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Effect of spacers on the electrostatic charge properties of metered dose inhaler aerosols

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Abstract

The electrostatic charge properties of commercial metered dose inhaler (MDI) aerosols, including Ventolin®, Flixotide®, Tilade® and QVAR®, sampled through new and detergent-coated AeroChamber® Plus spacers were studied using a modified 13-stage electrical low pressure impactor (ELPI) with aerodynamic cutoff diameters ranging from 0.028 to 10.07 µm. Aerosol particles deposited on the impactor stages according to their aerodynamic diameters and their charges were simultaneously measured by the electrometers. The deposited drug mass was assayed chemically using HPLC. The surface potential on the inner spacer wall was measured with an electrostatic probe before and after aerosol actuation. High surface potentials were found on the new spacers whereas the detergent-coated spacers had minimal charges due to the conductive coating. MDI aerosol charges were decreased when spacers were used but the charge profiles of the aerosols were not altered qualitatively. New spacers had the lowest throat deposition, fine particle dose, and net aerosol and fine particle charges as a result of high spacer retention. These trends were partially reversed by the detergent-coated spacers. In general, the charge per mass of drug (charge-to-mass ratio) for particles from detergent-coated spacers was higher than those from new spacers. This was thought to be due to the reduction of electrostatic deposition inside the spacer thus leading to particles carrying higher charges being sampled. The calculated number of elementary charges per drug particle ranged from zero to several hundred, which is sufficiently high to potentially affect lung deposition. The ELPI provided high resolution charge profiles on MDI aerosols delivered through spacers.

Keywords: Spacer; Electrostatic charge; ELPI; MDI; Pharmaceutical aerosol

1. Introduction

Spacer devices are used with metered dose inhalers (MDIs) to overcome problems in coordinating inhalation with actuation, especially in children, and reduce throat deposition of drug particles (Newman, 2004). These devices may be broadly classified into three groups according to their design, namely, tube spacers, holding chambers, and reverse-flow devices (Newman, 2004). The general term 'spacers' is used to describe these devices collectively in this paper. A spacer serves as a reservoir to hold the aerosol cloud for the patient to inhale through a one-way valve at a natural pace. It also provides a chamber in which MDI droplets may decelerate and evaporate to a smaller size before inhalation to reduce throat deposition and enhance penetration into the lungs (Barry & O'Callaghan, 1996).

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Most spacers are constructed with lightweight plastic materials for portability and durability. Plastics are electrical insulators, thus electrostatic charges may be generated and accumulated on spacer surfaces through contact and friction, or triboelectrification (Hendricks, 1973), during handling. Many studies have shown that spacer charges adversely affect drug output and consequently lung deposition due to particle retention inside the spacer (Barry & O'Callaghan, 1994, 1995; Dewsbury, Kenyon, & Newman, 1996; Piérart, Wildhaber, Vrancken, Devadason, & Le Souëf, 1999; Wildhaber, Devadason, Eber, Hayden, Everard, Summers et al., 1996). Conversely, a reduction in spacer surface charges counteracts this effect. This suggests that spacer drug retention is due to electrostatic particle deposition on the internal walls. Methods of varying degrees of effectiveness have been reported for the reduction or elimination of surface charges on plastic spacers (Barry & O'Callaghan, 1995; Kenyon, Thorsson, Borgstrom, & Newman, 1998; O'Callaghan, 1997; O'Callaghan, Lynch, Cant, & Robertson, 1993; Wildhaber, Devadason, Eber, Hayden, Everard, Summers et al., 1996; Wildhaber, Devadason, Hayden, James, Dufty, Fox, et al., 1996). The most popular method for charge reduction is coating the spacers with dilute surfactant solutions (Piérart et al., 1999; Wildhaber, Devadason, Hayden, James, Dufty, Fox, et al., 1996). Ionic surfactants were found to perform better than nonionic ones (Wildhaber, Devadason, Hayden, James, Dufty, Fox, et al., 1996). This supports the hypothesis that a conductive surfactant coating on the spacer surface is effective in dissipating charges (Kenyon et al., 1998). The optimal treatment was to immerse the spacer in a detergent solution followed by drip-drying without rinsing with water (Piérart et al., 1999). The use of commercial detergents is simple, economical, and relevant to patient use in the community setting, and thus this procedure was adopted in the present study.

Particles emitted from MDIs are known to be charged (Kwok, Glover, & Chan, 2005; Peart, Kulphaisal, & Orban, 2003). Electrostatic interactions between charges on these particles and those on spacer surfaces may contribute to spacer deposition (Dewsbury et al., 1996; O'Callaghan et al., 1993, Piérart et al., 1999; Wildhaber, Devadason, Eber, Hayden, Everard, Summers et al., 1996; Wildhaber, Devadason, Hayden, James, Dufty, Fox, et al., 1996). However, the electrostatic properties of MDI aerosols delivered via spacers have not been studied hitherto. An aerosol electrometer apparatus has been used by Peart et al. (Kulphaisal, Peart, & Byron, 2002; Peart et al., 2003, Peart, Magyar, & Byron, 1998; Peart et al., 2002) to measure charges sampled directly from MDIs. It is essentially a two-stage impactor with a Faraday pail as the second stage for collecting and measuring the net charge on fine particles $< 5\,\mu m$ (Peart et al., 2003). The limitation of this setup is that the charges and polarities among different size fractions could not be discerned as only one net charge was measured. Recently, a modified setup of the electrical low pressure impactor (ELPI) was used by Glover and Chan (2004) and Kwok et al. (2005) that provided more detailed charge and mass profiles on MDI aerosols. Discussion on the general instrumental setup and data treatment may be found in the above references. Although many studies had been conducted on the effect of spacer charges on MDI aerosol drug output by cascade impaction (Barry & O'Callaghan, 1995; O'Callaghan et al., 1993; Piérart et al., 1999, Wildhaber, Devadason, Eber, Hayden, Everard, Summers et al., 1996; Wildhaber, Devadason, Hayden, James, Dufty, Fox, et al., 1996), only the mass profiles were measured. The aerosol charge profiles were a major aspect missing from these studies because charge data cannot be obtained using conventional impactors. The ELPI overcomes this drawback and was employed in the present study to acquire a more complete understanding of the effects of spacers on aerosol charges.

The aim of the present study was to employ the modified ELPI to investigate charge and mass profiles of aerosols from commercial MDIs sampled through new and detergent-coated plastic spacers. This paper focuses on the AeroChamber® Plus spacer because it has a soft adaptor universal for the MDIs to provide a common sampling system.

2. Materials and methods

2.1. Metered dose inhalers, spacers, and sampling protocol

The four types of MDIs examined in the study were Ventolin® (100 μg salbutamol sulphate; Allen & Hanburys, Australia), Flixotide® (250 μg fluticasone propionate; Allen & Hanburys, Australia), Tilade® (2 mg nedocromil sodium; Aventis Pharma, UK), and QVAR® (100 μg beclomethasone dipropionate, 3M Health Care, UK). All are hydrofluoroalkane (HFA) products, with QVAR® being a solution formulation and the other three being suspensions. Nine new inhalers of each type were used before expiry, three without a spacer, three with new spacers and three with detergent-coated spacers. All MDIs were primed to waste prior to use according to the consumer medicine information leaflets.