200 nm depth of human alveoli. Also, covered by large nasal and pulmonary mucosal surfaces and tight junctions between the epithelial cells, this administration route is useful for the therapy of pulmonary diseases and for DD to the systemic circulation. The combined effect of the mechanical and biochemical barriers is that pulmonary bioavailability (for locally acting drugs) and systemic bioavailability (for systemically acting drugs) of drugs are low. Hence, efficient inhaler devices, proper inhalation techniques, and suitable microformulations or nanoformulations are strictly necessary.

of the pMDIs, (3) breath-actuated metered-dose inhalers, (4) DPIs, (5) Nebulizers, and (6) SMIs]. Section 6 is about Nanobiotechnology solutions against asthma and COPD. Section 7 addresses Nanobiotechnology solutions against pulmonary infections and cancer. Section 8 is a concluding remark section.

## 2. BENEFITS AND DRAWBACKS OF THE PULMONARY ROUTE OVER OTHER ADMINISTRATION ROUTES

DD to the lungs by inhalation offers an interesting route to noninvasive drug administration for either local or systemic effects. As it is depicted in Table 1, PDD has many advantages when compared with conventional drug administration, such as rapid onset of drug action

with high bioavailability, less systemic side effects than oral or parenteral routes, and the opportunity of a targeted drug therapy for respiratory diseases.

However, the efficacy of the inhaled drugs can be hampered by their rapid clearance in the lungs due to the mucociliary escalator, macrophage uptake, local metabolism, and translocation to the systemic circulation. Microcarriers and nanocarriers able to provide sustained drug release (SDR) in the lungs might improve the therapeutic outcomes of the inhaled formulations due to their retention in the lungs for an extended period of time and their local progressive release at therapeutic levels. Moreover, SDR formulations are also useful to avoid peaks of local drug concentrations that can be toxic for the lungs, as it occurs with cytotoxic drugs such as anti-neoplastics [7]. Because of the advantages offered by