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Review article

Co-suspension delivery technology in pressurized metered-dose inhalers for multi-drug dosing in the treatment of respiratory diseases

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ABSTRACT

Technologies for long-term delivery of aerosol medications in asthma and chronic obstructive pulmonary disease have improved over the past 2 decades with advancements in our understanding of the physical chemistry of aerosol formulations, device engineering, aerosol physics, and pulmonary biology. However, substantial challenges remain when a patient is required to use multiple inhaler types, multiple medications, and/or combinations of medications. Combining multiple drugs into a single inhaler while retaining appropriate dosing of the individual agents in the combination may enhance patient adherence to therapy and reduce device errors that occur when patients are using multiple inhalers. Pressurized metered-dose inhaler (pMDI) devices are widely used by patients for acute symptom relief as well as maintenance treatment, so the pMDI may be a suitable option with which to explore medication combinations. However, optimizing drug formulation remains a key challenge for pMDI delivery systems. This article introduces a new pMDI formulation approach: co-suspension delivery technology, which uses drug crystals with porous, low-density phospholipid particles engineered to deliver combinations of drugs to the airways with accurate and consistent dosing via pMDIs, independent of medication types and combinations. We describe the key characteristics of pMDIs, and discuss the rationale for the co-suspension delivery technology platform based on the limitations associated with traditional formulations. Finally, we discuss the clinical implications of co-suspension delivery technology for developing combination drug therapies administered by pMDIs.

Contents

Abbreviations: COPD, chronic obstructive pulmonary disease; DPI, dry powder inhaler; FDC, fixed-dose combination; HFA, hydrofluoroalkane; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; pMDI, pressurized metered-dose inhaler.

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1. Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are heterogeneous diseases with multiple components, including chronic inflammation, airway obstruction, and airway hyperresponsiveness [1]. Numerous medications are available for asthma and COPD, most of which are administered by oral inhalation devices [2,3]. The first propellant-based, pressurized metered-dose inhalers (pMDIs) were developed in the mid-1950s [4,5], beginning an era of portable and compact modern inhalers with highly efficient aerosolization engines.

Oral inhalation is the standard method of medication administration for patients with asthma [6] and COPD [7] as it achieves targeted drug delivery to the lungs. Direct administration to the airways has several advantages over systemic administration, including rapid delivery of low doses to the airways [3] and reduced potential for adverse events, as well as increased efficacy [8].

Asthma and COPD are distinct diseases with defined treatment paradigms and objectives, but are currently treated with many of the same classes of inhaled medications due to their overlapping disease features [2,7]. Moreover, both are chronic diseases that require continued maintenance therapies, often with escalating interventions [9,10]. Treatment escalation can involve administration of multiple drugs and may require use of multiple inhaler devices. The use of different drugs from different delivery systems can be confusing for patients, and potentially increase errors in inhaler technique. Thus, the availability of different fixed-dose combinations in a single inhaler device may be beneficial, allowing escalation or de-escalation without changing the inhaler device. Potential combinations include: (1) bronchodilator combinations (e.g., long-acting beta-agonist [LABA]/long-acting muscarinic antagonist [LAMA]) for patients with COPD; (2) an anti-inflammatory drug plus a bronchodilator (e.g., inhaled corticosteroid [ICS]/LABA) for patients with asthma or COPD; or, although currently still in clinical development, (3) triple therapy (e.g., ICS/LAMA/LABA) for patients with asthma or COPD.

Several inhalation delivery systems are currently available for patients, including pMDIs, dry powder inhalers (DPIs), soft mist inhalers, and nebulizers, each having its own advantages and challenges (Table 1) [3,8,11–15]. Each inhaler type delivers aerosols differently, requiring varying degrees of patient effort and coordination. Choosing the appropriate mechanism for inhaled drug delivery depends on several patient factors (Fig. 1) [18]. Although pMDIs require hand–breath coordination for drug delivery (corrected by addition of a spacer), they are among the most frequently prescribed devices, particularly for short-acting bronchodilators [3,12], and provide a suitable device option for patients with inadequate negative inspiratory flow, and those who are intubated or are on chronic mechanical ventilation [19,20] (Table 2).

