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The effect of vehicle on physical properties and aerosolisation behaviour of disodium cromoglycate microparticles spray dried alone or with L-leucine

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Abstract

The aim of this study was to improve the aerosolisation behaviour of disodium cromogycate (DSCG), using spray drying technique. The effect of vehicle on the drug particle properties was investigated. L-leucine was selected as a natural antiadherent amino acid to improve the deagglomeration of DSCG particles. Spray dried samples of DSCG alone or with L-leucine were prepared from water and ethanol under the same conditions. The powder properties of the samples were examined by laser diffraction, helium densitometer, X-ray diffraction, differential scanning calorimetry and thermogravimetric analysis. The in vitro deposition was determined, using an Andersen cascade impactor with a Spinhaler® at a flow rate of 60 l/min. An amorphous form of the drug was obtained when water was used. However, crystal transformation of original DSCG in the presence of ethanol during spray drying resulted in production of elongated particles. These particles exhibited improved aerodynamic properties, compared to the amorphous and commercial materials. Significant differences in fine particle fraction were observed using the two vehicles. Co-spray drying of DSCG and L-leucine improved the deposition profiles of the drug. These results indicated that the change in crystal structure of DSCG during spray drying process was susceptible to the nature of the vehicle. A crystalline form of DSCG with good aerodynamic properties was achieved during spray drying process. In addition, the processing of DSCG with L-leucine in a single step using ethanol resulted in an improvement in dispersion properties of the drug particles.

Keywords: Disodium cromoglycate; Dry powder inhalers; Spray drying; Vehicle; Crystal transformation; Aerodynamic behaviour

1. Introduction

Disodium cromoglycate (DSCG) has emerged as one of the first-line agents in the treatment of mild to

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moderate asthma (Gilman, 2001). Many formulations of the drug are now available for inhalation using different types of aerosol devices including nebulizers, metered dose inhalers (MDIs) and dry powder inhalers (DPIs). Most commonly, MDIs and DPIs are used to deliver the drug to the respiratory tract. They are portable and more cost-effective than nebulizers. The absence of propellants in the formulation of DPIs proposed them as a good alternative to MDIs. Since, the inhalation of drugs through DPIs is controlled by inspiratory effort, the emission of drugs is actually coordinated with the breath. This, in turn, overcomes the synchronization problems associated with MDIs.

DPI formulations consist of drug with an aerodynamic particle size ideally smaller than 5 μm (Zeng et al., 2001a). The common problems in the inhalation of these formulations are the stability of output and the presence of agglomerated particles in the air stream during inspiration through an inhaler (Lalor and Hickey, 1998). The flow and dispersion properties of these small particles are influenced by interparticle forces, including electrostatic, van der Waals, capillary and mechanical forces. The magnitudes of these forces are affected by several physichochemical properties of particles, including size distribution, morphology, density and surface composition (Prime et al., 1997). The design of the inhalers can also influence the dispersion and deagglomeration properties of drug particles. Several attempts have been made to optimize the dry powder formulations (Lucas et al., 1998; Tee et al., 2000; Rasenack et al., 2003) and the inhalers efficiencies (Brindley et al., 1995; Hodson et al., 1997; Casper et al., 1999). A recent study has suggested a more important role for powder formulation than the inhaler design (Steckel et al., 2003). Thus, it seems that particle engineering can play a significant role in the preparation of the materials intended for use in DPI formulations.

Spray drying is one of the techniques that has been widely used to manipulate the physical properties of pharmaceutical materials (Sacchetti and Van Oort, 1996). It is a process that produces particles from a solution or a suspension feed in a single step. There are several reports indicating the application of the spray drying in the production of powder formulations for inhalation (Chawla et al., 1994; Chan et al., 1997; Harjunen et al., 2002; Stahl et al., 2002). The effect of spray drying process on the physical and inhalation properties of DSCG were investigated and compared with those of mechanically micronised particles of the drug (Vidgren et al., 1987). Under the conditions used by Vidgren et al. (1987), the spray dried particles showed mean particle diameters smaller than the micronised particles and upon aerosolisation produced a respirable fraction about 2.6 times higher than the micronised one. However, the spray dried DSCG particles, which were prepared from an ethanol/water mixture, were found to be amorphous with higher moisture adsorption affinity as compared with the crystalline micronised particles. It is known that spray drying often results in the production of amorphous forms of the materials due to the rapid evaporation of the solvent. Spray drying of DSCG aqueous solutions at different feed concentrations and process conditions also resulted in the production of amorphous forms of the drug (Chew et al., 2000). No report investigating the effect of ethanol as a vehicle on the crystallinity of the spray dried DSCG was available. The first aim of this study was to compare the effect of water and ethanol separately on the physical and aerodynamic properties of spray dried DSCG microparticles as an aid to prepare an optimum formulation of the drug with improved deposition properties. The second aim was to spray dry DSCG from the two vehicles in the presence of L-leucine as an antiadherent, with a view to improve the deaggregation and dispersion properties of the drug containing microparticles upon aerosolisation.

2. Materials and methods

2.1. Materials

Micronized DSCG was kindly supplied by Profarmaco, Italy. Spinhaler® (Fisons, UK) was purchased from Iranian market. Absolute ethanol and L-leucine were purchased from Merck, Germany.

