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Preparation of spray dried submicron particles: Part B – Particle recovery by electrostatic precipitation

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ABSTRACT

The low bioavailability of poorly water-soluble drugs is currently one of the major focuses of pharmaceutical research. One strategy currently being investigated to overcome this limitation is to decrease the particle size of the active pharmaceutical ingredients (API). An innovative process for this is spray drying with spray conditioning, which can produce submicron particles. One challenge resulting from this process is the recovery of these dispersed particles from a gas flow. Electrostatic precipitation is a common technique for air purification purposes, but an adapted electrostatic precipitator (ESP) design is necessary to achieve high collection efficiencies.

The ESP design in this work uses the precipitation method of Penney filters which separates charging and collection into two stages. The ESP dimensions depend on various assumptions and simplifications. Several experiments were conducted to assess the performance of the ESP and characterize its behaviour in long-term tests. The crucial parameters in the charging process are the residence time as well as the operating voltage. These constraints were examined to enhance the collection efficiency. Based on these tests it was possible to determine a suitable charging length as well as the dimensions of the collection stage.

In conclusion, an ESP customized for collecting particles in the range of 0.1–1 µm was designed, built and tested, and collection efficiencies higher than 99% were achieved for submicron particle size distributions. For a robust process continuous cleaning of the charging stage is necessary.

1. Introduction

Poorly water-soluble pharmaceutical ingredients are a major challenge for oral drug administration. One technique to overcome this limitation is the use of particles in the submicron range (0.1–1 µm) in order to increase the specific surface area (Nernst, 1904) as well as the saturation concentration (Brunner, 1904) which is detailed in part A of this publication.

An innovative method for the production of these particles is spray drying dissolved material and pre-conditioning it in a cyclone before drying. Spray drying forms submicron particles that are dispersed in a gas stream. The collection and utilization of these manufactured particles is necessary for further processing. The collection efficiency of inertial separators, such as cyclones and scrubbers, drops significantly for submicron particles. In comparison, fibre filters and electrostatic precipitators (ESP) exhibit collection efficiencies higher than 95% in the submicron region (Fritz and Kern, 1992; Lützke and Wilkes, 1978). Fibre filter manufacturers like SEFAR or AFRPO are producing submicron particle filters with highest collection efficiency performances. The collection of these small particles on nanofiber membranes results in a high pressure drop which leads to a high collection surface and a difficult harvesting process. Deep filtration is also unsuitable for collecting submicron APIs because the particles are trapped in the fibre material, resulting in total loss of the API (Sparks and Chase, 2016). The powder collected on an ESP discharge electrode however, can be easily recovered. In addition, ESPs operate with negligible pressure losses, resulting in moderate operating costs when combined with low electrical currents (Parker et al., 1997).

Electrostatic precipitation is a common technique for collecting airborne particles (< 100 µm) e.g. in combustion processes with varying throughputs or gas loads. In combination with spray drying, electrostatic precipitators are only used as separators for high volume flows and for the collection of abrasive dusts. Even though ESPs typically have high capital and maintenance costs, a small scale precipitator with a high collection efficiency can be used economically for high-value pharmaceutical products (Masters, 1991). Collection with an ESP

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List of symbols

n	number of elementary charge on a particle
ε_0	electric constant, vacuum permittivity
d_p	particle diameter
k	Boltzmann constant
T	temperature
t	time
e	elementary charge
v_{O_2}	thermal ion velocity
v_r	radial velocity
η	dynamic viscosity
v_L	longitudinal velocity
N_0	ion density
m_{O_2}	ion mass
μ_{im}	ion mobility
n_n	number density of neutral gas molecules
A_{st}	collision cross section
I	electric current
j	electric current density
E	electric field strength
U	applied voltage
L	precipitator length
r	radius
R_{CE}	radius collection electrode
R_{FE}	radius inner field electrode
Cu	Cunningham correction
$\dot{V}$	volume flow

is advantageous for pharmaceutical applications because collection takes place on an even surface, which facilitates cleaning and heat sterilization.

In ESPs, airborne particles are charged by colliding with gas ions. The gas ions are generated by a corona discharge at a wire or a sharp edge. The charged particles are deflected in an electric field towards a grounded electrode where the collection occurs.

