TABLE 5
Advantages, Disadvantages, and Examples of Different Inhaler Devices—cont'd

Inhaler	Pressurized	Advantages	Disadvantages	Examples
SMI	No	Compact and portable Without propellants Multidose and consistent dosing Less oropharyngeal deposition	Require precise hand-to-breath coordination Relatively expensive Not available in most countries	Respimat

API, active pharmaceutical ingredient; *BA-MDI*, breath-actuated metered-dose inhalers; *CF*, cystic fibrosis; *COPD*, chronic obstructive pulmonary disease; *DPI*, dry-powder inhalers; *pMDI*, pressurized metered-dose inhalers; *SMI*, soft mist inhalers.

obstructive airway diseases. These portable multidose devices contain the drug in solution or suspension, which is then delivered as a precise volume of micronized particles dispersed in a propellant due to the action of a metering valve at each puff [66]. In the beginning, chlorofluorocarbons (CFCs) were used as propellants; however, because the Montreal protocol on substances that deplete the ozone layer was signed in 1987 [67], the CFC was replaced by hydrofluoroalkane (HFA)-134a or HFA227ea propellants that do not constitute a threat to the ozone layer.

One of the great advantages of pMDIs is that they are compact, portable, relatively cheap, and multidose devices. Besides, pMDIs are available for most inhaled medications, and most of the aerosol particles are in the optimal range for deposition in the lower respiratory tract, resulting in high reproducibility in each dosage [68, 69]. However, the misuse of pMDIs by the patients, even after repeated education, is one of the major causes of poorly controlled disease [70]. Not only the precise hand-to-breath coordination required by the device is difficult to address by the patients, but also the drug deposition in the mouth and the oropharynx is high, causing systemic adverse side effects. Besides, the lack of built-in counters results in frequent complaints from users who cannot predict when they should refill the device.

5.2. Accessories of the pMDIs

The spacers or valved holding chambers are accessories attached to the pMDIs to ensure the dosing of the pressurized system in patients who cannot coordinate the pulsation-aspiration technique. In this manner, the drug deposition in the oropharynx is allowing less the increased deposition in the lower respiratory tract when compared with the pMDIs alone. Nonetheless, these accessories make the device's price more expensive and less transportable for the patients [71].

5.3. Breath-Actuated MDI Devices (BA-MDIs)

Breath-actuated MDI devices (BA-MDIs) have emerged as an alternative to pMDIs for patients with poor coordination, when using the latter. BA-MDIs and pMDIs are pressurized systems, but BA-MDIs operation is based on a flow-triggered system driven by a spring that liberates the right dose of drug during inhalation. Therefore as they are actuated by the user's inhalation, no hand-to-breath coordination is needed and are easier to teach when compared with conventional pMDIs [72]. However, despite having all the advantages of pMDIs in addition to the unnecessity of a precise coordination technique, BA-MDIs require a higher inspiratory flow for triggering, and there are not enough drugs available to be administered with this device.

5.4. DPIs

DPIs arise as an alternative to the inhalers in pressurized cartridge to solve the problems of coordination between the activation of the device and the inhalation. Unlike pressurized systems, DPIs deliver the active pharmaceutical ingredient in a powdered formulation in the form of micronized particles in the respirable range as pure loose agglomerates or adhered to the surface of lactose carriers [19]. DPI devices can be classified into two large groups according to the dose delivered: single-dose and multidose devices. HandiHaler (Boehringer Ingelheim, D) and Aerolizer (Novartis Pharma, CH) are single-dose devices, whereas the Diskus (GlaxoSmithKline, United Kingdom) and the Turbuhaler (AstraZeneca, Sweden) are examples of multidose devices that either measure