2.2. Spray drying

A 8 g/100 ml solution of commercial DSCG (Profarmaco, Italy) in water was spray dried, using a lab scale spray dryer (Buchi 191, Buchi, Switzerland) with an inlet air temperature 100 °C, outlet temperature 70 °C, air flow rate at 800 Nl/h and pump setting 5. A suspension of 8 g/100 ml of commercial DSCG was also

prepared in absolute ethanol and spray dried at the same conditions that were used for the aqueous solution, except that the outlet temperature which was in the range 75 °C.

To evaluate the effect of L-leucine in the presence of the vehicles, the same solution and suspension of DSCG (8 g/100 ml), containing 800-mg L-leucine (10% with respect to the drug) were prepared and co-spray dried according to the above conditions.

Spray dried samples of L-leucine alone were also prepared using an aqueous solution or an ethanolic suspension under the same conditions. These samples were used as controls to investigate the absolute effect of the vehicle on the physical properties of L-leucine.

All samples were transferred to tight closed amber glass containers and stored in a desiccator over silica gel.

2.3. Particle size measurement

The particle sizes of samples were determined by laser diffraction (Malvern Mastersizer X, Malvern, UK). About 5 mg of each material was dispersed in 5 ml of *n*-butanol and sonicated (Starsonic 60, Liarre, Italy) for 3 min. A few drops of each sample were poured into the small volume cell of the instrument to obtain an obscuration of between 18 and 20%. The analysis was repeated in triplicate for each sample.

2.4. Particle density

The bulk density of the samples was determined by measuring the volume of a known mass of the material that had been poured into a 25-ml graduated cylinder. The true density was also determined using a helium pycnometer (Multipycnometer, Quantachrome, USA). Each sample was analysed three times.

2.5. Scanning electron microscopy (SEM)

The particle shape of the samples was evaluated by a scanning electron microscope (SEM) (Philips XL 30 scanning microscope, Philips, The Netherlands). Particles were coated with gold under vacuum (SCD 005 sputter coater, Bal-Tec, Germany) and examined at an acceleration voltage of 25 kV.

2.6. Infrared spectroscopy

Infrared spectra were obtained, using a FTIR spectrometer (Nicolet 550, USA). Samples were prepared in KBr discs and scanned from 400 to 4000 cm^{-1}.

2.7. X-ray diffraction (XRD)

The crystallinity of the materials were assessed with a X-ray diffractor (D5000, Siemens, Germany), using Cu Kα radiation, 40 kV and 30 mA. The samples were packed in a quartz holder and scanned in steps of 0.05° from 5 to 35° (2θ).

2.8. Differential scanning calorimetry (DSC)

The thermograms of the materials were determined, using a differential scanning calorimeter (PL-DSC, Polymer Laboratories, UK). Approximately, 4-mg of the materials was placed in aluminium pans and analysed under dry nitrogen purge. The temperature range was between 50 and 300 °C and the heating rate was 10 °C/min. Each sample was analysed in triplicate.

2.9. Thermogravimetric analysis (TGA)

The weight loss of vehicle as a function of temperature in each sample was determined, using a thermogravimetric analyser (Perkin-Elmer, USA). About 5 mg of each material was weighed and heated at the temperature range of 50–350 °C at a scanning rate of 10 °C/min under nitrogen purge.

2.10. Determination of DSCG and L-leucine contents in co-spray dried materials

Ten samples were taken in a random manner from each co-spray dried material obtained from water or ethanol. The quantity of DSCG in each sample was measured using UV spectrophotometry at 326.5 nm (Chew et al., 2000). The amount of L-leucine in each sample was calculated by subtraction of DSCG content from the total weight.

2.11. In vitro deposition

Two capsules, each containing 20-mg of DSCG, were introduced separately to an Andersen cascade

impactor via a Spinhaler®. After aerosolisation of the powders for 4 s at a flow rate of 60 l/min, the inhaler, capsule shells, throat, preseparator, the seven stages and plates and filter were washed with purified water. The concentration of DSCG in each sample was determined, using UV spectrophotometry (Chew et al., 2000).

Fine particle dose (FPD) was determined as the amount of drug deposited on stage 1 to the filter. The effective cut-off diameter of stage 1 of Andersen cascade impactor at 60 l/min was reported to be <6.18 μm (Zeng et al., 2001b). Fine particle fraction (FPF) was calculated as the percentage of the ratio of FPD to the total amount of the drug recovered per capsule. The emitted dose (ED) was defined as the total drug recovered from throat, preseparator, the seven stages and plates and filter. The percentage emitted was calculated as the ratio of ED to the total drug recovered per capsule, expressed as percentage. Dispersibility was defined as the ratio of FPD per ED percentage.

3. Results and discussion

3.1. Physical characteristics

3.1.1. Samples containing DSCG alone

Table 1 shows the particle size distribution data for all of the samples. The commercial DSCG was shown to have a volume median diameter ($d_{50\%}$) of 1.52 μm with a mode at 2.07 μm. The SEM photograph suggests a prismatic, columnar shape for the commercial DSCG crystals with a particle size predominantly smaller than 5 μm (Fig. 1a). This sample exhibited a suitable particle size distribution for inhalation and was used as a control for spray dried materials without any further micronization.

