J. Pharm. Pharmacol. 2000, 52: 13–17
Received July 5, 1999
Accepted August 16, 1999

Triboelectrification of Spray-dried Lactose Prepared from Different Feedstock Concentrations

ORLA E. CASSIDY, PAUL A. CARTER, GEOFF ROWLEY AND DAVID R. MERRIFIELD*

*Institute of Pharmacy and Chemistry, University of Sunderland, Sunderland, and *SmithKline Beecham Pharmaceuticals, Worthing, West Sussex, UK*

Abstract

Powder systems may acquire electrostatic charge during various pharmaceutical processing operations and may give rise to difficulties in handling and powder flow, mainly due to adhesion/cohesion effects. We have investigated the electrostatic charging of spray-dried lactose prepared from different feedstock concentrations using a laboratory spray-dryer.

Triboelectrification of the spray-dried lactose samples was effected through contact with the stainless steel surface of either a mixing vessel or a cyclone separator. Results from both techniques showed differences in charge accumulation and particle-steel adhesion between the spray-dried lactose samples. As the feedstock concentration used to produce the spray-dried lactose was increased in the range 10–50% w/v, the mean charge on the lactose decreased from $-20{\cdot}8$ to $-1{\cdot}3\,\mathrm{nC\,g^{-1}}$ and $-54{\cdot}9$ to $-4{\cdot}1\,\mathrm{nC\,g^{-1}}$ for the mixing vessel and cyclone separator, respectively, with a corresponding decrease in adhesion. In addition, as the feedstock concentration was increased from 10 to 50% w/v, decreases were obtained in surface area values (1·06 to $0{\cdot}56\,\mathrm{m^2\,g^{-1}}$), pore diameter (198·7 to 83·5 μm) and pore volume (1·09 to $0{\cdot}75\,\mathrm{cm^3\,g^{-1}}$), and together with differences in crystal form correlated with the charge and adhesion results.

The results suggested that the feedstock concentration could have a considerable influence on the charging and adhesional properties of spray-dried lactose. This may have relevance during pharmaceutical processing and manufacturing operations.

Electrostatic charge of powder systems arising from triboelectrification during processing operations, e.g. milling, mixing and pneumatic transport, may give rise to powder cohesion and particle adhesion to the surface of the processing equipment. Interparticulate or particle/substrate collisions lead to charge accumulation which is influenced by several factors, including particle size and shape (Carter et al 1992, 1998), contact area and frequency of contact (Lowell 1990), nature and work function of the contacting materials (Elsdon & Mitchell 1976; Bailey 1984), contact surface roughness and contamination (Eilbeck et al 1992, 1999), and atmospheric humidity (Nguyen & Nieh 1989; Mackin et al 1993).

Spray-dried lactose is a commonly used pharmaceutical excipient produced from a suspension of crystalline lactose in saturated lactose solution. The spray drying process involves atomization of the liquid into a spray, spray/air contact, drying of the spray and separation of the particulate solid (Masters 1991). The characteristics of spray-dried powders, e.g. particle size and shape, bulk density, flow, moisture content and porosity, are influenced by the choice of operating conditions (Fell & Newton 1971). This work addresses the hypothesis that differences in charging tendency may exist between samples of spray-dried lactose prepared from a range of feedstock concentrations.

Correspondence: O. E. Cassidy, Institute of Pharmacy and Chemistry, University of Sunderland, Sunderland, UK.

Materials and Methods

Preparation of spray-dried lactose

Feedstocks in the range (10–50% w/v) were prepared by heating aqueous solutions or suspensions of microfine ($<10\,\mu$m) α-lactose monohydrate (Lactochem) for 1 h at 50°C. The feedstocks were introduced with constant stirring into the laboratory

spray-dryer (Buchi 190) at 6 mL min^{-1} with inlet and outlet temperatures of 115 and 52–58°C, respectively. The samples were further dried under vacuum and silica gel at 60°C for 24 h and stored in sealed glass containers before characterization and charge measurement.