Despite the suitability and applicability of pMDIs in asthma and COPD therapy, important medicines and their combinations remain unavailable in this delivery device given the challenges of formulating them with modern hydrofluoroalkane (HFA) propellant systems. Co-suspension delivery technology utilizes a new pMDI formulation method in which drug crystals are suspended in the propellant by engineered low-density phospholipid particles. This article aims to introduce this new formulation approach for pMDIs to clinical audiences. It discusses the rationale for the co-suspension platform, and outlines its features. The clinical implications of this formulation method for developing combination drug therapies administered by pMDIs are also described.

2. Characteristics of pMDIs

A pMDI is a portable, multi-dose, pressurized reservoir device system consisting of an aluminum canister, which rests within a plastic actuator, and delivers drugs via an orifice in the actuator (Fig. 2) [12,21]. The canister contains either a suspension of micronized drug crystals or a solution of drug with a co-solvent, in a propellant, or sometimes in a propellant mixture. Suspension formulations often contains a surfactant (e.g., oleic acid or lecithin) to reduce particle agglomeration [12,21]. Use of a closed pressurized reservoir within a canister protects ingredients from sources of product degradation, including microbial contamination, moisture, oxygen, and light.

When the canister is pressed onto the actuator, the formulation is released from the metering chamber of the valve into air via the actuator orifice, which causes the propellant to be converted into microdroplets that contain drug. The propellant droplets evaporate immediately, resulting in aerosolized drug microcrystals or co-solvent droplets containing drug ready for inhalation (Fig. 2) [12]. The pMDI propellant drives the drug formulation through the actuator orifice at a high velocity (>30 m/s for the now phased-out chlorofluorocarbons and approximately 2–8.4 m/s for the newer HFA propellants) [22,23]. Propellants are gaseous at atmospheric pressure [21], but are contained in their liquid form in the pMDI canisters. As the force of propellant evaporation provides the energy for drug aerosolization, a patient's inspiratory effort is required only for inhalation of the aerosol.

3. Challenges of aerosolized delivery with pMDIs

Although pMDIs are widely used for respiratory medications, a number of challenges remain that affect drug development in this inhaler type. Several physical and chemical attributes of the pMDI system govern the performance of pMDIs. The pMDI container must be able to withstand the pressure created by the propellant, and the internal surface of the container must be designed to reduce adhesion of drug particles and their chemical degradation [21]. A fine balance of complex compositional and physicochemical properties is required to achieve consistency and stability in suspension formulations. Inability to completely optimize these properties can lead to significant dosing variability [24,25]. When suspended in propellants, drug crystals tend to form large flocculates to minimize surface energy. This, in turn, leads to density-driven creaming or sedimentation that can result in variable metering and dosing [24–26]. No known surfactant is available to prevent this tendency. The rate of flocculation depends on the concentration of the suspended drug, particle size distribution, and the number of drugs in the suspension; thus, poor colloidal stability is often magnified in combination formulations due to differences in these factors among multiple drug microcrystals [25]. Additionally, solubility issues with HFA-based propellants introduced challenges in the development of formulations for pMDIs [27]. To help address these issues, solution-based formulations have been developed by adding co-solvents to propellants [28].

Particle aerodynamics plays an important role in drug delivery to the lungs and present important challenges to device design and particle engineering. The delivered dose and its distribution within the airways are influenced by the patient's inspiratory maneuver, aerodynamic particle size distribution, and airway anatomy [14]. Smaller particles penetrate more deeply into the lung, whereas larger particles have a greater propensity for deposition in the oropharynx and upper airways, particularly at higher inspiratory flow rates [29]. Particles with an aerodynamic diameter of 1–5 μm are deposited in the airways and alveoli [30]. Most particles >10 μm are deposited in the oropharynx and subsequently swallowed,

Table 1
Types of commonly used inhalers.

