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Influence of relative humidity on the electrostatic charging of lactose powder mixed with salbutamol sulphate

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ABSTRACT

In this study, electrostatic charging of lactose and its mixtures with salbutamol sulphate (SS) were studied as a function of relative humidity (RH). Powder adhesion onto a steel pipe surface was also investigated. The powders were charged by sliding in a steel pipe. Increase in RH decreased the charging of lactose and mixtures, but the effect on SS was not evident. Furthermore, the charge of the mixtures reversed from negative to positive as RH was increased and remained positive as the samples were again dried. Humidification also changed the adhesion behavior of the mixtures onto the pipe surface.

1. Introduction

Electrostatic charging, or triboelectrification, of powders has a significant effect in the pharmaceutical industry. The charging arises from powder–powder and powder–surface contacts. The packing behavior, flowability, and manufacturing of powders, among other things, may be hampered as a result [1]. In dry powder inhalers (DPIs), the drug is mixed with an additive powder, for instance with lactose, in order to improve the dosing accuracy and the flowability of the drug particles [2–4]. Frictional contacts with these two unlike powders cause bipolar charging which can lead to different problems [5–7]. The oppositely charged drug particles may adhere on the carrier particles and end up in throat instead of lungs [8]. Moreover, if electrostatic separation occurs during the transportation, mixing, or handling, the concentrations of the drug–additive mixtures may considerably differ from the planned concentrations [8]. The charging may be reduced, for example, by increasing humidity since it drastically decreases resistivity [9–13]. However, the powders used in pharmaceutical industry are often sensitive to moisture.

Salbutamol sulphate (SS) is a common antiasthmatic drug which is typically used by DPIs as an immediate treatment of asthma [14]. Charging of SS and lactose has been studied previously, for instance, by Rowley [15] and Elajnaf et al. [11]. Rowley concluded that lactose particles adhering to the inner surface of a cyclone charger resulted in lower specific charge values for lactose than with a clean surface. He also noticed that as the amount of SS was increased in lactose–SS mixtures, the specific charge decreased, and that in single powder systems the bigger particles tended to charge less than the smaller particles. Elajnaf et al. on the other hand charged these same powders, among others, in a cylindrical mixing vessel in different relative humidities. They observed, for example, that the specific charge of powders and adhesion of SS to a surface reduced as humidity was increased.

In this study, SS in pure form and as mixtures with lactose monohydrate was charged by sliding in a steel pipe. Sliding experiments with a steel pipe were used to simulate transportation circumstances in various humidities. The charging was also studied as a function of the amount of powder adhered onto the surfaces since it has been reported that the triboelectrification may strongly change when the surface gets contaminated by adhered powder particles [5,16–18].

2. Materials and methods

2.1. Materials

Lactose monohydrate and micronized SS samples were supplied

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by Orion Oyj (Espoo, Finland) and were used as received. In addition to pure samples, mixtures containing 1.0 wt% and 2.0 wt% of SS in lactose were studied to simulate the concentrations in DPIs.

2.2. Scanning electron microscopy

Scanning electron microscope (SEM) images were taken with Zeiss Sigma VP field emission SEM (Germany). The SEM samples were sputter coated with platinum before the imaging.

2.3. Charge and adhesion measurements

The charging measurement set-up consisted of a grounded pipe of stainless steel (length 500 mm, inner diameter 25 mm) with the angle of 50° in relative to horizontal level (Fig. 1). Prior to each set of measurements, the pipe was carefully cleaned with tap water, purified water, and ethanol. Powder samples with a typical mass of 0.05–0.1 g were charged by sliding in the pipe. After sliding, the powder samples dropped into a plastic cup that was inside a Faraday cup. The charge Q was measured with a Keithley 6514 electrometer (Keithley Instruments). The slid powder sample was weighed together with the plastic cup in order to observe the sample mass m. Furthermore, charge-to-mass ratio or the specific charge Q/m was calculated. This was repeated, without cleaning the pipe, until approximately 4 g of powder was transferred. For pure SS, the measurements were made until 2 g was collected due to limited amounts of samples available. The mass of the inserted powder was also weighed in order to determine the amount of powder, which adhered onto the pipe.

The relative humidity (RH) of the surrounding air was varied from 36 RH% to 93 RH% with an air conditioner. RH was measured right next to the pipe using Humicor type HRT probe (Coreci, Lyon). When humidity had reached steady state, the samples were placed on flat metallic sample containers on a grounded table. This ensured that the samples had absorbed water from the surrounding air before the measurements and that any initial charge on the particles would decay to ground.