The spray drying processes produced microparticles with different particle size distribution patterns and shapes, depending on the nature of vehicle, which had

Table 1
Particle size distribution and densities of the materials (mean, $n = 3$)

Sample	Particle size (μm)		Density (g/ml)	
	$d_{50\%}$	Mode (s)	Bulk	True
DSCG				
Commercial	1.52	2.07	0.35	1.60
Spray dried from water (DSCG-SDW)	2.25	3.01, 0.72	0.37	1.61
Spray dried from ethanol (DSCG-SDE)	4.55	6.75	0.10	1.62
DSCG + L-leucine				
Spray dried from water (DSCG/Leu-SDW)	2.67	3.35, 0.83	0.34	1.57
Spray dried from ethanol (DSCG/Leu-SDE)	5.08	7.55	0.08	1.64

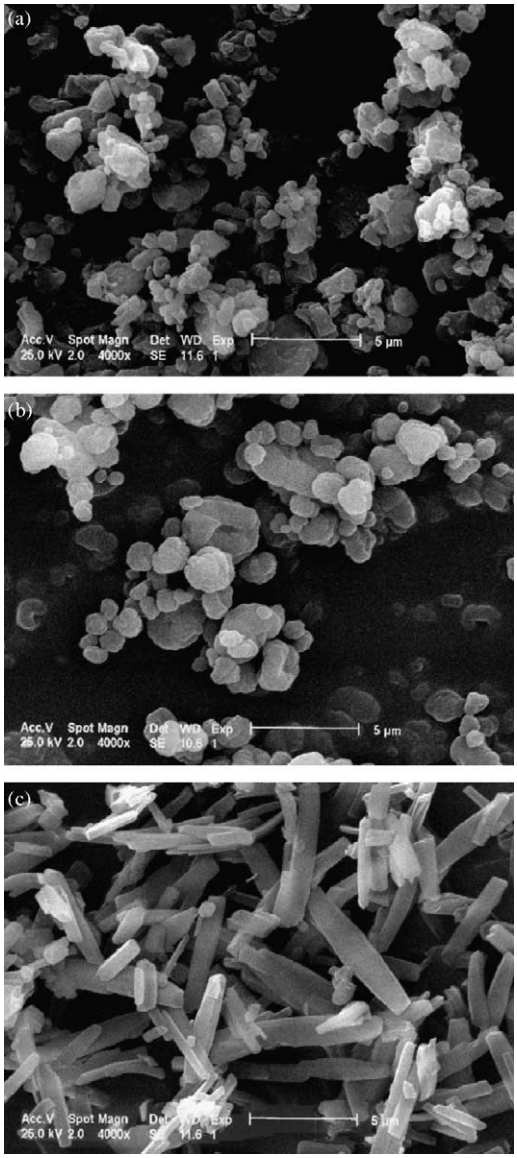

Fig. 1. Scanning electron micrographs of (a) commercial DSCG, (b) DSCG spray dried from water (DSCG-SDW), (c) DSCG spray dried from ethanol (DSCG-SDE).

been used in the preparation of the feed. The spray dried DSCG microparticles obtained from aqueous solution (DSCG-SDW) was shown to have a bimodal particle size distribution with a $d_{50\%}$ of 2.25 μm. No definite crystal structure was shown by these particles (Fig. 1b). The DSCG spray dried from ethanol (DSCG-SDE) exhibited the highest value of $d_{50\%}$, which was approximately 3.0 times that of the commercial one. Such a difference in $d_{50\%}$ was attributed to the differences in the particle shape of the materials. As shown in Fig. 1c, the crystals formed in the presence of ethanol during spray drying process were more elongated with flat surface and well-defined edges.

The true density value of the commercial sample was close to that of the spray dried samples ranging from 1.60 to 1.62 g/cm^3. These values were closely in agreement with recent results reported for DSCG (Young et al., 2003).

On the contrary to the true density values, it was found large differences in the bulk density values of the samples. Spray dried sample processed from ethanol exhibited the lowest bulk density value among the samples (Table 1). This result suggested a loose packing arrangement for DSCG-SDE particles. The SEM photograph of the particles supported these findings. As can be seen in Fig. 1c, the elongated particles of DSCG-SDE sample interact with each other in a loosely manner.

The infrared spectra of the samples were not different (Fig. 2), indicating the similarity of vibration in bonding energies. Fig. 3 shows XRD patterns for all DSCG samples. The broad (halo) scattering pattern (Fig. 3b) confirmed an amorphous nature for DSCG-SDW, consistent with a previous report (Chew et al., 2000). The presence of sharp diffraction peaks in the patterns of the commercial DSCG (Fig. 3a) and DSCG-SDE (Fig. 3c) indicated crystalline nature for these two samples. It has been previously reported that DSCG exists as a crystalline hydrate phase, which converts reversibly to liquid crystalline phases under certain circumstances (Cox et al., 1971). The XRD pattern of the hydrate phase was reported to change considerably with the change in environmental relative humidity. The appearance and disappearance of some XRD peaks at different relative humidities were attributed to the change in α angle of the crystal (Chen et al., 1999). The pattern of commercial DSCG obtained in this study was similar to the pattern reported by Cox

