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A small volume spacer for use with a breath-operated pressurised metered dose inhaler

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Abstract

A small volume spacer, the Optimiser, has been evaluated for use with the Easi-Breathe breath-operated inhaler. Oropharyngeal deposition in healthy subjects was reduced by 80% by the use of the spacer. The Optimiser spacer removes most of the non-respirable drug, without compromising the fine particle dose delivered from the Easi-Breathe inhaler.

Keywords: Small volume spacer; Breath-operated inhaler; Oropharyngeal drug deposition

Breath-operated metered dose inhalers improve drug delivery to the lungs of patients who have difficulty in using standard pressurised metered dose inhalers (MDI) correctly (Newman et al., 1991). Such inhalers are designed to aid co-ordination by actuating at a pre-determined point during inspiration. Actuation of the Easi-Breathe breath-operated inhaler (Norton Healthcare) occurs at an air flow rate of approximately 20 l/min, which is readily achievable by most patients using MDIs (Fergusson et al., 1991). Such an air flow is likely to be reached early during inspiration, thereby facilitating lung deposition (Farr et al., 1995). Breath-operated inhalers, however, do not protect against oropharyngeal drug deposition. A combination of a breath-operated inhaler with a small volume spacer offers the advantages of improved co-ordination and reduction in oropharyngeal deposition, without the inconvenience of a large volume spacer. Impinger deposition studies, high speed photographic imaging of flume geometry and gamma scintigraphic imaging of drug deposition in healthy subjects, have been undertaken to assess the utility of a small volume spacer, the Optimiser (Norton Healthcare), used with the Easi-Breathe inhaler.

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Table 1
Effect of the spacer on drug deposition in the four-stage liquid impinger

	Beclomethasone dipropionate			Salbutamol
	50 μg	100 μg	250 μg	100 μg
Spacer deposition (%)	27	34	39	31
Reduction in deposition on inlet, stages 1 and 2 (%)	70	69	70	72
Change in deposition (μg/actuation):				
stage 3	+1	+2	+9	+2
stage 4	0	+1	+1	+1

The Easi-Breathe inhaler is essentially similar to a standard metered dose inhaler with a mechanism added to actuate the MDI canister early during inhalation. The Optimiser spacer comprises a plastic tube having a cross section 2.5 × 3.3 cm. It has an overall length of 10 cm and a volume of approximately 50 ml.

Aerosol particle size measurements have been carried out using a four-stage liquid impinger (Apparatus C, Inhalanda, 1993). The drug was delivered into the impinger from an Easi-Breathe inhaler, both with and without an Optimiser spacer. The mechanism for automatically actuating the inhaler was removed, and the canisters fired manually, to ensure aerosol collection at the recommended constant air flow rate of 60 l/min. Measurements were carried out on three canisters each of beclomethasone dipropionate 50, 100 and 250 μg/actuation (Beclazone, Norton Healthcare) and salbutamol 100 μg/actuation (Salamol, Norton Healthcare). Assays of the drug deposited in each stage of the apparatus, the inlet, spacer and actuator, were undertaken by high performance liquid chromatography.

The impinger deposition data (Table 1) show that the spacer removed between 27 and 39% of the total doses. For each formulation, this corresponded with a reduction of about 70% of the delivered dose associated with aerosol particles having aerodynamic diameters greater than 6.8 μm; depositing in the inlet, stage 1 and stage 2 of the impinger. The spacer had little effect on the quantity of drug deposited in stages 3 and 4 (the fine particle dose).

Photographs were taken of the flumes of salbutamol 100 μg/actuation, delivered from the inhaler with and without the spacer. The pictures had a field of view extending to 8 cm beyond the mouthpiece and were recorded at varying time intervals up to 250 ms following actuation. Illumination of approximately 500 ns duration was provided by a high-energy, argon gas stabilised spark unit.

As shown in Fig. 1, attachment of the spacer had a marked effect on the structure of the flume. The aerosol flume emerged from the actuator with a well-defined conical shape. After traversing the spacer, it was emitted with a more cloud-like appearance. Over the first 5 cm after leaving the actuator, the flume had an average velocity of 8 m/s, compared with 1 m/s after leaving the spacer. Thus the attachment of the Optimiser results in the aerosol particles being inhaled at the velocity of the inspired air, about 1.5 m/s.