Characterization of spray-dried lactose

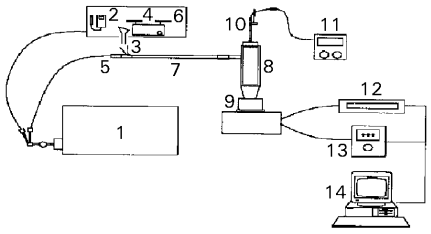
Moisture content of the samples was determined gravimetrically after storage under vacuum and silica gel at 60°C. Following storage, particle size distribution was determined using laser light scattering (Malvern Mastersizer 2600) for each sample dispersed in *n*-butanol following sonication for 10 s. Scanning electron microscopy (Stereoscan 200, Cambridge Instruments) provided photomicrographs of surface features. Specific surface area, particle density, pore size and specific optical rotation were determined using nitrogen gas adsorption (Flowsorb II 2300, Micromeritics), helium pycnometry (Accupyc 1130, Micromeritics), mercury porosimetry (Poresizer 9310, Micromeritics) and polarimetry (ADP220, Bellingham and Stanley), respectively.

Charging with Turbula apparatus

Preliminary charge studies at approximately 40% relative humidity (r.h.) were undertaken by agitating 1·0-g samples of the spray-dried lactose in a 0·1-L cylindrical stainless steel mixing vessel on a Turbula mixer (Glen Creston TC2) at 30 rev min^{-1} for 2 min (Mackin et al 1993; Carter et al 1998). Samples were then poured in a reproducible manner over a 1-min period into a Faraday well connected to an electrometer (Keithley 610C) to measure charge. Powder adhesion to the inside surface of the mixing vessel was determined after each charging procedure using a qualitative scale as follows: 0 absent; 1 low; 2 moderate (approximately half the surface covered); 3 extensive.

Charging with cyclone apparatus

The cyclone apparatus described previously (Carter et al 1992, 1998; Eilbeck et al 1999) incorporated pneumatic powder feed, triboelectric charging via a stainless steel cyclone separator, and charge and mass measurement using a modified Faraday well (Figure 1). The spray-dried lactose samples (1·0 g) were fed into the venturi system via the stainless steel vibratory feeder and conveyed along the stainless steel horizontal pipe using dry compressed air (Jun-Air 2000) at 8 m s^{-1} and $< 10\%$ r.h. An alpha polonium-210 radioactive charge neutralizer



1 Compressor
2 Relative humidity probe
3 Venturi funnel
4 Vibratory feeder
5 Ionization nozzle
6 Sealed chamber
7 Feed pipe
8 Cyclone
9 Faraday well and balance
10 Pitot tube
11 Flow meter
12 Balance electronics
13 Electrometer
14 Computer

Figure 1. Cyclone apparatus for electrostatic charge measurement of powders.

(Eilbeck et al 1992) was used to establish a baseline charge on the powder before entry into the cyclone separator via a tangential input pipe. The powder was separated from the carrier gas following triboelectric charging through contact with the cyclone wall and deposited in the Faraday well connected to an electrometer (Keithley 610C) and force compensation load cell (Precisa 400M) for real time measurement of charge and mass, respectively. Drug adhesion to the inside surface of the cyclone was estimated using the scale given above.

Results and Discussion

Characterization of spray-dried lactose

Data obtained and results calculated for yield, moisture content, particle size and particle density are shown in Table 1 for the spray-dried lactose samples produced from the range (10–50% w/v)

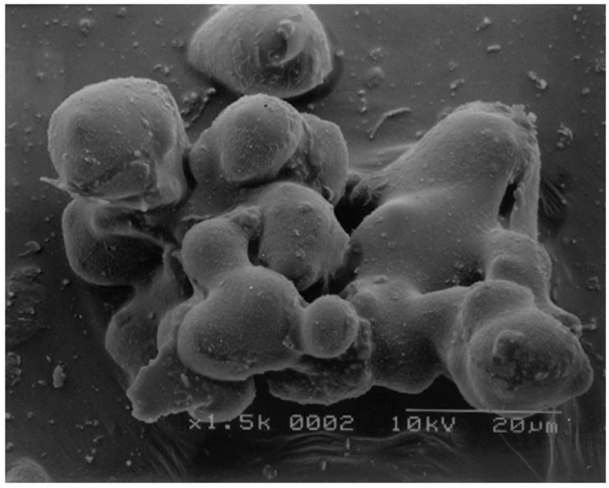


Figure 2. Photomicrograph of spray-dried lactose sample from 10% w/v feedstock concentration at magnification ×1500.

