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Influence of a biosurfactant on reentrainment and de-aggregation of powders

Introduction

Inhalation of medicines in the form of aerosol is a common method of therapy of lung diseases (asthma, COPD, pneumonia, cystic fibrosis, etc.) [1]. In all types of inhalers, aerosol particles with the preferential size 1–5 µm must be formed *in situ* just before the inhalation starts. They are usually produced either by liquid atomization (pneumatic or ultrasonic) or by resuspension of fine powders. The last method became very popular in the recent years due to technical problems with the new pressurized inhalers without CFC [2]. Although dry powder inhalers (DPIs) are easy to use and well accepted by patients, they usually exhibit non-optimal performance, seldom releasing more than 40% of fine particles (< 5 µm). Reasons of that are related to the intrinsic properties of powder particles [3]. These properties are responsible for strong inter-particle cohesion and prevent the existing powder aggregates from breaking apart required for the release of fine particles during inhalation. Known strategies of improvement powder de-aggregation are related to induction of flow turbulence [4] or flow intermittence [5] to create high shear stresses in the gas phase. Different approach should focus on the reduction of inter-particle forces. In this paper we search the possibility of improvement of powder aerosolization by modifying powder particle morphology and surface properties.

Methods

Powders used in the experiments were produced in the laboratory system presented in fig. 1. Solutions of lactose (5–10%) were atomized in the ultrasonic nebulizer 1 (*Medbryt*, Poland). The wet aerosol was mixed with the stream of air heated to 120°C in the programmable furnace 2 (*Czylok*, Poland). The mixture was dried in the expansion chamber 3. The powder was collected in the cyclone and fibrous filter 4 connected in series, while the flow of filtered air was measured with the rotameter 5. Solution was atomized with the rate of approximately 1 cm^3/min, and the total airflow in the system was maintained at 20 dm^3/min.

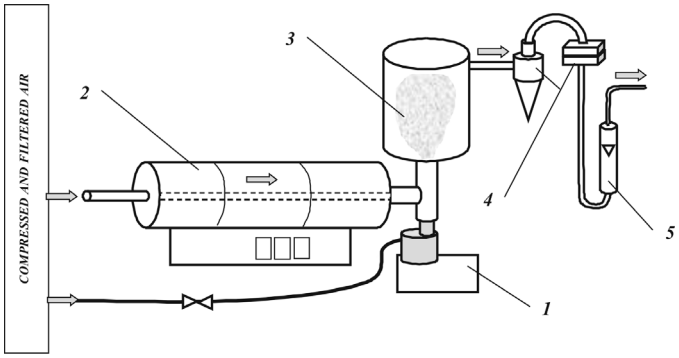


Fig. 1. Scheme of the experimental set-up: *1* – ultrasonic nebulizer, *2* – tubular furnace (heater), *3* – expansion chamber, *4* – fibrous filter, *5* – flowmeter

Biosurfactant used as an adjuvant (0,1% w/w) to lactose solution was *Exosurf Neonatal* (GSK, UK). It is a medicine used as a substitute of natural lung surfactant primarily in the curing of the respiratory distress syndrome of premature babies. This biosurfactant is composed of colfosceril (DPPC) with small amounts of palmitic acid and tyloxapol.

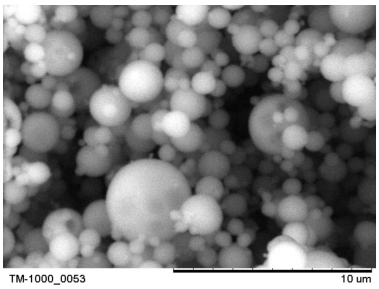
Collected powder was analyzed under the scanning microscope (*Hitachi* TM1000, Japan). The powder was also aerosolized in a commercial inhaler (DPI cyclohaler) operated at 60 dm^3/min. Particle size distribution of emitted aerosols was determined in the range 0,6–30 µm with the white-light spectrometer (*Palas*, Germany).