Inhaler	Formulation	Metering System	Comments
pMDI (±spacer)	Drug suspended or dissolved in propellant, with surfactant and co-solvent	Metering valve and reservoir	**Pros:** Ubiquitous; best device to produce aerosols; usable in ventilator circuits; patients and clinicians very familiar with this device; commonly used rescue inhaler
			Cons: Some patients have difficulty with hand–breath coordination (corrected by use of a spacer); some formulation and development challenges
Breath-actuated MDI	Drug suspended in propellant	Metering valve and reservoir	**Pros**: No hand–breath coordination required; easy to use
			Cons: Not widely available for patient use
DPI	Drug blend in lactose; drug alone; drug/excipient particles	Capsules, blisters, multi-dose blister packs, reservoirs	**Pros:** Easy to use
			Cons: Significant inspiratory flow rate dependence; high throat deposition; significant drug interactions during storage; formulation and development challenges for combinations
SMI	Aqueous solution or suspension	Unit dose blisters or reservoirs	**Pros:** Low throat deposition
			Cons: Risk for clogged nozzles; requires dose and inhaler manipulations by patient (i.e., must be assembled); difficult to dose combinations accurately; requires sterility
Nebulizer	Aqueous solution or suspension	Nebule dispensed into reservoir chamber of nebulizer	**Pros:** Suitable for use by any patient type (no minimum inspiratory flow rate or hand–breath coordination required); good for ventilator circuits
			Cons: Marketed as two products: device and drug; requires sterility; prone to clogged nozzles; requires dose and inhaler manipulations by patient; difficult to administer drug combinations

DPI, dry powder inhaler; MDI, metered-dose inhaler; pMDI, pressurized metered-dose inhaler; SMI, soft mist inhaler.
Sources [12–15].

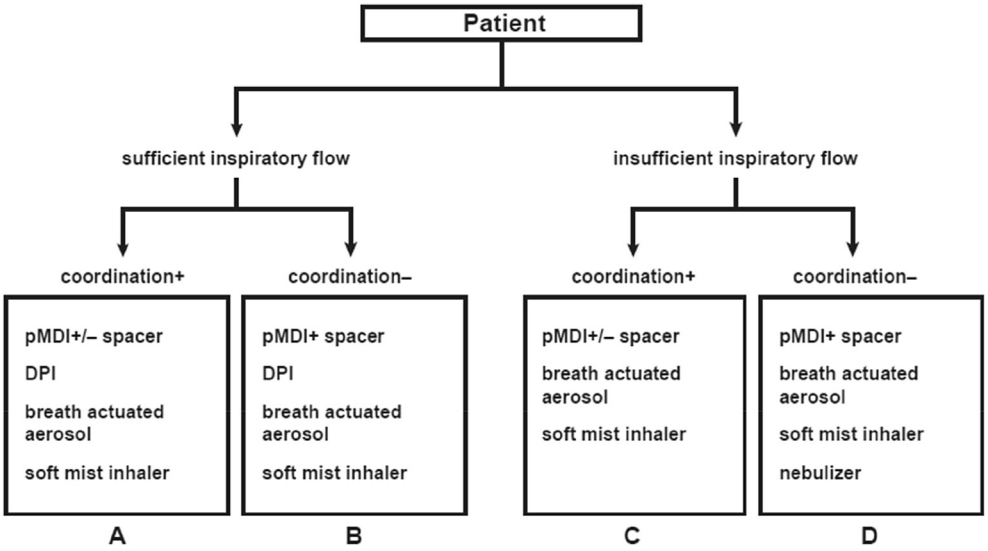

Fig. 1. Decision tree for inhaler choice. Decision tree showing how to choose the best inhaler type for a specific patient. Reprinted from Respiratory Medicine, Vol 107(12), P.N.R. Dekhuijzen, W. Vincken, J.C. Virchow, N. Roche, A. Agusti, F. Lavorini, W.M. van Aalderen, D. Price, Prescription of inhalers in asthma and COPD: Towards a rational, rapid and effective approach, 1817–1821, Copyright 2013, with permission from Elsevier [18]. DPI, dry powder inhaler; pMDI, pressurized metered-dose inhaler.