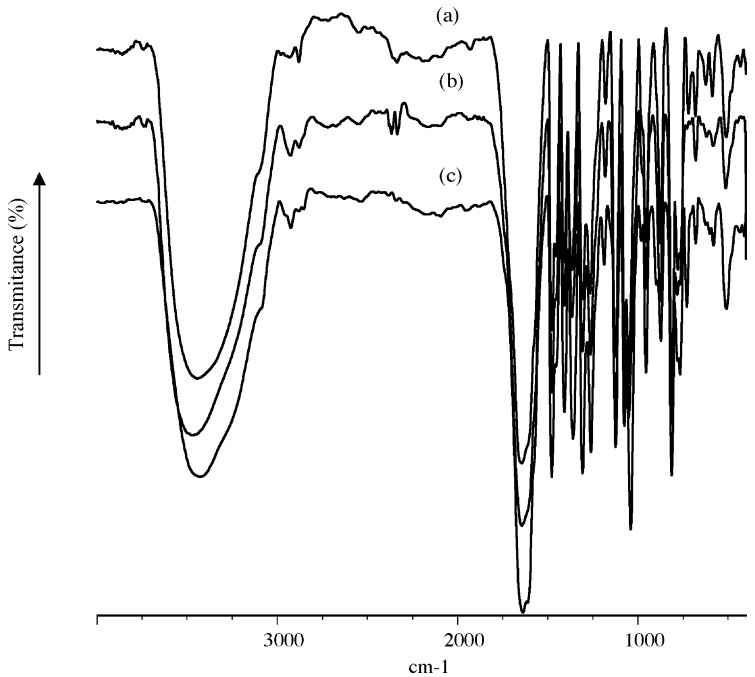

Fig. 2. Infrared spectra of the DSCG samples at 4000–400 (cm^{-1}) region: (a) commercial DSCG, (b) DSCG-SDW, (c) DSCG-SDE.

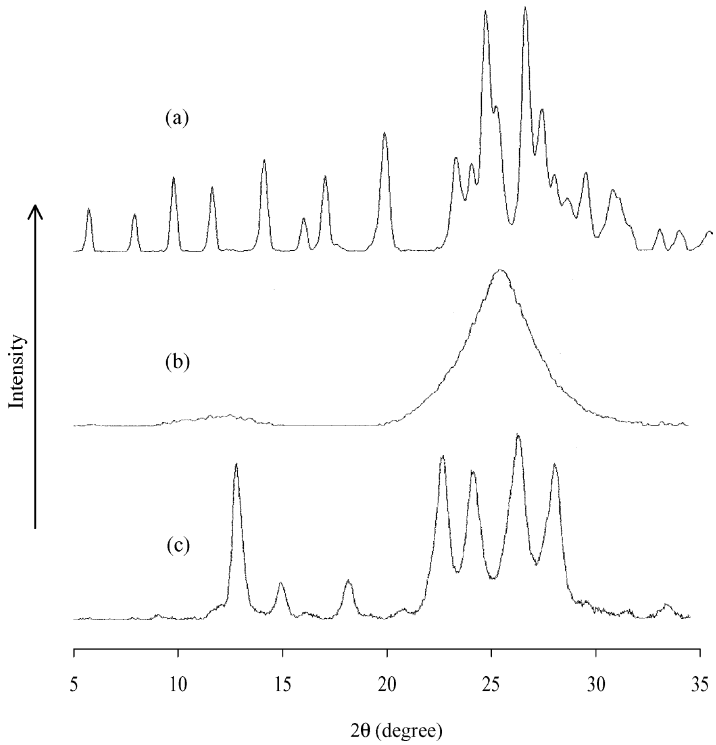

Fig. 3. X-ray diffraction patterns of various DSCG samples: (a) commercial DSCG, (b) DSCG-SDW, (c) DSCG-SDE.

et al. (1971). DSCG-SDE exhibited diffraction peaks at 23.06°, 24.59°, 26.54° and 28.47° 2θ close to the corresponding peaks for commercial DSCG. On the contrary, the diffraction peak at 13.06° 2θ observed for DSCG-SDE was absent at the scattering pattern of commercial crystal. No diffraction peak was also observed for DSCG-SDE below 10° 2θ, in contrast to the commercial crystal and to those reported for DSCG hydrates in the literature (Cox et al., 1971; Chen et al., 1999). The XRD pattern of DSCG-SDE was also different from that was reported by Stephenson and Diseroad (2000) for desolvated crystals of DSCG which were isolated upon the addition of ethanol into a saturated aqueous solution of DSCG. These findings suggested the production of a new crystalline form of DSCG during spray drying from ethanol.

The DSC and TGA thermograms of all samples are shown in Figs. 4 and 5, respectively. The DSC thermogram of the commercial drug showed a dehydration endotherm at 75–130 °C, followed by a melting endotherm at 262.5 °C (Fig. 4a) which corresponded to the two steps in the TGA plot (Fig. 5a). Previous studies have shown that up to nine water molecules can be accommodated in the crystalline structure of one DSCG molecule, depending on the relative humidity (Cox et al., 1971). The dehydration process of DSCG lattice was reported to be non-uniform, because of the presence of two types of water molecules in the crystalline structure of the drug; sodium-coordinated water and water in lattice channels (Stephenson and Diseroad, 2000). The start of dehydration of commercial DSCG at 75 °C in this study, might be related to the loss of water in lattice channels followed by the evaporation of metal-coordinated water molecules at higher temperatures. The weight loss up to 130 °C for this sample was about 8.0%, according to the TGA analysis. DSCG-SDW showed a broad dehydration endotherm ranged from 52–130 °C (Fig. 4b), corresponding to the weight loss of 11.5% observed in TGA (Fig. 5b). This sample displayed a melting endotherm at 253.1 °C, followed by an exo-endotherm at 260–275 °C leading to a product that decomposed at 295 °C. The TGA