Büchi Labortechnik introduced the Nano Spray Dryer B-90, which produces submicron particles at the laboratory scale at very low concentrations (Lee et al., 2011). It has already been shown that producing submicron APIs in the B-90 can increase the bioavailability in rats by a factor of 7.5 (Nazarov et al., 2015) at particle yields from 50 to 90% (Büchi Labortechnik GmbH, 2017; Gu et al., 2018; Li et al., 2010). The particles are separated in the B-90 in a single-stage electrostatic precipitator. The fractional efficiency in the submicron range is specified to be 90% (Büchi Labortechnik GmbH, 2017). Even if collection does not reduce efficiency in the ESP on a laboratory scale, the efficiency will decrease over time at the production scale due to increased resistance caused by the build-up of powder on the collection electrode.

The aim of the approach discussed herein is to enhance the production rate of submicron particles by improving the powder recovery.

The aim of this study was to design and build an electrostatic precipitator for submicron particles. The design was validated with two model compounds for various operation conditions. Mannitol was used as a crystalline model material and povidone as an amorphous model material.

An overview of the main unit operations of the process is shown in Fig. 1. For the production of submicron particles a two-fluid nozzle in combination with a cyclone is used. This setup allows droplets larger than the cut-off size diameter to be recycled, droplets in the desired size range (smaller than the cut-off size diameter) pass through the dip tube and enter the drying chamber where submicron particles are formed. The main difference to the setup described in part A of this research is the exchange of the fibre filter collection unit with a customized ESP.

2. Materials, methods & ESP setup

2.1. Materials

Collection experiments were conducted with spray dried submicron mannitol (Pearlitol® 160C, Roquette® Pharma, Lestrem, France) and polyvinylpyrrolidone (povidone) (Kollidon® K30, BASF, Ludwigshafen, Germany) particles.

2.2. Methods

2.2.1. Preparation of submicron particles

Mannitol and povidone were dissolved in deionized water (10 wt-%) and spray dried at 80 °C with a resulting production rate of 1 g submicron particles per hour. The preparation of spray dried submicron particles is detailed in part A of this research. The fine dispersed particles enter the precipitator after the drying step.

2.2.2. Electrostatic precipitator

An ESP was build based on the design calculations discussed in Section 3.1. A schematic of the ESP as well as a photograph is shown in Fig. 2.

This ESP consists of two stages (charging and collection stage). It is mounted vertically, which simplifies sealing the top of the apparatus. The outer pipe is grounded, acts as a receiving electrode in the charging stage for ions and as a collecting electrode for charged particles in the collection stage. The inner pipe forms the field electrode required to

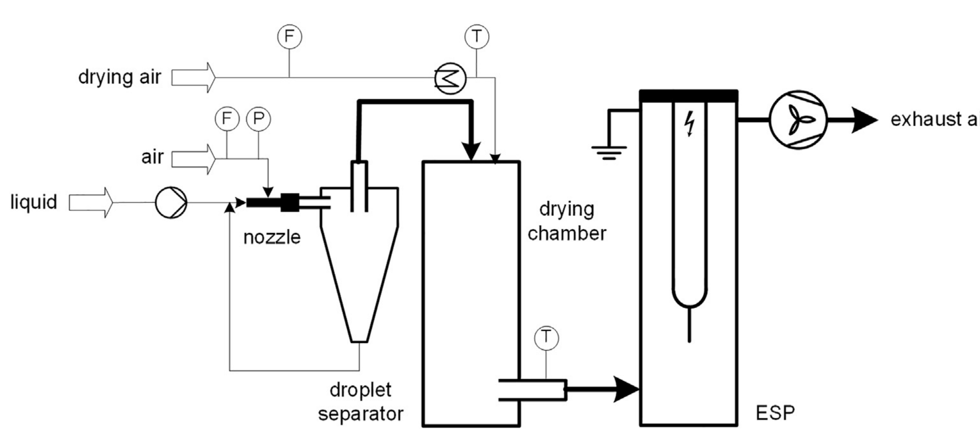

Fig. 1. Schematic of the setup for spray drying experiments including the two stage ESP.