whereas particles <1 μm are mostly exhaled [31]. A range of aerosol particle size (i.e., aerodynamic particle size distribution) is required for broad deposition in the airways, posing a particular challenge for pMDI drug formulations in which drug-crystal-to-drug-crystal interactions often defeat the ability to generate consistent aerodynamic particle size distribution. In addition, rapid spray velocity causes oropharyngeal deposition, as can large droplet size [21]. Lung deposition is further dependent on patients' inspiratory flow rate for particles sized 1–5 μm and >10 μm [22,32]. In general, to decrease oropharyngeal deposition, drugs should possess a diameter of <5 μm [33,34].

Studies have demonstrated that patient adherence can increase when multiple drugs are combined in a single device [35]. However, combining drugs within a single device is challenging [36]. The inability to achieve aerosol performance equivalency for individual drug components from combination inhalers versus single component inhalers—termed the co-formulation effect—causes additional technical limitation for these products [36,37].

4. Co-suspension delivery technology

A recent advancement that helps to address the challenges of

Table 2
Advantages and disadvantages of standard pMDIs.

Advantages	Disadvantages
Portable, compact, ready to use after shaking	Require propellants
Short treatment time	Hand–breath coordination for actuation often needed (although this can be corrected by use of a spacer)
Multi-dosing device	Upper limit to dose content
Relatively inexpensive	Potential for high oropharyngeal deposition (up to 50%–80%) due to high spray velocity, leading to complications (dysphonia, candidiasis)
Contents remain stable and mostly free of environmental influences (e.g., humidity, light, oxygen)	Certain major drug classes not yet available as pMDIs (e.g., LAMA)
Delivers precise, consistent doses with each actuation (when used properly[a])	
Does not require critical inspiratory flow	
Available for a wide variety of drugs	
Patient preference	

LAMA, long-acting muscarinic antagonist; pMDI, pressurized metered-dose inhaler.
[a] Contents shaken well, patient inhales fully. Precision of dosing tends to diminish as canister approaches empty.
Sources [12,13,16,17,22,64].

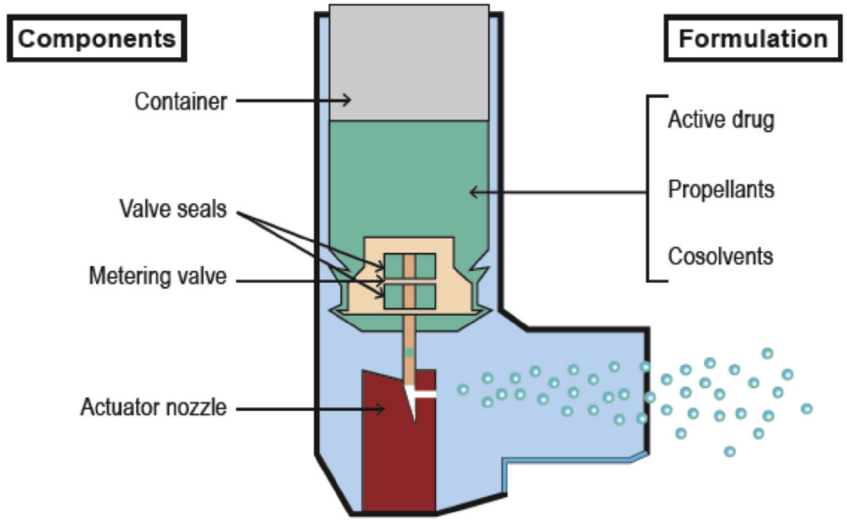

Fig. 2. Schematic of a pMDI and its components. Detailed schematic diagram of a pMDI and its individual components. Adapted from F. Lavorini, The challenge of delivering therapeutic aerosols to asthma patients, ISRN Allergy 2013 (2013) 17 [12]. This work is licensed under a Creative Commons Attribution 3.0 Unported License. https://creativecommons.org/licenses/by/3.0/.

