Drug Development and Industrial Pharmacy, 24(11), 1083–1088 (1998)

COMMUNICATION

Measurement of Electrostatic Charge Decay in Pharmaceutical Powders and Polymer Materials Used in Dry Powder Inhaler Devices

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ABSTRACT

The electrostatic charge generated on drug/excipient particles during the formulation, manufacture, and use of pharmaceutical dry powder inhaler (DPI) devices may significantly affect the performance of such devices. An experimental investigation has been undertaken of charge accumulation and decay on compacts of selected powders (lactose and salbutamol sulfate) and a device material (polyvinyl chloride, PVC) used during the formulation, manufacture, and use of DPIs. Significant differences in charge acquisition and decay for the three materials have been demonstrated after charging using a corona electrode. PVC acquired the highest charge, which decayed rapidly in 30 min toward the value prior to exposure to corona. Lactose and salbutamol acquired similar charge values, which decayed to zero after 30 min for lactose, whereas salbutamol retained a significant charge after 120 min. The significant differences in charging propensity among drug, excipient, and device materials may have relevance in DPI formulation, manufacture, and use.

INTRODUCTION

Triboelectrification describes a contact charging process involving friction and sliding effects; it is frequently encountered during pharmaceutical powder processing operations and has been identified in the mechanisms of adhesion and cohesion (1). Interparticulate or particle/substrate collisions invariably lead to a net electrostatic charge on a powder sample that may be positive or negative and is often a complex bipolar system (1,2). Triboelectrification has been shown to be influenced by several factors, including particle shape and size (3), nature

and work function of the contacting materials (4), contact area and frequency (5), surface roughness and purity (6), and atmospheric conditions (7).

Dry powder inhaler (DPI) formulations often consist of small quantities (<1% w/w) of micronized (<5 μm) drug particles (e.g., salbutamol) adhered to coarser (70–90 μm) excipient particles (e.g., crystalline lactose), ideally forming an ordered mix. The liberation of drug following delivery from an inhaler device will permit deposition in the respiratory tract; however, deep lung deposition from dry powder complexes is small and variable. For instance, 5% (w/w) (8) and 16% (w/w) (9) have been quoted and attributed to inertial deposition in the oropharynx region and adhesion/cohesion effects. The electrostatic charge on drug/excipient particles acquired from particle/substrate or interparticulate contact and discharge after triboelectrification (10) may affect mixing performance, passage through the inhalation device, and deposition in the respiratory tract (11).

Due to the lack of detailed work in the literature and the suggested strong influence of electrostatic charging during the formulation, manufacture, and use of DPIs, there is a clear need to investigate the charge acquisition and decay, as well as interactions between charged materials and a substrate. The principal aim of this work was to develop a system to investigate the charge and discharge properties of pharmaceutical drugs/excipients and materials (e.g., polymers) used in DPI formulation, manufacture, and use. An increased understanding of the role of electrostatic phenomena in DPI technology will contribute to the knowledge required to improve the manufacture of, and drug delivery from, DPIs.

EXPERIMENTAL

Materials

The materials used were salbutamol sulfate BP (micronized; GlaxoWellcome), crystalline lactose BP (Lactochem), and polyvinyl chloride (PVC) porous powder (Corvic, ICI).

Methods

Sample Preparation

The unlubricated powder samples (approximately 35 mg) were compressed by manual operation (Manesty F1 single punch) to produce flat-faced cylindrical tablets of 4.8-mm diameter. The tablets were stored in closed containers in air of 0.8% relative humidity (RH) prior to charging.

Sample Charging

A compact was placed on an earthed surface and exposed to a corona charging needle (−1.1 kV) for 3 min at a separation distance of 300 μm under ambient conditions (12).

Charge Decay Using Faraday Well

The magnitude/sign of the charge was determined immediately and then at selected time intervals by transferring the compact using an earthed instrument to a Faraday well connected to an electrometer (Keithley 610C). The charge and charge decay were determined for 15 compacts of each of the three materials.