The powder samples were inserted into the pipe with a grounded metallic spatula under an AC neutralizer to minimize the sampling charging. In a previous study it was shown that the sampling charge with this arrangement is negligible [18]. In addition, the set-up as well as the measurer were all grounded. When weighing the samples, the plastic cup that contained the sample was sealed with aluminum foil. The scale was also wrapped with aluminum foil both on the inside and on the outside. The arrangements were made to ensure that the electric forces caused by the charged powder would not affect the weighing.

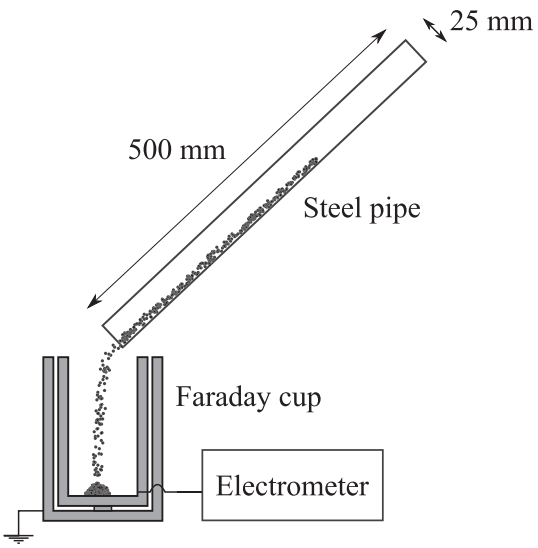

Fig. 1. The measurement set-up (not to scale).

2.4. Gas perfusion calorimetry

Isothermal gas perfusion calorimetric (IGPC) measurements were performed with TAM 2277 Thermal Activity Monitor (Thermometric Ab, Sweden) equipped with a gas perfusion accessory. Pure lactose, SS and a 1.0% SS–lactose mixture were weighed into stainless steel ampoules for the measurement. The samples were exposed to a sequence of humidification (95 RH%) and drying steps (0 RH%) over a 24 h period. For reference purposes, a sample of the SS–lactose blend was preconditioned by storage for at least 16 h at 25 °C under 94 RH%, generated by a saturated KNO_3 solution.

3. Results and discussion

3.1. SEM images

SEM images of lactose and SS are presented in Fig. 2. From the images, it can be seen that the particle size range of lactose was broad: the size of the largest particles were some hundreds of microns whereas the fines were 1 μm in diameter. The coarse lactose particles were covered with fine lactose particles. The largest of the micronized SS particles were elongated but the fines were more spherical.

3.2. Charge measurements

3.2.1. Lactose

The specific charge of lactose as a function of the cumulative mass of the powder transferred down the steel pipe in different relative humidities is presented in Fig. 3a. In the figure, each data point represents one sliding. It can be noticed that increasing the relative humidity from 36 RH% to 93 RH% decreased the charging distinctly from -5.4 ± 0.8 nCg^{-1} to -0.5 ± 0.2 nCg^{-1}, respectively, even though the absolute value of the charge at 54 RH% (-0.7 ± 0.1 nCg^{-1}) was slightly smaller than at 73 RH% (-1.2 ± 0.3 nCg^{-1}). Additionally, at a low humidity, the measured values had more variation than in higher humidities.

3.2.2. Salbutamol sulphate

As seen in Fig. 3b, the effect of relative humidity for charging of SS was indistinct. As a function of the cumulative mass of powder transferred, the charge values decreased slightly: In the beginning of the measurements, the specific charge was up to $+15.5$ nCg^{-1} but decreased to approximately $+5$ nCg^{-1} at the end of the measurements. Fluctuation of the values diminished to some extent as more powder was fed into the pipe.

3.2.3. Lactose–SS mixtures

The specific charge of mixture containing 1.0% of SS in lactose is presented in Fig. 3c. First, at humidities 36 RH% and 54 RH%, the mixture charged negatively to -3.3 ± 0.6 nCg^{-1} and -3.0 ± 0.9 nCg^{-1}, respectively. After this, when humidity was increased to 73 RH%, the sign of the charge changed to positive and the average was $+1.2\pm0.4$ nCg^{-1}. When the humidity was further increased to 93 RH%, the charge dropped to very close to zero, while the small measured values were still positive. After the humidification, measurements were made at 35 RH% to see whether the sign would change back to negative. However, the charge values were yet again positive, average value being $+11.6\pm2.1$ nCg^{-1}.

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