PHARMACEUTICAL TECHNOLOGY

Effects of Electrostatic Charging on Pharmaceutical Powder Blending Homogeneity

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ABSTRACT: During the pharmaceutical powder blending process, electrostatic charges generate and accumulate unavoidably due to particle–particle and particle–wall collision. The effect of electrostatic charging on pharmaceutical powder blending homogeneity was investigated on two binary blending systems: (1) lactose as an excipient with caffeine as an Active Pharmaceutical Ingredient (API) and (2) Microcrystalline Cellulose (MCC) with caffeine. Three different blending procedures were conducted: (1) conventional blending without any charge control, (2) blending with simultaneous charge neutralization, and (3) blending combined with a corona charging process. It was found that the average API concentration variation increases with the increase of charge-to-mass ratio of final blend samples. In other words, the presence of uncontrolled electrostatic charges has an adverse effect on powder blend uniformity. Elimination or minimization of electrostatic charges also appears to have a negative impact on powder blend uniformity. In contrast, blending of positively charged excipient material and negatively charged API material leads to a better blend uniformity. The controlled electrostatic charging opens an opportunity for improving uniformity of the pharmaceutical blending process. © 2008 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 98:2412–2421, 2009

Keywords: electrostatic charges; blend homogeneity; charge neutralization; corona charging

INTRODUCTION

Most pharmaceutical powders are dielectric materials and are often unavoidably charged during manufacturing process due to inter-particle and particle–wall collisions. The electrostatic charges of both positive and negative polarities give rise to attractive or repulsive electrostatic forces between the individual particles. As a result, electrostatic charging may cause the agglomeration or segregation of particles during powder dispersion, transport, and other handling process.

Previous studies found that charged particles may lead to the contamination of equipment as the charged particles adhere to the inner walls. The contaminating particles have significant

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effects on the charging behavior of powders and thus introduce variations in charging during the processing.[1–3] A study carried out by Murtomaa and Laine[4] showed that the charging behavior of glucose might be drastically changed with the addition of lactose particles into the powder flow. Lactose tended to adhere to the contact surface more easily than glucose. This resulted in the electrostatic separation and the variation of the powder concentration until a steady state of charging was reached.[4,5]

Electrostatic charging also has significant effect on powder blending performance. For example, it was found that the total adhesion forces between drug and excipient particles decreased with the electrostatic charge decay during storage.[3] In another case, the active pharmaceutical ingredient (API) concentration changed in dry powder inhalation (DPI) formulations after triboelectrification with steel and polyamide contact surfaces.[6] In Staniforth's work[2] it was observed that optimization of the triboelectric charging conditions may improve the stability of the ordered powder mix. When the drug and excipient particles carried opposite charges, the mix was less prone to segregation.

In the current study, the effect of electrostatic charging on pharmaceutical powder blending homogeneity was investigated systematically. Three different types of blending experiments were conducted. The first was the conventional blending process without any control on electrostatic charges. The second blending process was carried out while neutralizing the charge with a charge neutralization apparatus. The third experiment was carried out by first charging the excipient and the API powders with opposite polarities and then by mixing the excipient and API components carrying opposite charges. The polarity and magnitude of charging of powder was controlled by using a corona charger. The blending homogeneity of the mixture after each blending method was then analyzed to see how the presence of electrostatic charges affected the blend quality.

EXPERIMENTAL

Materials

Two kinds of excipient materials were used in the experiments: one was lactose (Pharmatose® DCL14, DMV International, Veghel, The Netherlands); the other was Micro-crystalline Cellulose (MCC; Celphere® CP-102, Asahi Kasei Chemicals Corporation, Tokyo, Japan). The API in the binary blending system was anhydrous caffeine (CAS Number: 58-08-2, Sigma–Aldrich, St. Louis, MO). The materials used in the experiments were stored at ambient condition ($23 \pm 2^{\circ}$C, $42 \pm 3\%$ RH). All the blending experiments in this study were carried out at the same condition.

Blending Process With Uncontrolled Electrostatic Charges

A cylindrical stainless steel blender with a diameter of 45 mm and a height of 21 mm was used in these blending experiments. Lactose was loaded from the top of the blender followed by the addition of caffeine into the blender. The materials were blended for 30 min with a constant rotational speed of 10 rpm and a fill volume of 40%. A total of 10 samples were taken from the final blend using a grounded metal spatula. This is to minimize the effect of extra charges brought by the spatula itself and/or generated during sampling on the surface charges of the samples taken. Five samples were scooped from the top of the powder bed (one spot at the center and the other four near to the wall, at the upper, lower, left, and right position to the center, respectively); the other five samples were taken from the bottom following the same pattern. The same sampling procedures were used throughout the study. The sample weight was around 1–1.5 g, comparable to the weight of a tablet dose. The net charge-to-mass ratio of each sample was determined by using a Faraday Cup and an Electrometer (Model 210-HS, Trek Inc., Medina, NY) together with a balance (Mettler Toledo, Greifensee, Switzerland). Subsequently, the concentration of caffeine in each sample was analyzed by an UV spectrophotometer (Model 8452A, Hewlett Packard, Palo Alto, CA) at the wavelength $\lambda = 274$ nm. The same experiment was repeated three times and a total of 30 samples were collected and analyzed in the end.

The blending experiments were conducted for four binary systems including lactose–2 wt% caffeine system, lactose–5 wt% caffeine system, lactose–10 wt% caffeine system, and MCC–5 wt% caffeine system. In addition, another blending experiment was implemented on the lactose–5% caffeine system where the pure lactose particles