Preparation of Nanostructural Dextran-Based Carrier Particles for Drug Delivery to the Lungs

Katarzyna Jabłczyńska, Ewelina Widyńska, Tomasz R. Sosnowski

Faculty of Chemical and Process Engineering, Warsaw University of Technology, POLAND, Warsaw, Waryńskiego Street 1, E-mail: k.jablczynska@ichip.pw.edu.pl

Abstract – Particle engineering can be used to design inhalation drug carrier that will combine advantages of nano- and microparticles. This work present a review of research on dextran-based nanostructural powder prepared using the spray drying method. The shape of powder particles is shown to depend on the applied drying process parameters and additives used. It was proved that surface morphology of particles strongly affects powder aerosolization performance. Tested powders demonstrated a good restoration of the initial nanoparticles size distribution after rehydration. All these features allow to consider dextran-based nanostructural particles as new attractive carriers for drug delivery to the lungs.

Key words – nanostructural powder, particle engineering, spray drying, polysaccharide particles, inhalation therapy.

I. Introduction

The activity of pharmaceutical products, and hence the effectiveness of medical treatment, depends not only on the drug itself but also on the properly designed carrier that is able to deliver the drug to the desired site of action inside the organism. Nowadays, when the number of newly discovered active substances constantly decreases, research on the formulation of the already known drugs becomes more important in the field of pharmacy.

In case of aerosol therapy, the role of an active substance carrier can be played by a powder particle, which - after depositing in deep parts of respiratory system – will be able to decompose and release the therapeutic agent. It will happen only if the particle has suitable size and shape and is easily dispersed in air, but at the same time - is physicochemically stable during storage. Fulfilling these requirements is a task for particle engineering utilizing the advanced process technologies [1].

II. Conception of nanostructural carriers

Usage of nanoparticles in formulations intended for inhalation brings certain benefits such as adsorption enhancement, phagocytosis avoidance and additional effect of targeting cancer cells.

Assemblage of nanoparticles into the micrometric particles allows to avoid problems with nanoparticles aerosolization and increases their deposition in the lungs.

This work presents the extension of recently reported research related to preparation and characterization of dextran-based nanostructural powder with the potential use in aerosol therapy [2]. Proposed powder particles are microsized aggregates of dextran nanoparticles, which break up and create nanosuspension after hydration.

III. Powder preparation

Powders were produced in the spray drying process using laboratory scale apparatus Mini Spray Dryer B-290 (Büchi, Swizterland). Dextran nanoparticles suspension obtained according to protocol described in [3] was fed into pneumatic nozzle and dispersed to the form of fine droplets aerosol. After solvent evaporation in the drying chamber, the produced particles were separated in the high efficiency cyclone and collected. Different characteristics of powders were obtained by changing flow stream of drying air and inlet temperature of air.

IV. Morphology of the powder particles

The powders were characterized by means of scanning electron microscopy using SEM, model TM1000 (Hitachi, Japan). Depending on the applied process parameters, different particle morphologies was obtained. Two utmost forms of particles are shown in Figs. 1 and 2.

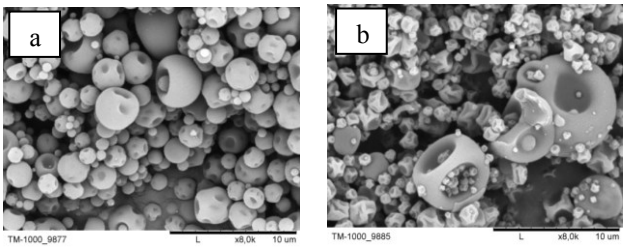

Fig. 1. SEM pictures of powders obtained by spray drying of dextran nanosuspension: a) airflow 7 m^3/h, 100°C; b) irflow 14 m^3/h, 220°C.

The first one, with smooth surface and some cavities, was produced at the most calm drying conditions, while the latter one, having a highly corrugated surface, was obtained at the highest inlet air temperature and airflow, i.e. the fastest obtainable drying rate.

V. Powder aerosolization and aerosol size distribution

Powders were aerosolized in the cyclohaler-type dry powder inhaler (DPI) at the moderate stream of air equal (60 dm^3/min). Particle size of produced aerosols was determined using the cascade impactor (NGI – Copley Scientific, UK). Fig. 2 presents the aerosol particle size distribution obtained with NGI for two types of powders. It can be seen that the spherical particles of powder obtained at low drying temperature are aerosolized more easily and thus finer aerosol is produced. The second powder contains almost 45% of aggregates with aerodynamic diameter larger than 8.06 μm which do not disintegrate in the airflow.

VI. Additives

Pharmaceutical powders can be further developed by the addition of auxiliary substances to the precursor suspension. Fig. 3 shows example morphologies of the particles produced with leucine (left) and ammonium bicarbonate (right).