administering multiple drugs by a single pMDI has been the development of a novel co-suspension delivery technology platform. This technology creates a uniform formulation of drugs in their micronized crystalline form, and minimizes the potential for drug–drug interactions for multi-drug combinations within a single inhaler device (Fig. 3A) [25]. This homogenous suspension is maintained for 30 s after shaking [25,38,39], compared with drug-crystal-only-based formulations, which can separate rapidly [40].

The co-suspension delivery technology uses engineered, low-density phospholipid particles in HFA propellant to suspend micronized drug crystals uniformly [25,36]. The drug crystals form strong associations with the porous phospholipid particles (Fig. 3A) [25,36], and drug-to-porous-particle ratios are selected such that the interaction between drug crystals is minimized (Fig. 3A and B).

The drug-free phospholipid particles are prepared by spray-drying an emulsion of distearoylphosphatidyl-choline (a synthetic, long-chain, fully saturated phosphatidylcholine) and anhydrous calcium chloride (to improve the physical stability of the lipid particles), in a 2:1 M ratio, using an emulsion of perfluorooctyl bromide and water to form the porous architecture. The removal of perfluorooctyl bromide and water during the spray-drying process creates a dry powder comprising physically and chemically stable porous microstructured phospholipid particles [25,36]. The spray-drying process imparts a low-density solid-foam nanostructure within, and an amphiphilic corrugated surface on, the phospholipid particles [25]. The amphiphilic corrugated surface potentially reduces cohesion between particles, leading to decreased aggregation rates in the propellant [25]. The porous particles possess long-term physical and chemical stability under most practical conditions of storage and handling of the pMDIs. After these particles are emitted from the pMDIs, and after they enter the lungs, their porous microstructure absorbs moisture when exposed to airway temperature and humidity. This leads to their complete collapse into a mucous-like structure, which merges with the local airway mucosal surface. Any drug particles associated with the porous particles are separated, either in airways or on the airway surface. The porous particles thus naturally assimilate into the lung mucosal environment, while allowing the drug crystals to provide their desired pharmacological action.

Co-suspension delivery technology may overcome many of the technical challenges associated with pMDI suspension formulations (Table 3) [21,24,25,41–46]. This technology combines multiple drugs into a single pMDI with reduced potential for drug–drug co-formulation interactions, while maintaining suspension uniformity, physicochemical stability, and consistent drug delivery at both delivered dose and aerosolization levels [44,45]. As more patients are being treated with drug combinations, co-suspension delivery technology provides a means to deliver multiple drugs from a single pMDI while maintaining drug delivery similar to the individual drug pMDIs.