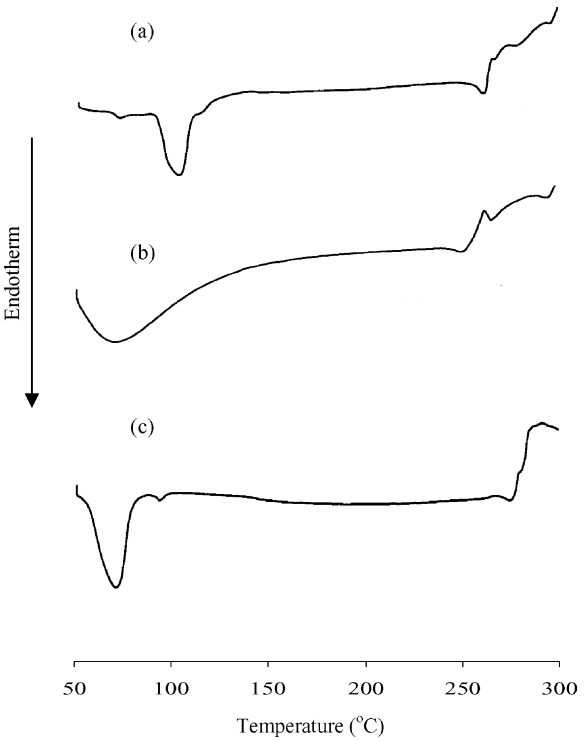

Fig. 4. DSC thermograms of (a) Commercial DSCG, (b) DSCG-SDW, (c) DSCG-SDE.

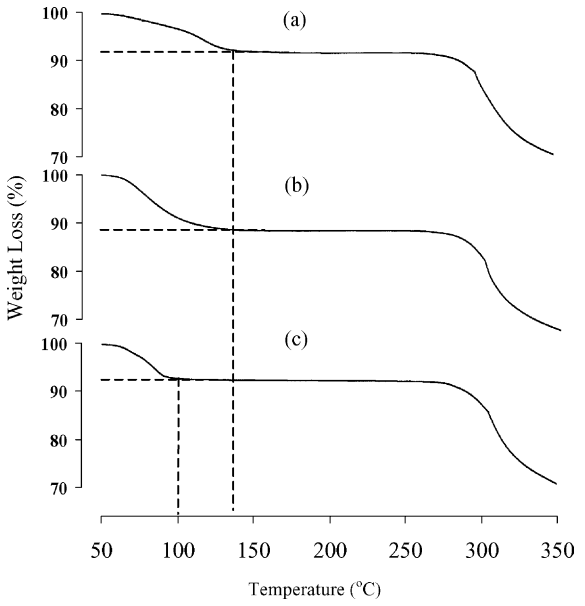

Fig. 5. TGA thermograms of (a) Commercial DSCG, (b) DSCG-SDW, (c) DSCG-SDE.

curves clearly showed the decomposition process for all samples at temperatures higher than 300 °C. In the DSC thermogram of DSCG-SDE a large desolvation endotherm at 60–85 °C and a small dehydration endotherm a 90 °C, followed by a melting endotherm at 275.2 °C was observed (Fig. 4c). The presence of desolvation endotherm at lower temperature suggested the presence of ethanol in the sample. This suggestion was supported by TGA analysis because this sample lost most of its vehicle/solvent below 80 °C (Fig. 5c), close to the boiling point of ethanol. The weight loss up to 100 °C for this sample was about 7.0%.

3.1.2. Co-spray dried samples containing DSCG and L-leucine

The laser diffraction particle size analysis showed that size distribution of co-spray dried samples of DSCG and L-leucine had not been changed substantially as compared with the corresponding samples of the drug spray dried alone under the same conditions (Table 1). This result was unexpected especially for the sample spray dried from ethanol because the particle size of the original (commercial) L-leucine was completely different from the original (commercial) DSCG sample and both materials were not soluble in ethanol. To explain this finding, L-leucine was spray dried, using the same vehicles and conditions in the absence of the drug. The particle size of original L-leucine was substantially reduced upon spray drying of the material from its aqueous solution (Fig 6). The particle size of this spray dried sample of L-leucine ($d_{50\%}$ = 5.94 μm) was comparable to the particle size of DSCG-SDW ($d_{50\%}$ = 2.25 μm).

The presence of L-leucine particles in the co-spray dried sample obtained from water (DSCG/Leu-SDW) were confirmed by SEM (Fig. 7a and c). From the SEM pictures, it is clear that spray dried L-leucine obtained from aqueous solutions was comprised of hollow spherical microparticles, consistent with the previous finding (Lucas et al., 1999).

The characteristic XRD peaks of the commercial L-leucine appeared at 6.12°, 24.39° and 30.61° 2θ (Fig. 8a). Spray dried samples of L-leucine alone showed peaks at reflection angles similar to the original material (Figs. 8b and d). The presence of L-leucine was also confirmed by the appearance of a reflection peak at 6.12° 2θ in the XRD patterns of co-spray dried samples (Fig. 8c and e).