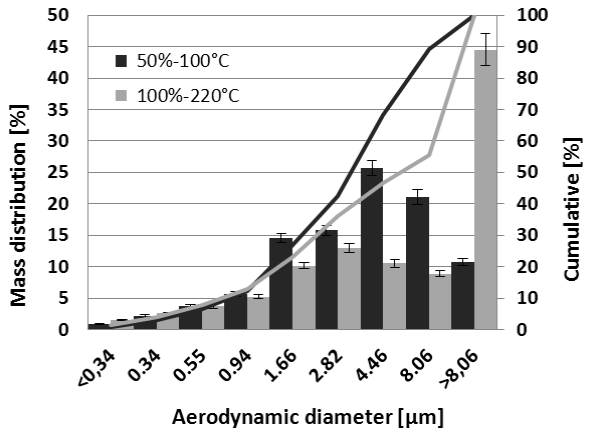

Fig. 2. Particle size (aerodynamic diameter) distribution by mass of aerosols generated in the DPI from two tested powders

It is evident that additives influence the morphology of powder particles. In the leucine-dextran (10:90) powder some perfectly spherical, hollow particles are present. In the powder produced with 2% ammonium bicarbonate, all particles have spheroidal shape and almost none cavities on their surface can be seen. In contrast to the expectations, both additives had negative impact on the powder aerosolization ability (data not shown).

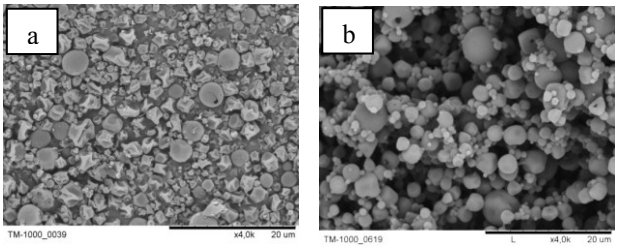

Fig. 3. Sample SEM pictures of powders obtained by spray drying (14 m^3/h, 220°C) of nanosuspension with additives of: (a) leucine; (b) ammonium bicarbonate

VII. Nanoparticles reconstitution

The most important thing in the evaluation of the nanostructural powder quality was its ability to create the nanosuspension in an aqueous environment. Tests performed using nanoparticle tracking analysis (NTA – Malvern Instruments, UK) showed that hydrated powders restore the initial size distribution of nanoparticles (i.e. the size which was found in the precursor nanocolloid). Size distributions of nanoparticles in the precursor and in the reconstructed nanosuspension are shown in Fig. 4.

Conclusions

Presented investigations prove that the proper controlling of the parameters of spray drying allows to convert dextran nanosuspension to powders with the required quality regarding their further application in aerosol therapy. Additives can be used to tune powder particle morphology, however fine particles with smooth surface can be produced without any additional substances. Such inhalable powders can be applied as efficient precursors of nanoparticles that can serve as potential drug carriers.

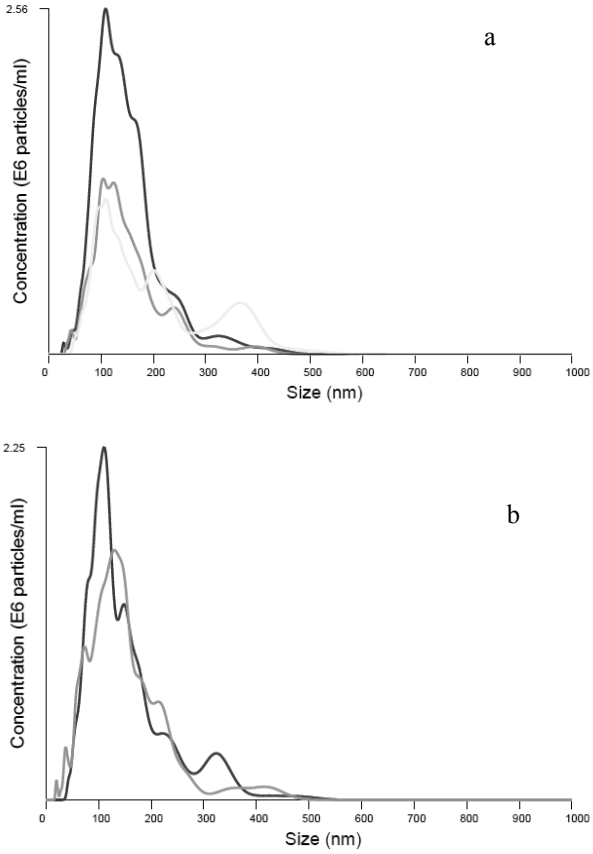

Fig. 4. Size distribution of dextran nanoparticles in aqueous phase before spray drying (a) and after rehydration of dry particles (b)

References

[1] L. Gradoń, T.R Sosnowski, "Formation of particles for dry powder inhalers", Adv. Powder Technol., vol. 25, pp. 43-55, 2014.

[2] K. Jabłczyńska, M. Janczewska, A. Kulikowska, T. R. Sosnowski, "Preparation and characterization of biocompatible polymer particles as potential nanocarriers for inhalation therapy", Int. J. Polym. Sci., vol. 2015, article ID: 763020 (8 pages), 2015.

[3] Wasiak I., Kulikowska A., Janczewska M., Michalak M., Cymerman I.A., Nagalski A., Kallinger P., Szymanski W.W., Ciach T., "Dextran nanoparticle synthesis and properties", PLoS ONE vol. 11(1), e0146237, 2016.

Acknowledgement

Work financed by National Science Centre (Poland) - project No. NCN 2014/13/N/ST8/01667.