Charge Decay Using Capacitive Probe

The compacts were transferred to the earthed stainless steel substrate of an apparatus incorporating a high-resolution capacitive probe system (Fig. 1) (13), and the surface charge was mapped at a probe separation distance of 100 μm at chosen time intervals. The sample under investigation was placed on the rotating steel turntable (30 rpm; 5-cm diameter) that was stepped under computer control to allow radial scanning. The fixed capacitive probe (25-μm sensing head) provided a signal that was amplified and digitally converted using a PC30AT (Amplicon) converter to provide voltage-time traces. These experimentally determined traces were in the form of a derivative signal to improve resolution, and mathematical integration was necessary to recover the true voltage-time trace. Approximately 30 traces were collected for each sample as the sample was progressively advanced beneath the probe, and these traces were grouped (Surfer, Golden Software, Inc.) for display as 3-D charge profile plots. A short vertical metal wire charged to a known potential was to be used to calibrate the system and estimate the signal broadening function; however, this was not installed for this work, so arbitrary units are used to represent charge values.

RESULTS AND DISCUSSION

Data obtained and results calculated for preliminary charge measurement using the Faraday well are displayed in Table 1 for compacts of salbutamol sulfate, lactose, and PVC. The specific charge (nC g^{-1}) was calculated for each material, and the results represent the mean (% coefficient of variation, cv) of charge measurement for 15 compacts. Generally, the results presented in Table 1 indicate that salbutamol, lactose, and PVC compacts have

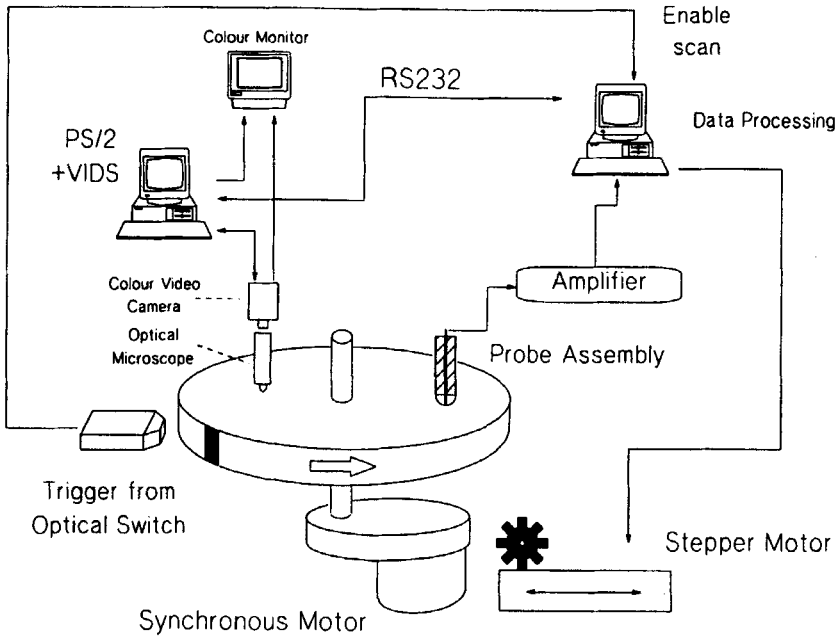

Figure 1. Schematic of capacitive probe apparatus.

different charge accumulation and decay properties. PVC acquired the highest charge from the corona device (-16.9 nC g^{-1}), which decayed almost to the intrinsic charge (charge before exposure to corona) after 30 min. Lactose and salbutamol acquired similar charges from the corona device (-7.4 and -7.8 nC g^{-1}, respectively), which were significantly lower than the charge acquired by PVC ($p < 0.05$). The charge decayed to zero after 30 min for lactose, whereas salbutamol retained a significant charge (-3.3 nC g^{-1}) after 120 min. Differences in intrinsic electrical properties among lactose, salbutamol sulfate, and PVC have been demonstrated previously (14), with lactose compacts giving lower values for capacitance (2.65 pF) than salbutamol sulfate (3.49 pF) under ambient conditions, with PVC showing considerably higher values (6.95 pF). An association between charge accumulation and capacitance of the three samples and the sources of differences in their electrical properties is to be investigated.