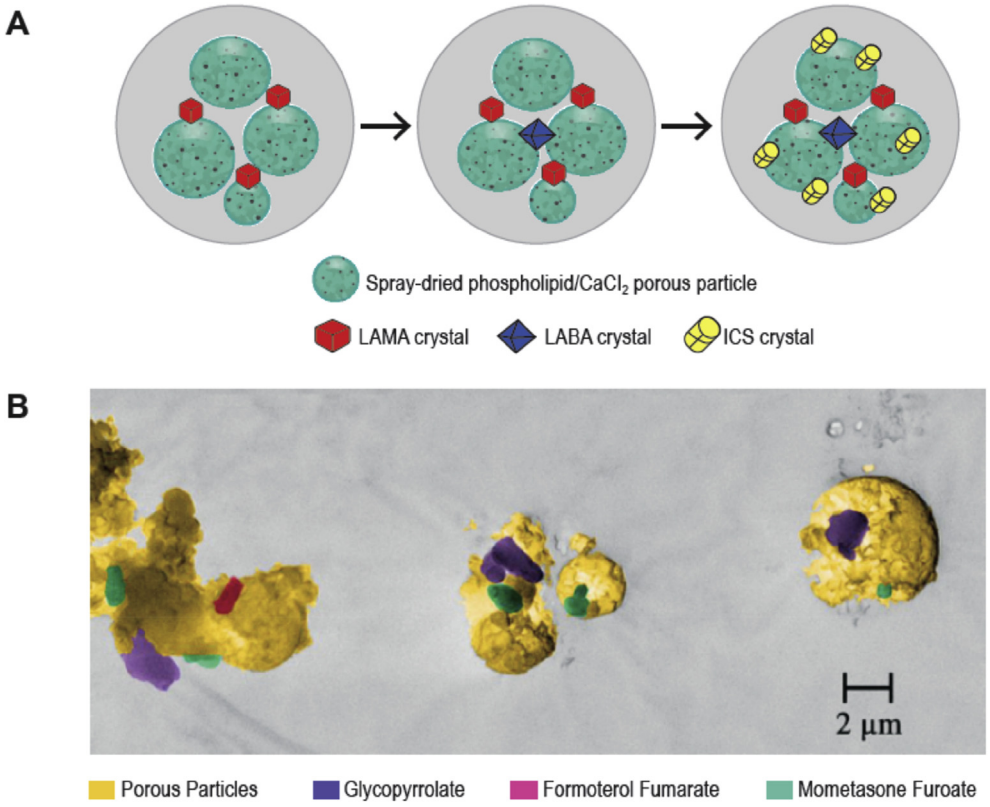

Fig. 3. Micronized drug crystal co-suspension with porous particles. A) Schematic representation of the phospholipid microparticles interacting with the micronized drug crystals while suspended in a propellant droplet. B) Color-coded micrograph of agglomerates emitted from a pMDI containing micronized crystals from three different drugs co-suspended with porous microparticles. Reprinted with permission from R. Vehring, D. Lechuga-Ballesteros, V. Joshi, B. Noga, S.K. Dwivedi, Cosuspensions of microcrystals and engineered microparticles for uniform and efficient delivery of respiratory therapeutics from pressurized metered dose inhalers, Langmuir 28(42) (2012) 15015–15023 [25]. Copyright 2012. ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic agonist. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

5. Co-suspension delivery technology consistency and robustness during patient use

A series of experiments testing the consistency and robustness of co-suspension delivery technology-based drug delivery demonstrated highly reproducible dose delivery and aerosol performance, with >99% of doses remaining within the target dose range, and no differences detected between monotherapy and combination product drug delivery [47].

In addition, tests mimicking various patient use and misuse scenarios using co-suspension delivery technology pMDIs (e.g., varying degrees of shaking before drug delivery, dropping the device, delays between shaking and drug delivery, and a wide range of inhalation flow rates used to inhale the delivered dose) have shown consistent drug delivery across the different scenarios [47].

6. Lung deposition from co-suspension delivery technology formulation-based pMDIs

Particle size of a delivered dose aerosol is a key factor dictating where the drug will deposit in airways. The co-suspension delivery technology aerodynamic particle size distribution results for the combination of glycopyrrolate and formoterol show a broad distribution of aerosolized particle sizes with a mass median aerodynamic diameter of approximately 3 µm, geometric standard deviation of about 1.7 [25,47–49], and an 'extra-fine' particle size (below 1.5 µm) fraction of approximately 25%. This is a size distribution considered ideal for delivering drugs to central and peripheral airways simultaneously [29], and does not focus solely on one segment of particle size range.

Lung deposition using co-suspension delivery technology has also been assessed using gamma-scintigraphy in healthy volunteers [48]. A LABA/LAMA fixed-dose combination (FDC) formulation was shown to deliver a high lung fraction (38.4 ± 10% of emitted dose) with negligible exhaled fraction (0.25 ± 0.26% of emitted dose). Subject-by-subject deposition patterns revealed both central and peripheral airway drug exposure with an outer/inner lung ratio of 0.57 ± 0.13 [48].