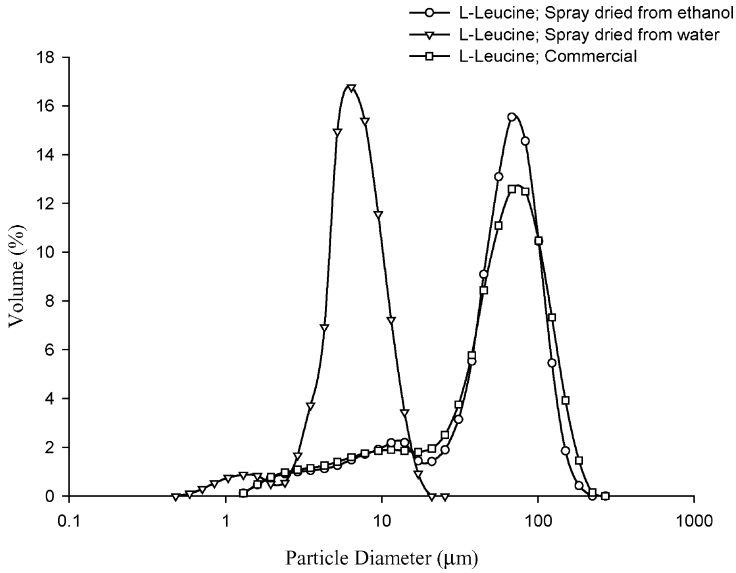

Fig. 6. Particle size distribution of different forms of L-leucine as measured by laser diffraction method.

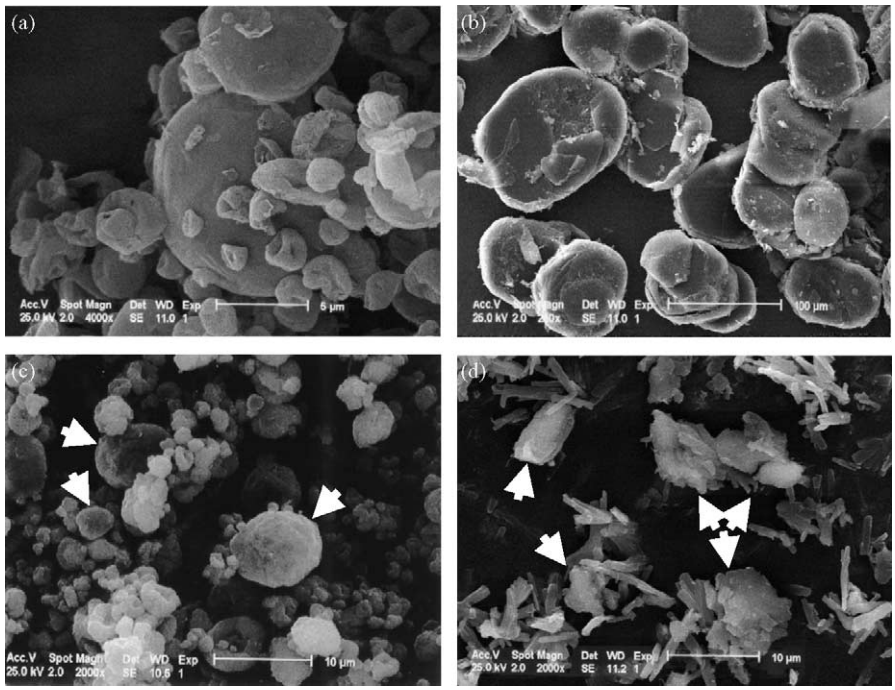

Fig. 7. Scanning electron micrographs of (a) L-leucine spray dried from water, (b) L-leucine spray dried from ethanol, (c) DSCG and L-leucine co-spray dried from water (DSCG/Leu-SDW), (d) DSCG and L-leucine co-spray dried from ethanol (DSCG/Leu-SDE). White arrows indicate L-leucine particles in co-spray dried samples.