Drug deposition studies were carried out in eight healthy subjects, aged 22–54 years. All gave informed consent and the study was approved by the Ethics Committee of Nottingham University Medical School and the Administration of Radioactive Substances Advisory Committee (ARSAC) of the Department of Health.

Canisters of beclomethasone dipropionate 100 μg/actuation were radiolabelled to deliver 10 MBq technetium-99m per dose at the time of administration (Hardy et al., 1993). Andersen impactor deposition studies confirmed that the radiolabelling did not affect the particle size distribution and that the technetium deposition matched that of the drug. Each subject was dosed with a single actuation from the Easi-Breathe inhaler on two occasions at least 2 days apart, in a randomised order, with and without the Opti-

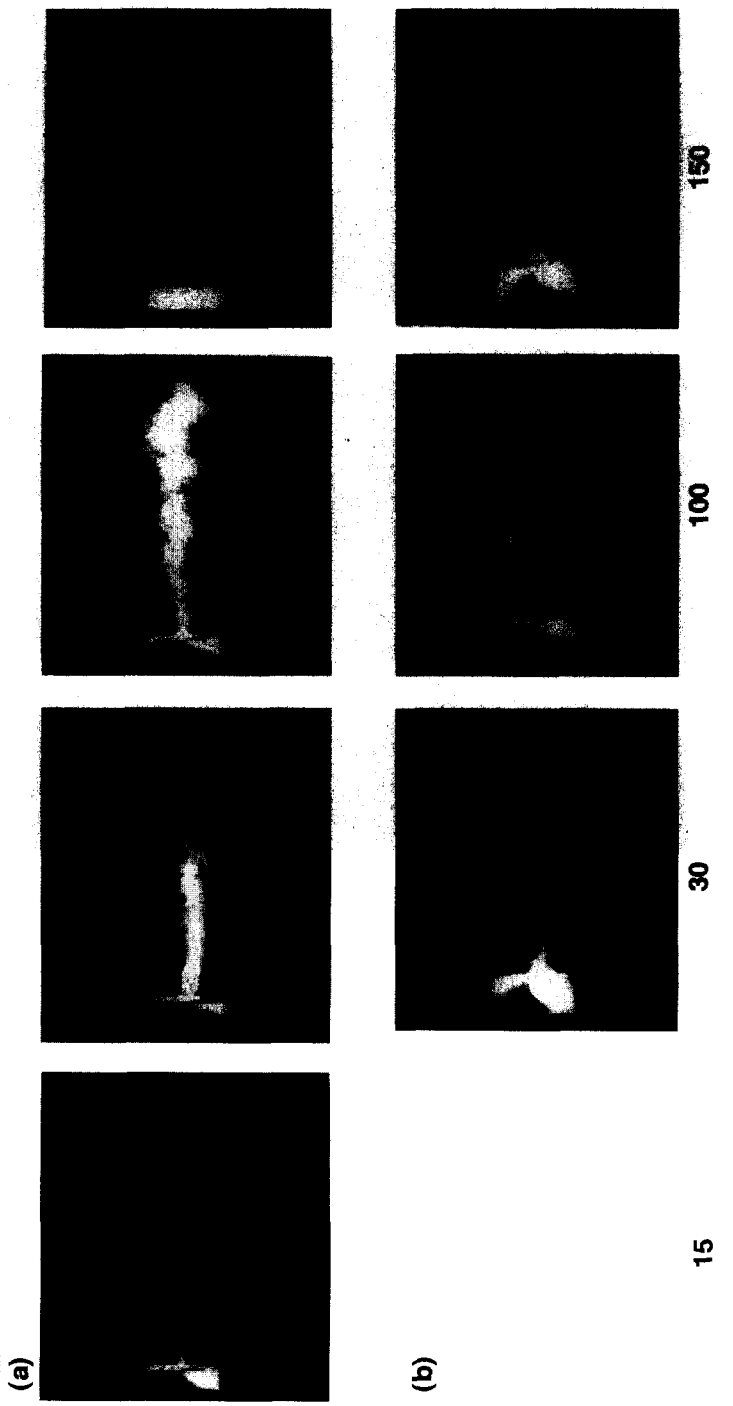
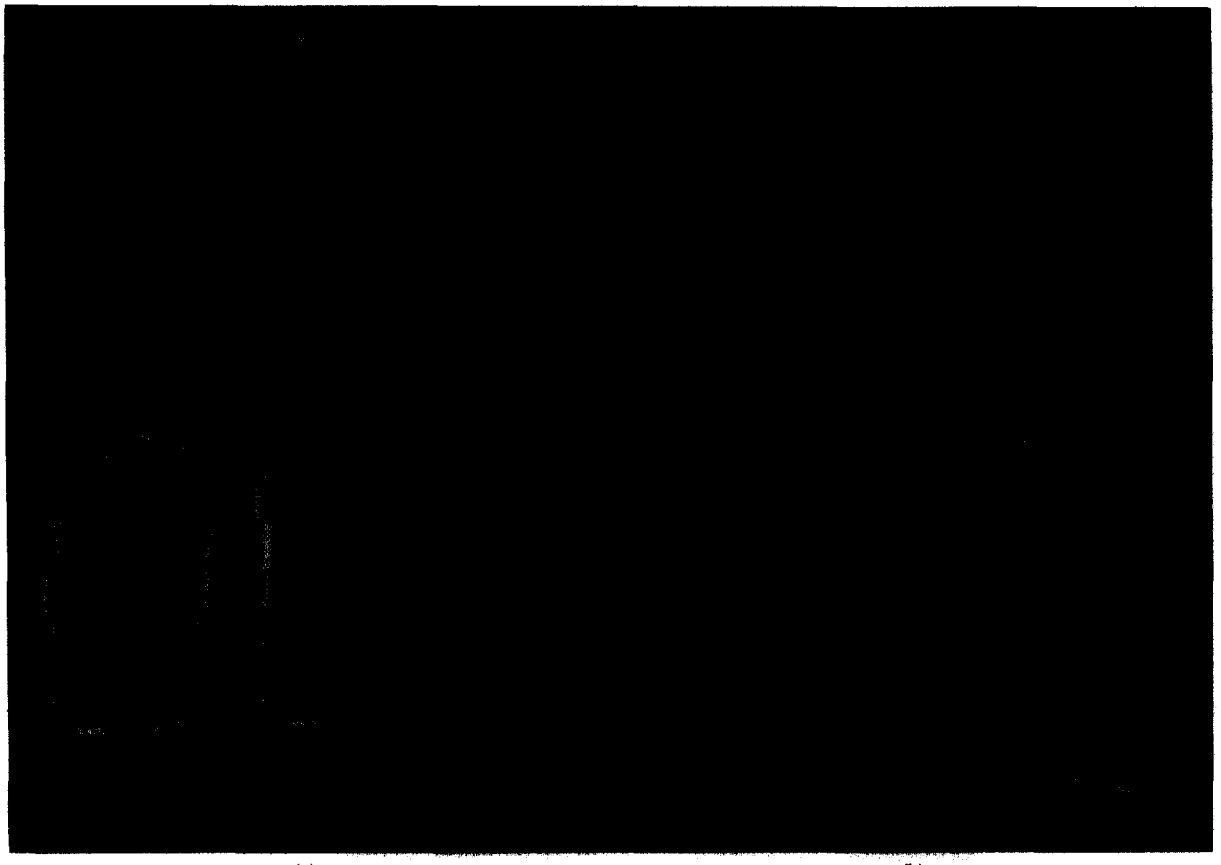


Fig. 1. Aerosol flumes from (a) the actuator and (b) the spacer.



(a) (b)

Fig. 2. Drug deposition in the same subject from the Easi-Breathe inhaler (a) without a spacer and (b) with the Optimiser.

miser spacer. The distribution of the radioactivity was recorded using a gamma camera. Transmission images with technetium-99m and an image with the subject inhaling krypton-81m were also recorded. The count rates detected were corrected for background counts, radioactive decay during the imaging period, and attenuation of the radiation by the geometric mean method (Forge et al., 1993). Data were expressed as proportions of the dose.

Imaging showed that a mean of 55% of the dose was deposited in the Optimiser spacer. The effectiveness of the spacer in removing the large aerosol droplets is apparent in the gamma camera images recorded 2 min after dosing (Fig. 2). The spacer reduced the oropharyngeal deposition by 80%, in agreement with previous findings in which small spacers have been shown to reduce oropharyngeal deposition by over 70% (Ashworth et al., 1991; Hardy et al., 1993).

The use of the Optimiser spacer with the Easi-Breathe breath-operated inhaler offers the advantages of improved co-ordination and reduction in oropharyngeal deposition compared with dosing from a standard MDI, without compromising the fine particle dose.

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