Figures 2–4 illustrate the mean charge decay of three tablets of salbutamol sulfate, PVC, and lactose, respectively, following corona charging and scanning with the capacitive probe. These curves were constructed by taking the maximum values from 3-D charge profile plots;

Table 1

Preliminary Charge Values Measured by Faraday Well for Salbutamol Sulfate, Lactose, and PVC Compacts Before and After Corona Exposure

Material	Compact Mass (mg) (% cv)	Mean Charge (nC g^{-1}) Immediately Before Charging	Mean Charge (nC g^{-1}) Immediately After Charging	Mean Charge (nC g^{-1}) After 30 min	Mean Charge (nC g^{-1}) After 120 min
Salbutamol	33.8 (7)	−0.27 (67)	−7.8 (25)	−4.1 (21)	−3.3 (26)
Lactose	40.9 (3)	0.00 (—)	−7.4 (34)	0.00 (—)	0.00 (—)
PVC	35.7 (1)	−1.06 (56)	−16.9 (14)	−2.7 (52)	−1.8 (17)

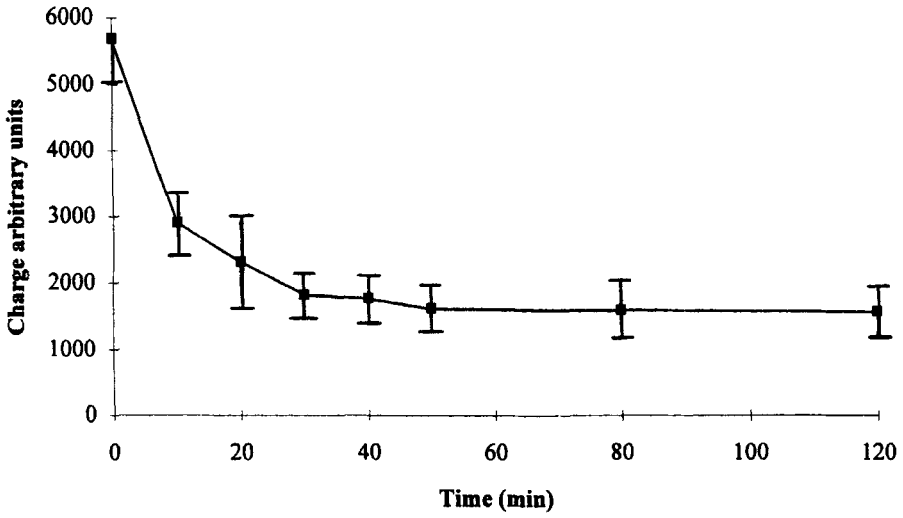

Figure 2. Charge decay of salbutamol sulfate compact.

a selected example is shown in Fig. 5, which represents the charge distribution over a salbutamol sulfate compact immediately after corona exposure. Figures 2–4 confirm differences in charging and charge decay, with salbutamol sulfate retaining a significant charge after 120 min. Coelho and Ecopol (15) suggested that charge decay should follow an exponential route provided the mechanism of decay is by conduction and the material is ohmic, that is, the current passing through the sample is proportional to the potential difference applied. Insulating materials such as those used for this study are unlikely to be ohmic, but by approximation, it is possible to construct plots of ln charge versus time and thus calculate decay rate constants for each material (Table 2).

The values in Table 2 show the highest decay rate for lactose (0.12 min^{-1}) and a higher decay rate for PVC (0.08 min^{-1}) than salbutamol sulfate (0.03 min^{-1}), which confirms the preliminary findings of this study. The results from this work provide a good estimate for charge decay that clearly differentiates the charge decay properties for the three substances.