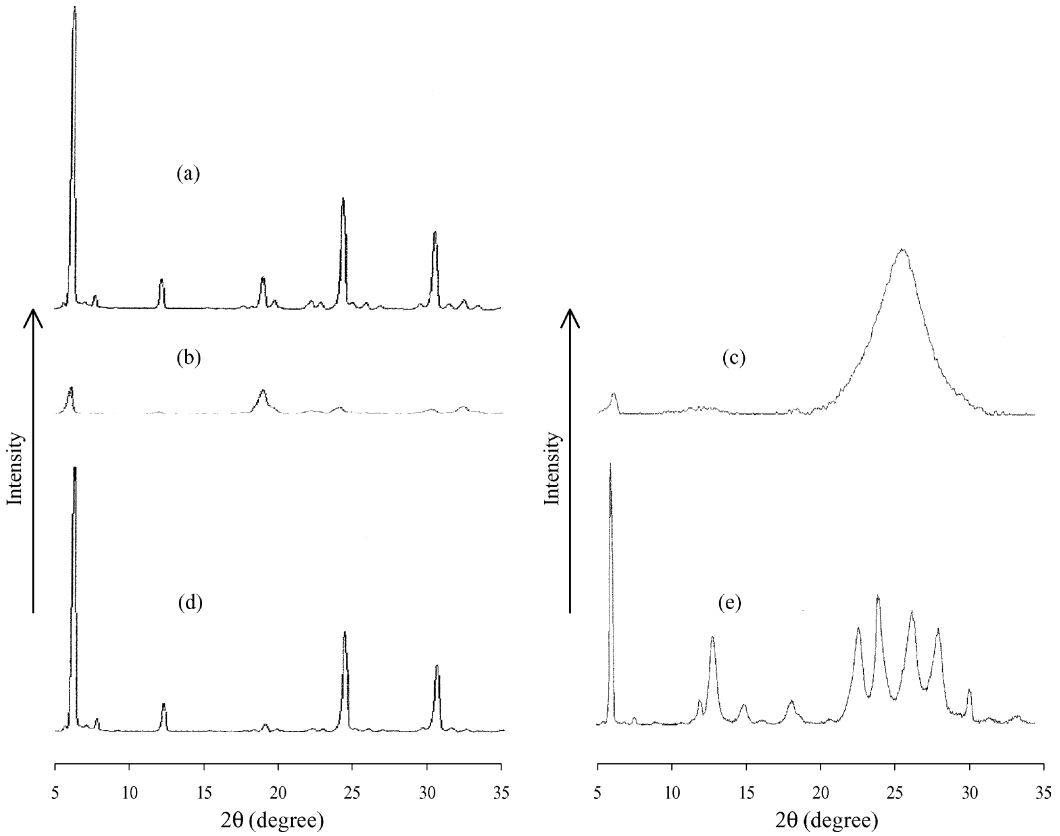

Fig. 8. X-ray diffraction patterns of various L-leucine containing samples: (a) commercial L-leucine, (b) L-leucine spray dried from water, (c) DSCG/Leu-SDW, (d) L-leucine spray dried from ethanol, (e) DSCG/Leu-SDE.

As shown in Fig. 6, the particle size of commercial L-leucine was not susceptible to the presence of ethanol during the spray drying process. The main mode (at about 64.17 μm) in particle size distribution of L-leucine spray dried from ethanol was far from the respirable size range. Theoretically, it is expected to find a small mode at about 64.17 μm in particle size distribution of the sample of DSCG and L-leucine co-spray dried from ethanol (DSCG/Leu-SDE), contrary to the measured finding (Table 1). This finding could be better explained by SEM photographs of the samples (Fig. 7). The estimated particle size observed in SEM of L-leucine spray dried alone from ethanol was in the range, which was obtained by laser diffraction analysis. As might be expected, the presence of L-leucine had no effect on the morphology and size of the drug particles (compare Figs. 1c and 7d). The interesting finding was the change in size and morphology of L-leucine particles in the presence of the drug during spray drying from ethanol (Fig. 7b and d). It is likely that the microenvironment changes during DSCG crystal transformation observed in the presence of ethanol induced these changes in the L-leucine particles.

3.2. *In vitro deposition*

3.2.1. *Samples containing DSCG alone*

Deposition data for DSCG after aerosolisation of the samples at 60 l/min through a Spinhaler®, using an Andersen cascade impactor, are presented in Fig. 9a. The amounts of DSCG deposited on various stages of the Andersen cascade impactor varied for different samples. This result suggested different aerodynamic properties of the drug particles aerosolised from commercial and spray dried samples. Table 2 shows the mass median aerodynamic diameter (MMAD) of

Table 2
Mass median aerodynamic diameter (MMAD), giametric standard deviation (GSD), fine particle fraction (FPF), emission percent and dispersibility of DSCG from different samples (mean ± S.D., $n = 3$)

Sample	MMAD (μm)	GSD (μm)	FPF (%)	Emission (%)	Dispersibility (%)
DSCG (commercial)	3.85 (±0.07)	2.75 (±0.05)	9.86 (±0.33)	43.58 (±0.85)	22.63 (±1.20)
DSCG-SDW	3.55 (±0.04)	2.02 (±0.02)	7.36 (±0.43)	32.17 (±0.10)	22.87 (±1.28)
DSCG-SDE	3.23 (±0.06)	1.72 (±0.02)	21.03 (±1.53)	60.54 (±3.91)	34.90 (±4.77)
DSCG/Leu-SDW	3.11 (±0.05)	1.74 (±0.02)	18.68 (±1.66)	42.06 (±2.81)	44.38 (±0.99)
DSCG/Leu-SDE	3.00 (±0.12)	1.74 (±0.09)	35.73 (±0.43)	60.71 (±6.89)	58.91 (±1.34)

the drug calculated from the deposition data. In contrast to $d_{50\%}$ values, the MMAD of DSCG-SDE was smaller than the other samples. It is known that aerodynamic diameters of fibres and needle-like particles are approximately equal to their shortest dimension (Hinds, 1999). The favourable aerodynamic behaviour of elongated particles was previously reported to be for cromoglycic acid (Chan and Gonda, 1989), steroid KSR-592 (Ikegami et al., 2002) and salbutamol sulphate crystals (Larhrib et al., 2003), according to their in vitro deposition data. The FPF and percentage emission of DSCG-SDE were higher than the commercial DSCG and DSCG-SDW, indicating a favourable deposition pattern for the elongated DSCG-SDE particles. These elongated particles also showed a lower GSD value, which indicated that the aerosolised par-