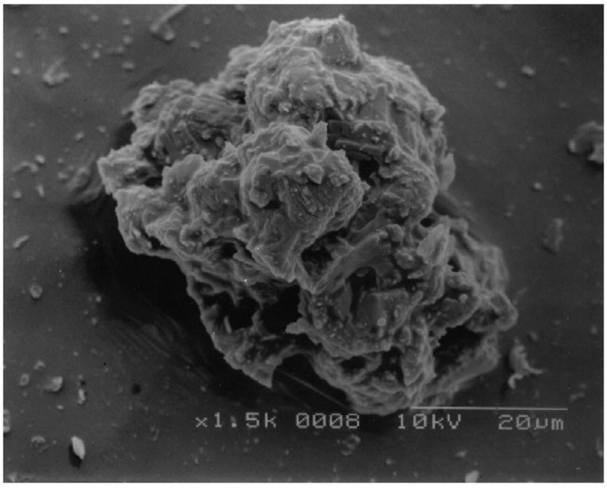


Figure 3. Photomicrograph of spray-dried lactose sample from 50% w/v feedstock concentration at magnification $\times 1500$.

of feedstock concentrations. The values show a decrease in yield with increase in feedstock concentration, due partly to the change in rheological properties of the feedstock from that of a solution to a slurry. The particle size distributions for the samples were similar for each feedstock concentration and within the approximate range of 5–110 μm, although the results in Table 1 show variation in size ranges and median values (22·9–34·4 μm) which does not correlate with feedstock concentration. Previous work (Fell & Newton 1970) suggested that lower concentration lactose feedstock solutions will give smaller particles than higher concentrations (up to 15% w/v), however this study did not demonstrate this with the 10% and 20% w/v lactose solutions giving median values of 27·8 and 22·9 μm, respectively. Surface area was found to decrease with increase in feedstock concentration and this effect may be due to differences in porosity between the samples, since a decrease in both pore size and cumulative pore volume with increasing feedstock concentration was demonstrated (Table 2). In addition, electron photomicrographs for spray-dried lactose samples

Table 2. Porosimetry and polarimetry of spray-dried lactose produced from a range (10–50% w/v) of feedstock concentrations.

Feedstock (% w/v)	Porosimetry		Polarimetry	
	Mean pore diameter (μm)	Cumulative pore volume ($cm^3\,g^{-1}$)	Percent α-lactose	Percent β-lactose
10	198·7 (46·5)	1·09	38·6 (1·2)	61·4 (1·2)
20	187·1 (34·2)	0·93	37·5 (1·4)	62·5 (1·4)
30	138·3 (31·6)	0·88	42·9 (0·9)	57·1 (0·9)
40	97·9 (37·5)	0·86	58·5 (2·1)	41·5 (2·1)
50	83·5 (0·4)	0·75	63·2 (2·5)	36·8 (2·5)

Standard deviation shown in parentheses.

from 10 and 50% w/v feedstock concentrations (Figures 2 and 3, respectively), provide evidence of larger pores and a more open structure for the 10% w/v sample. The spray-dried lactose sample from the 50% w/v concentration (Figure 3) suggests the presence of a crystalline α-lactose monohydrate structure whereas the sample from the 10% w/v concentration (Figure 2) shows predominantly amorphous material, indicated by a less irregular surface.

Charging with Turbula apparatus

Results for the charging investigations with the Turbula apparatus are shown in Table 3 for the spray-dried samples agitated in the stainless steel vessel. The specific charge ($nC\,g^{-1}$) was calculated for each sample and the results represent the mean (% coefficient of variation) for five determinations. The charge results are also presented as $nC\,m^{-2}$. The values in Table 3 show that all the samples gave a net electronegative charge following agitation in the vessel and low values for variation, however differences in charging tendency are shown between the samples with a decrease in the magnitude of charge and variation with increase in feedstock concentration. Stainless steel is found near the electropositive end of the triboelectric

Table 1. Characterization of spray-dried lactose produced from a range (10–50% w/v) of feedstock concentrations.