7. Clinical potential for triple combination therapy using co-suspension delivery technology

Combining an ICS, LABA, and/or LAMA in the treatment of asthma and COPD has been shown to provide clinical benefits for patients due to their complementary mechanisms of action [36]. For patients requiring multiple inhaled medications, administration of these medications through a single device as a FDC may improve adherence [50]. ICS/LABA FDCs have been approved and available for the treatment of asthma and COPD for many years. LABA/LAMA FDCs for the treatment of COPD have become available in a DPI and a soft mist inhaler, and most recently, in a pMDI using co-suspension delivery technology.

Investigational use of triple therapy with an ICS, LAMA, and LABA in patients with COPD has demonstrated significant benefits compared with LAMA monotherapy [51,52] and compared with ICS/LABA FDC [53–55]. The recently issued 2017 Global Initiative

Table 3
Challenges of pMDI inhalers overcome by co-suspension delivery technology.

Challenges	Results with co-suspension delivery technology
Combining multiple drugs into a single inhaler without altering delivery of each individual drug	• The drug crystals are irreversibly associated with the porous particles, helping to ensure uniform drug delivery. • Avoids drug–drug interaction with multiple drugs within a single inhaler device, retaining drug delivery characteristics of each individual drug.
Poor suspension stability	• Creates a uniform suspension of multiple drugs. • Porous particle–drug crystal mixtures remain afloat, instead of sedimenting. The mixtures eventually cream, and keep the drug crystals floating. Lifting and gentle shaking are often sufficient to redisperse the co-suspension into a uniform suspension. • Irreversible binding of drug crystals to porous particles creates stable colloids, wherein the drug crystal attached to the particles remain in suspension, rather than needing individual components to go into suspension.
Formation of large drug-crystals agglomerates	• The engineered phospholipid particles prevent drug–drug crystal agglomeration by keeping them afloat and apart from each other. • Ensures consistent delivery of the dose and retains the physicochemical properties of each drug. • Gentle shaking redisperses co-suspension flocculates.
Inconsistent and irreproducible drug delivery over time	• Reduced drug–drug crystal interaction in co-suspension leads to consistent dose delivery and aerosolization over time, regardless of nature and number of drug types, and quantity of each drug. • Provides broad applicability for the clinic
High spray velocity causes high oropharyngeal deposition	• Co-suspension utilizes the low spray–velocity HFA propellant. • Low-density porous particles tend to form a more uniform cloud, with particles sized for optimal delivery to the airways.

HFA, hydrofluoroalkane.
Sources [21,24,25,41–46].

for Chronic Obstructive Lung Disease (GOLD) guidelines recommend triple therapy as a treatment option for COPD patients with a greater symptom burden and at greater risk for exacerbations (i.e., GOLD D patients) [7]. Indeed, a real-world study of prescribing patterns for patients with COPD on maintenance medications showed that 46% of patients classified as GOLD D stepped up to triple therapy within 1 year after initial diagnosis [56]. Triple therapy has traditionally required the use of multiple inhaler devices. It is widely believed that a single-inhaler FDC option would be appropriate for patients requiring triple therapy. In September 2017, a dry powder inhaler with triple therapy FDC (vilanterol/umeclidinium/fluticasone furoate) was approved by the FDA for the long-term maintenance treatment of patients with COPD [57]. A triple therapy FDC (formoterol/glycopyrrolate/budesonide) MDI to maintain continuity of inhaler type from rescue medication MDIs to approved dual maintenance therapy (glycopyrrolate + formoterol, or budesonide + formoterol) FDC MDIs is in development [58–60].