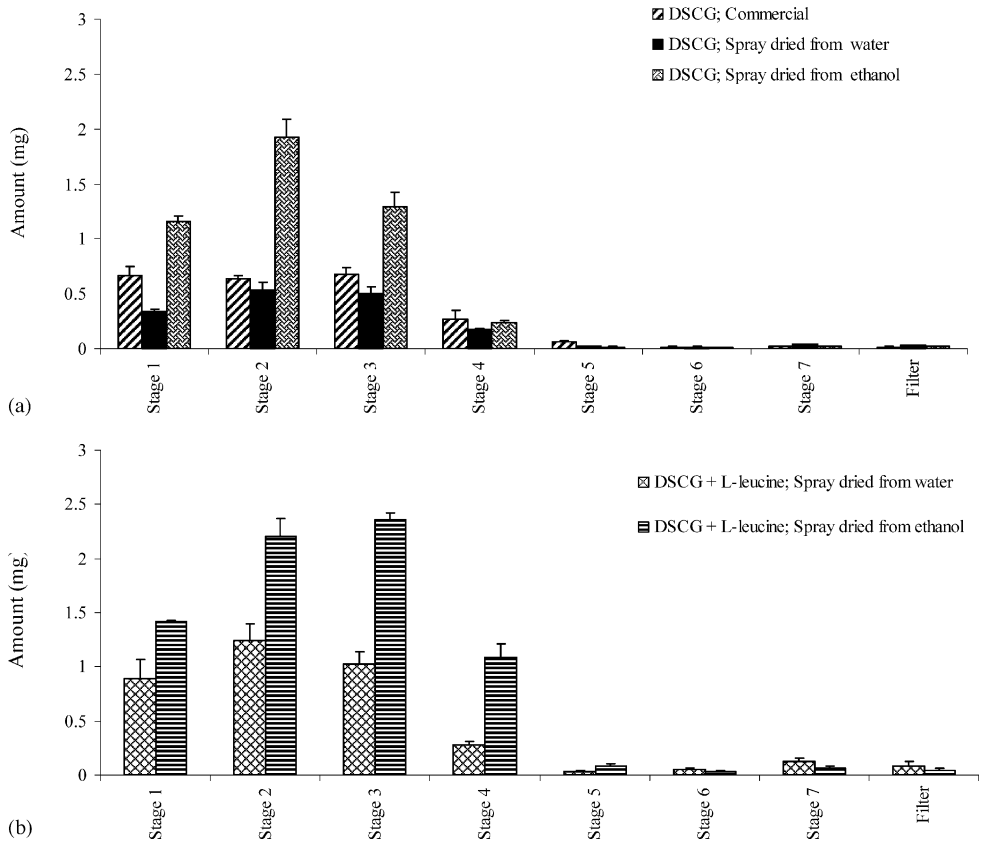

Fig. 9. The deposition of DSCG aerosolised from samples, containing the drug alone (a), or with L-leucine (b) using an Andersen cascade impactor at 60 l/min (mean ± S.D.).

ticles were more narrowly distributed in size, in comparison with the particles aerosolised from the other samples.

The higher dispersibility value of DSCG-SDE particles in comparison to the other samples suggested the presence of lower interactions between these particles, consistent with the low bulk density value of the sample (Table 1) and the SEM picture (Fig. 1c).

The emission of DSCG-SDW was lower than that was obtained from the other samples. This was attributed to the increased adhesive force between adjacent particles induced by the higher water content. Decreased deposition of DSCG due to increased water content was reported previously (Young et al., 2003).

3.2.2. *Co-spray dried samples containing DSCG and* L*-leucine*

The amounts of DSCG in co-spray dried samples obtained from water and ethanol were found to be 82.2% (±0.6) and 95.1% (±0.9), respectively. The corresponding percentage of L-leucine content was 17.8% (±0.6) for the sample obtained from water and 4.9% (±0.9) for the sample obtained from ethanol. The data indicated the presence of different concentrations of L-leucine in the finished products, compared to the initial concentrations in the feeds (9.1% with respect to the total solid content). These differences were due to the different percentage recovery of L-leucine during spray drying from water and ethanol. The MMAD value calculated for DSCG/Leu-SDE was lower than that was obtained for DSCG/Leu-SDW (Table 2).

Fig. 9b shows clearly higher deposition of the drug on stages 1, 2, 3 and 4 of the Andersen cascade impactor for DSCG/Leu-SDE. In contrast, DSCG/Leu-SDW showed a lower percentage emission, suggesting the presence of large agglomerates in the sample similar to the results observed for DSCG-SDW. The use of ethanol resulted in the production of a sample with the higher FPF, percentage emission and dispersibility of the drug, compared to the sample obtained from water. Therefore, it can be concluded that the particle morphology of DCSG can play a more important role on the aerosolisation of the drug than the antiadherent effect of L-leucine. DSCG-SDE exhibited a higher PFP than DSCG/Leu-SDW. This finding was also supported the importance of particle morphology in the drug aerosolisation capability.

4. Conclusion

Crystalline DSCG can be obtained by spray drying, using ethanol as a vehicle. The solid characteristics of the products depended on the nature of vehicle employed for preparation of the feed. The application of water in the preparation of the feed resulted in the production of an amorphous material with its characteristic features. Processing of the drug using ethanol as vehicle resulted in the formation of a crystalline material with particle size, morphology, XRD and thermal properties completely different from the commercial crystalline material.

Engineering DSCG particles by spray drying using ethanol as the vehicle improved their deposition profiles compared to the commercially available material. DSCG-SDW exhibited lower deposition profiles, compared to the other samples.

L-leucine exhibited completely different behaviours during spray drying with DSCG, susceptible to the nature of vehicles. It is surprising that smaller-sized L-leucine particles were formed during spray drying from ethanol in the presence of DSCG particles. DSCG/Leu-SDE exhibited the maximum deposition of the drug on stages 1, 2, 3 and 4 of the Andersen cascade impactor, compared to all other samples tested in this investigation. These results indicate that co-spray drying of DSCG and L-leucine, using ethanol resulted in the production of particles with improved aerodynamic behaviour and deagglomeration capability.

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