the dose from a powder reservoir or contain premetered individual doses that are dispensed from blisters, disks, dimples, tubes, or strips depending on the manufacturer's design [73].

DPIs are light, compact, and portable devices and do not contain propellant aerosol systems. The main advantage they present is their capacity of being actuated by the breath; consequently, they do not require hand-to-breath coordination to deliver the precise drug amount to the respiratory tract. However, patients still need a deep and forceful inhalation action to disaggregate the powder formulation into respirable particle sizes; otherwise, the delivery to the lungs is not assured. Moreover, DPIs are sensitive to moisture, are not recommended for children under 5 years of age, and are not suitable for individuals with lactose allergy.

5.5. Nebulizers

Nebulizers are devices that transform suspensions or solutions of drugs into aerosols to be inhaled through a face mask or a mouthpiece. Three different types of nebulizers are available depending on the technology that is used to generate aerosol particles: the jet nebulizer, the ultrasonic nebulizer, and the vibrating mesh nebulizer [1]. Although they are bulky, they tend to be contaminated with environmental microorganisms and must be plugged into an electrical outlet or power adaptor. There is no need of any special inhalation technique to use them, patients can be treated with drugs that are not available as MDIs or PDIs, and they have no age restrictions.

5.6. SMIs

The Respimat is an SMI developed by Boehringer Ingelheim (Germany), characterized by functioning as a nebulizer because it transforms an aqueous liquid solution containing the drug into aerosolized droplets in the respirable range. Unlike nebulizers, an SMI is handheld, a multidose device, and offers consistent dosing with less oropharyngeal deposition and high lung deposition. An adequate coordination of inhalation with actuation is required [74].

6. NANOBIOTECHNOLOGY SOLUTIONS AGAINST ASTHMA AND COPD

Respiratory diseases are complex and challenging pathologies creating a worldwide warning because at least 1 billion people suffer from either chronic or acute respiratory illnesses. Moreover, five of these pathologies are among the most frequent causes of severe sickness and death in the world. In 2017, the World Health Organization (WHO) reported about 65 million and 334 million of people with moderate to severe COPD and asthma, respectively, independent of ages, ethnicity, and location. COPD is a group of lung irreversible pathologies such as chronic bronchitis and emphysema and both combined sometimes.

Asthma is an inflammatory pathology linked with reversible contraction of the bronchial airways. Also, the number of people with asthma and COPD is rising because of air contamination, deficient sanitary and household conditions, malnutrition and hunger, making the respiratory infections one of the top three reasons of death and disability among both children and adults. For example, 3 million people die worldwide from COPD every year, and asthma affects at least 14% of children [75]. The economic impact of respiratory diseases affects seriously the health care systems. The mortality of population affected by respiratory pathologies increased 18% from 1990 to 2017 [76]. Besides, the mortality due to COPD is approximately eight times greater when compared with asthma [77]. Recent reports made only in the United States during 2010 and 2011 revealed that the total COPD and asthma treatment costs were projected to be approximately US$ 50 billion and US$ 56 billion, respectively [78, 79]. The increased global burden and impact of respiratory diseases can be associated with several factors such as low sociodemographic index and safety limitations of quality medicines in several regions of the world and because of the trend of aging population.

Conventional medicines for asthma and COPD try to improve the health conditions of patients by not only reducing the major symptoms immediately but also control their evolution [80]. The most common drugs for both pathologies are bronchodilators that are β_2-adrenergic receptor agonists (Fig. 5) and anticholinergics that are antagonists to the muscarinic receptors (Fig. 6). Bronchodilators bind with the β_2-adrenergic receptor that triggered a metabolic cascade by the activation of adenylate cyclase, increasing the levels of cAMP and consequently, activate PKA that phosphorylates the myosin light-chain kinase, reducing the muscle contraction for short term in the case of salbutamol or for long term in the case of formoterol and salmeterol. There are at least seven β_2-adrenergic receptor agonists in the market with similar physicochemical properties (Table 6).

The approved and marketed muscarinic receptor antagonist drugs such as the anionic aclidinium, glycopyrronium, ipratropium, tiotropium, and umeclidinium block the acetylcholine receptors, preventing the acetylcholine's binding with the receptor to halt smooth muscle contraction and reducing mucus secretion,