Co-suspension delivery technology has been used to combine two bronchodilators, glycopyrrolate and formoterol, in a commercially-approved single pMDI in the United States. Use of this format resulted in consistent, reproducible, dose-proportional drug delivery during various in vitro studies at a wide range of doses for each of these two drugs, achieving comparable dose-response curves to their respective monotherapy formulations [44]. In vitro dose-ranging studies have also demonstrated the ability of this technology to formulate nanogram-level doses of medications without interfering with drug performance [44]. This allowed for a wide range of doses to be tested in clinical trials, providing full dose-response characterization, and eliminating confounding of clinical assessments by drug delivery differences. Several other drug candidates and their combinations are currently under investigation in both COPD [58–61] and asthma [62,63].

Recent investigations with co-suspension delivery technology have shown that the three major drug classes for treating asthma and COPD (ICS, LABA, and LAMA, each with differing pharmacological and physicochemical properties) can be consistently and precisely delivered by a single pMDI FDC, compared with giving each component individually, or as a two-drug combination pMDI administered sequentially with one monocomponent pMDI [25]. Furthermore, triple-drug combinations formulated using co-suspension delivery technology demonstrated in vitro aerodynamic size distributions, optimally and similarly sized for each drug's delivery to the airways (2–3 μm) [25,30], as well as consistency across the monocomponent, and dual- or triple-combination formulation types [25].

Analysis of a co-suspension delivery technology-based triple combination therapy pMDI demonstrated that, after actuation, the drug crystals showed negligible inter-crystal interactions, remained attached to the porous particles when actuated in a dry environment (Fig. 3B), even after the inhalers were stored for 3 months at 40°C and 75% relative humidity [25], and maintained drug delivery attributes across monocomponent and combination formulations. Similarly, analysis of another triple-combination pMDI therapy using an alternate ICS showed similar aerosol performance across mono, dual, and triple FDC combination therapies [45]. In addition, pharmacokinetic data in healthy subjects showed that the triple combination was bioequivalent to a traditional formulation of LABA/ICS pMDI [45]. This drug delivery evidence provides robust scientific foundations for the extensive clinical research required to show the benefits of triple-drug combination therapy on lung function and symptoms for patients with COPD and asthma. Ultimately, the development of pMDIs with co-suspension delivery technology may allow for wider utilization of this dosage form in the management of respiratory diseases.

The scientific improvement in drug delivery with co-suspension MDI technology is expected to allow rapid development of a wide variety of drugs and their combinations, accompanied by accurate and reproducible dose delivery. While co-suspension delivery technology is not designed to address the potential limitations related to pMDI device-handling, developing a formulation platform that has the potential to improve patient adherence to therapy would be of significant value in the context of both asthma and COPD. Consequently, further development of this technology should be expected.

8. Summary

Although pMDIs are currently the most widely used aerosol delivery devices, challenges associated with pMDIs have meant that major drug classes and their combinations are not available for this inhaler type. As a result, there is a need for alternative formulation and delivery approaches. In its fundamental form, co-suspension delivery technology is a simple and versatile formulation platform for pMDIs. The platform uses drug crystals, which are

the naturally stable form of a drug, and phospholipid porous particles, which are naturally buoyant low-density particles, together. This approach allows the potential to formulate drugs with a wide range of pharmacological properties, physicochemical attributes, and doses, whether alone or in combinations. Thus, co-suspension delivery technology provides an opportunity to combine multiple drugs with highly variable characteristics in the same pMDI device while maintaining uniformity and suspension stability, thereby overcoming the variability associated with conventional formulations. Consistent delivery of small and large molecules can now be contemplated from one inhaler. This formulation approach has shown the ability to target all regions of lungs consistently. In addition, the co-suspension delivery technology formulation has been shown to have consistent drug delivery across various pMDI patient-use scenarios. By solving some of the longest-standing challenges with pMDI-based drug delivery, the co-suspension delivery technology has the potential to enable development of multiple therapies in one inhaler type and increase patient adherence to therapy.

Summary of conflicts of interest

GTF has received grants, personal fees, and non-financial support from AstraZeneca LP. AJH has nothing to disclose. SD is an employee of Pearl Therapeutics, a division of AstraZeneca LP.

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