Results and discussion

Both types of powders obtained in the drying process were composed of particles within inhalable size-range (1–5 µm) as shown in fig. 2.

It can be noticed that, in contrast to lactose particles, particles produced from lactose/biosurfactant solution were larger, non-spherical and slightly corrugated. The most probable explanation comes from a more deformable air/liquid interface of droplets with the biosurfactant that is caused by a decreased surface tension and *Marangoni* effects. These effects can be created during contraction of the surfactant-enriched

a)



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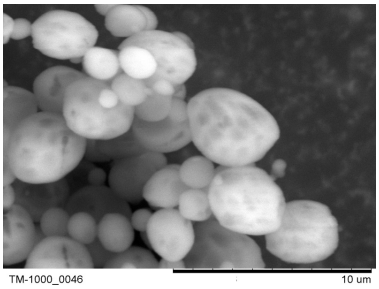

Fig. 2. SEM photographs of lactose particles (a) and lactose/biosurfactant particles (b)

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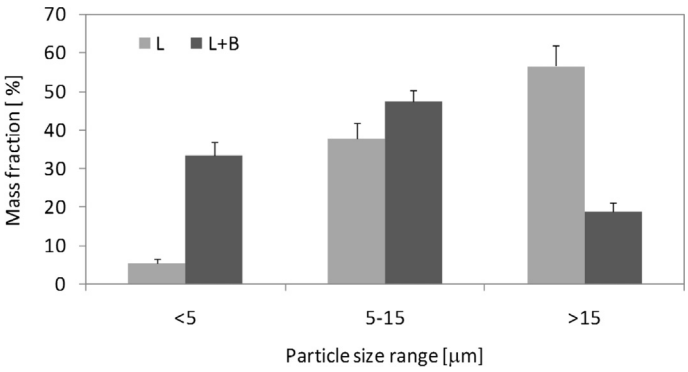

Fig. 3. Distribution of aerosol mass among different particle sizes: *L* – lactose, *L* + *B* – lactose/biosurfactant

interface resulting from drying process. Surface deformation may also lead to uneven drying rates in different regions of droplets, which resulted in surface corrugation of the formed particles.

The cumulative results of resuspension studies for both types of powders, shown in fig. 3, indicate that lactose particles are aerosolized mainly as aggregates, while lactose/biosurfactant particles are de-aggregated significantly easier. As a result, only 5% (by mass) of aerosolized lactose is contained in particles smaller than 5 μm. In the case of lactose/biosurfactant, the fraction of particles smaller than 5 μm is increased to 35%. It means that a higher mass of lactose/biosurfactant particles will be able to penetrate into the respiratory system during inhalation when compared to the aerosol produced from pure lactose. Easier de-aggregation of lactose/biosurfactant particles may be explained by their shape and morphology. Both prevent close packing due to the increase of inter-particle distance. It is expected that the surface of such particles is enriched in surfactant molecules oriented with lyophylic fragments towards the gas-phase. This can lead to another, molecular-scale steric effects, which reduce the adhesion forces. In addition, hydrophobic surface of lactose/biosurfactant molecules will repel water, making such particles more resistant to undesirable effects caused by air humidity (vapor condensation and liquid–bridging [3]).

Conclusions

It was demonstrated that particles produced by spray-drying from lactose solutions with 0,1% addition of biosurfactant (*Exosurf Neonatal*) are resuspended easier than particles of pure lactose produced in similar conditions. This effect is attributed to modified shape and surface properties of lactose/biosurfactant particles, being an outcome of interfacial surfactant adsorption during formation and evaporation of aerosol droplets. Better powder de-aggregation results in a higher fraction of aerosol particles smaller than 5 μm (35% for lactose/biosurfactant vs. 5% for pure lactose), what is advantageous for inhalation therapy. It is therefore concluded that application of biocompatible surface-active adjuvants during preparation of medicinal powders by spray-drying may be beneficial for the quality of aerosol releases from dry powder inhalers, leading to the increase of available lung dose of inhaled medicines.

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