Feedstock (% w/v)	Yield (%)	Moisture content (% w/w)	Median size (μm) [10–90%]	Surface area ($m^2\,g^{-1}$)	Mean particle density ($g\,cm^{-3}$)
10	49·3	1·13	27·8 [5·8–107·1]	1·06	1·61 (1)
20	58·3	2·05	22·9 [4·7–80·6]	0·79	1·58 (2)
30	37·3	2·88	29·5 [6·2–77·8]	0·79	1·56 (1)
40	29·9	2·94	34·4 [7·7–90·5]	0·65	1·54 (0·1)
50	18·9	1·95	26·7 [6·4–108·5]	0·56	1·54 (0·1)

Percent coefficient of variation shown in parentheses.

Table 3. Charge values ($nC\,g^{-1}$) from the Turbula apparatus for spray-dried lactose samples produced from a range (10–50% w/v) of feedstock concentrations.

Feedstock (% w/v)	Mean charge ($nC g^{-1}$)	Mean charge ($nC\,m^{-2}$)	Adhesion score
10	−20·8 (1·8)	−19·6	1
20	−10·7 (0·8)	−13·4	1
30	−6·6 (0·7)	−8·3	1
40	−2·3 (0·4)	−3·5	0
50	−1·3 (0·4)	−2·3	1

Percent coefficient of variation shown in parentheses.

series (Ally & Klinzing 1985) and hence will theoretically readily donate electrons to lactose. Carter et al (1997) showed that when undertaking triboelectrification studies with powders in a closed vessel, the net charge acquired by the powder is influenced by the sample mass, the material of the contact surface and volume of the vessel. It was suggested that particle–particle interactions play an important role in governing the final net charge, and adhesion to inner surfaces enhances such interactions. However, adhesion of the spray-dried lactose in this vessel was generally low (Table 3) and thus the acquisition of charge was predominantly through metal/particle contact. Specific surface area, cumulative pore volume and mean pore diameter decreased as the feedstock concentration was increased. This evidence suggests that the contact area during triboelectrification may be different for the different spray-dried lactose samples and this may contribute to the overall differences in charge acquisition for these samples.

Polarimetry measurements on the samples (Table 2) revealed an increase in the % α content and a decrease in the % β content as the concentration of feedstock was increased. In addition, 8–10% w/w amorphous material was detected by differential scanning calorimetry (DSC 1B, Perkin Elmer) in the 10 and 20% w/w samples whereas samples produced from the higher feedstock concentrations did not show amorphous content. There is a correlation between the decrease in electrostatic charge and the increase of α-lactose and corresponding decrease in β-lactose in the spray-dried lactose samples, as the feedstock concentration was increased. This finding has important implications for spray-dried lactose excipients used commercially in direct tablet compression, where β-lactose may be present in small quantities. It is clear that further detailed work on the charging of α- and β-lactose would be useful in order to aid the interpretation of results for triboelectrification of spray-dried lactose.

Charging with cyclone apparatus

The values in Table 4 show the specific charge ($nC\,g^{-1}$) calculated for each spray-dried lactose sample for charging in the stainless steel cyclone apparatus and the results represent the mean (% coefficient of variation) for five determinations. The charge results are also presented as $nC\,m^{-2}$. As with the Turbula charging apparatus, the mean specific electronegative charge values for the samples decreased with increase in feedstock concentration, however higher magnitude electronegative charges were obtained for all samples with the cyclone due to increased triboelectrification in this apparatus. Generally, there was a greater extent of adhesion to the inner surface of the stainless steel cyclone than the mixing vessel for each sample, in addition to higher values for charge variation with the cyclone. Adhesion was greater for the lactose samples produced from the lower feedstock concentrations as shown by the values in Table 4 obtained by visual inspection of the inner cyclone surface. Further evidence for this effect is given by the reduction in powder deposited in the Faraday well for the spray-dried lactose from lower feedstock concentrations. For example, the mean values for powder deposition in the Faraday well ranged from 57% w/w for the lactose from the 10% w/v feedstock to 78% w/w for the lactose from the 50% w/w feedstock.

Adhesion may be due to high particle charge:mass ratios, surface asperities, contact surface roughness and particle deformation on substrate contact. However, the charge:mass ratio for the powder adhered to the inner surfaces of the apparatus was not determined in this particular study. Recent work in these laboratories with crystalline lactose has revealed a higher net charge:mass ratio for adhered powder than the powder initially deposited in the Faraday well. For example, crystalline lactose (median size 43·5 μm) gave a mean charge:mass ratio value for adhered powder ($-223\,nC\,g^{-1}$) that was considerably greater than the powder initially deposited ($-78\,nC\,g^{-1}$).