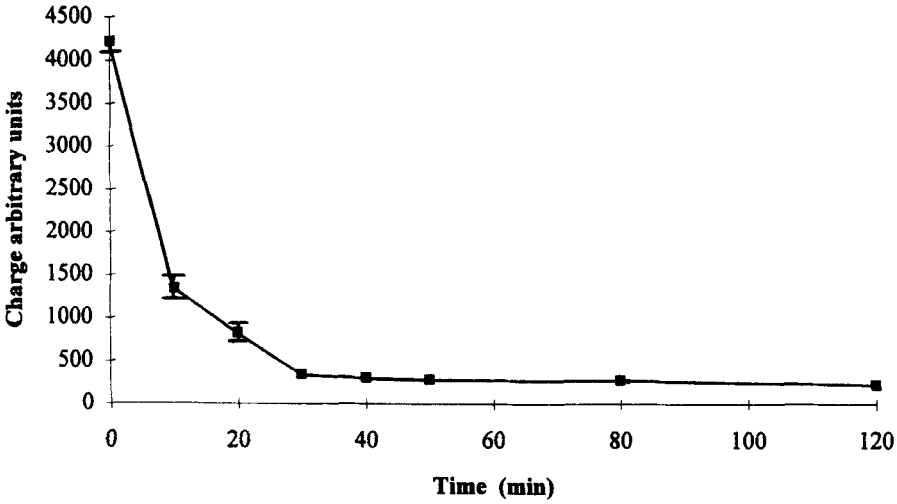

Figure 3. Charge decay of PVC compact.

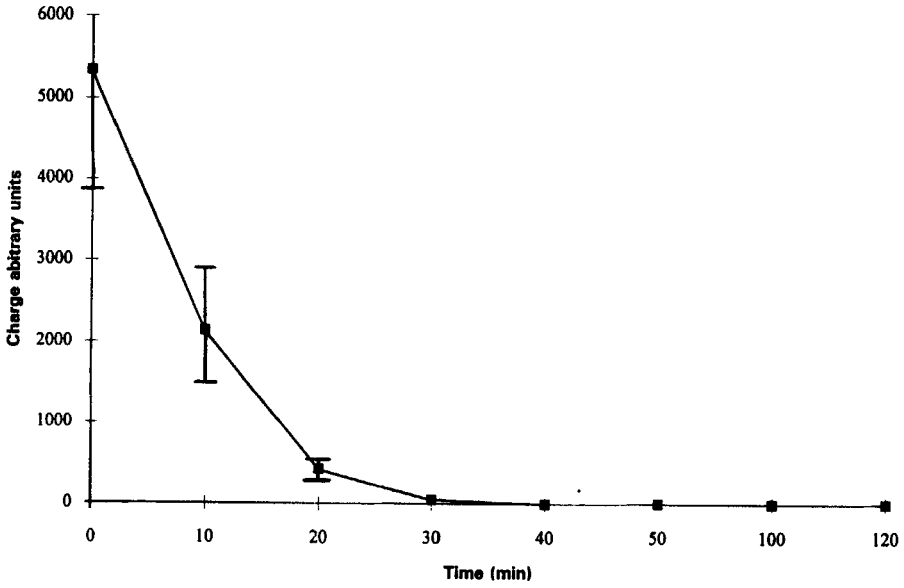

Figure 4. Charge decay of lactose compact.

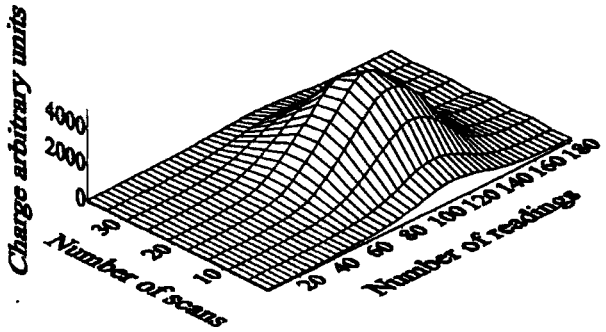

Figure 5. Charge distribution over a salbutamol sulfate compact.

CONCLUSIONS

The measurement of charge and charge decay on pharmaceutical powders and a polymer used in DPIs has been undertaken using a (1) Faraday well method and (2) capacitive probe method. Differences in charging and charge decay after exposure to a corona needle have been demonstrated with both methods among salbutamol sulfate, lactose, and PVC compacts. These preliminary findings show significant differences in charging propensity among drug, excipient, and device materials that may have relevance in DPI formulation, manufacture, and use. The methods used in this study will enable further detailed investigations of powders and DPI device materials to be undertaken under controlled charging conditions.

Table 2

Decay Rate Constants for Salbutamol Sulfate, Lactose, and PVC

Material	Decay Rate Constant (min^{-1})
Salbutamol	0.03
Lactose	0.08
PVC	0.12

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