Table 4. Charge values ($nC\,g^{-1}$) from the cyclone apparatus for spray-dried lactose samples produced from a range (10–50% w/v) of feedstock concentrations.

Feedstock (% w/v)	Mean charge ($nC\,g^{-1}$)	Mean charge ($nC\,m^{-2}$)	Adhesion score
10	−54·9 (14·9)	−51·8	3
20	−40·3 (3·1)	−50·4	2–3
30	−16·9 (6·9)	−21·2	2
40	−10·1 (2·6)	−15·5	1–2
50	−4·1 (1·5)	−7·3	1–2

Percent coefficient of variation shown in parentheses.

Although particle–particle and particle–substrate interactions may be responsible for a complex bipolar charging in a system and hence affect the final net charge, in this study the high adhesion values were associated with high net negative charge values. The decrease in electrostatic and adhesional properties of the spray-dried lactose samples as feedstock concentration was increased was confirmed by both the high (cyclone) and low (mixer) energy triboelectrification processes.

This study has investigated the electrostatic charging of spray-dried lactose prepared from different feedstock concentrations and has demonstrated differences in charge accumulation and particle-steel adhesion between samples. Differences in surface area, porosity and crystal form of the spray-dried lactose samples may help to explain the considerable differences in charging and adhesion, however further detailed work is required to investigate the effect of these properties of spray-dried lactose on charge acquisition and decay.

Acknowledgements

The authors acknowledge the work of Ms Hanh Nguyen for technical assistance and SmithKline Beecham Pharmaceuticals for financial support.

References

Ally, M. R., Klinzing, G. E. (1985) Inter-relation of charging and pressure drops in pneumatic transport. Powder Tech. 44: 85–88

Bailey, A. G. (1984) Electrostatic phenomena during powder handling. Powder Tech. 37: 71–81

Carter, P. A., Rowley, G., Fletcher, E. J., Hill, E. A. (1992) An experimental investigation of triboelectrificationin cohesive and non-cohesive pharmaceutical powders. Drug. Dev. Ind. Pharm. 18: 1505–1525

Carter, P. A., Rowley, G., McEntee, N. J. (1997) An investigation of experimental variables during triboelectrification studies on powders. J. Pharm. Pharmacol. 49 (Suppl. 4): 23

Carter, P. A., Cassidy, O. E., Rowley, G., Merrifield, D. R. (1998) Triboelectrification of fractionated crystalline and spray-dried lactose. Pharm. Pharmacol. Commun. 4: 111–115

Eilbeck, J., Rowley, G., Fletcher, E. J., Smith, I. (1992) An investigation of the effects of contact surface on triboelectrification in pharmaceutical powder systems. Proc. 11th Pharm. Tech. Conf. 2: 358–366

Eilbeck, J., Rowley, G., Carter, P. A., Fletcher, E. J. (1999) Effect of materials of construction of pharmaceutical processing equipment and drug delivery devices on the triboelectrification of size-fractionated lactose. Pharm. Pharmacol. Commun. 5: 429–433

Elsdon, R., Mitchell, F. R. G. (1976) Contact electrification of polymers. J. Phys. D: Appl. Phys. 9: 1445–1460

Fell, J. T., Newton, J. M. (1970) The characterization of the form of lactose in spray-dried lactose. Pharm. Acta. Helv. 45: 520–522

Fell, J. T., Newton, J. M. (1971) The production and properties of spray-dried lactose. Pharm. Acta. Helv. 46: 226–235

Lowell, J. (1990) Contact electrification of silica and soda glass. J. Phys. D: Appl. Phys. 23: 1082–1091

Mackin, L. A., Rowley. G., Fletcher, E. J., Marriott, R. (1993) An investigation of the role of moisture on the charging tendencies of pharmaceutical excipients. Proc.12th Pharm. Tech. Conf. 2: 300–317

Masters, K. (1991) Spray Drying Handbook. 5th edn, Longman (UK) and J. Wiley and Sons (US)

Nguyen, T., Nieh, J. (1989) The role of water vapour in the charge elimination process for flowing powders. J. Elect. 22: 213–227