Aerosolizing PulmoSol™ and PulmoSphere™ with the PreciseInhale® system

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Conclusions

PreciseInhale is capable of aerosolizing both PulmoSol and PulmoSphere powders to respirable particle sizes and with yields suitable for use in pre-clinical studies. Using as little as 1.5 mg of test article, the delivery efficiency was > 60 %, with respirable aerosols of ≈ 2 μm MMAD.

Introduction

The PreciseInhale system (**fig 1**) enables aerosol generation and precise dosing of small quantities of test article in pre-clinical studies. It fulfils a critical need in screening drug candidates with limited availability of study material. This study evaluated the performance of PreciseInhale when used with highly-dispersible, spray-dried, engineered PulmoSol and PulmoSphere placebo particles supplied by Novartis. PulmoSol particles are typically used to formulate macromolecules for pulmonary delivery. PulmoSphere particles are phospholipid-based, small porous particles. Compared to standard micronized drugs, these types of engineered particles enable higher delivery efficiencies to the lungs with less sensitivity to the surface properties of the given test article.

Figure 1. Schematic diagram of the PreciseInhale system.

Aim

The aim of this study was to investigate the performance of the PreciseInhale system when aerosolizing PulmoSol and PulmoSphere placebo particles.

Methods

Aerosol generation

Aerosol generation was performed using the PreciseInhale system. The aerosol generation parameters, i.e. the generation pressure, the choice of nozzle and time of exposure were optimized prior to testing. An initial quantity of 0.5 - 1.5 mg of material was aerosolized in each test and the efficiency was quantified gravimetrically by comparing the dispersed aerosol collected on a filter with the amount of starting material. Generation pressure was set to 10 bars, which is relatively low in the 10 - 160 bars pressure range. This was to minimize the risk of the pressure having a negative impact on the particles and and also to get a high efficiency through the PreciseInhale. The exposure flowrate used was 400 mL/min.

Aerodynamic particle size determination

The mass median aerodynamic diameter (MMAD) of each aerosol was determined using a Marple personal cascade impactor with cut points from 0.5 to 21.3 μm. The filters were gravimetrically analyzed.

Visualization of the particles

Aerosols were deposited on 13 mm diameter glass cover slips and analyzed by scanning electron microscopy (SEM).

Results

The efficiency of aerosol generated by PreciseInhale was above 60 % (n=5) for both PulmoSol and PulmoSphere. The MMAD for PulmoSol was 1.95 ± 0.13 μm (**fig 2a**) and for PulmoSphere the MMAD was 2.14 ± 0.31 μm (**fig 2b**) (n=3). The SEM images of the deposited aerosols showed intact particles (**fig 2**).
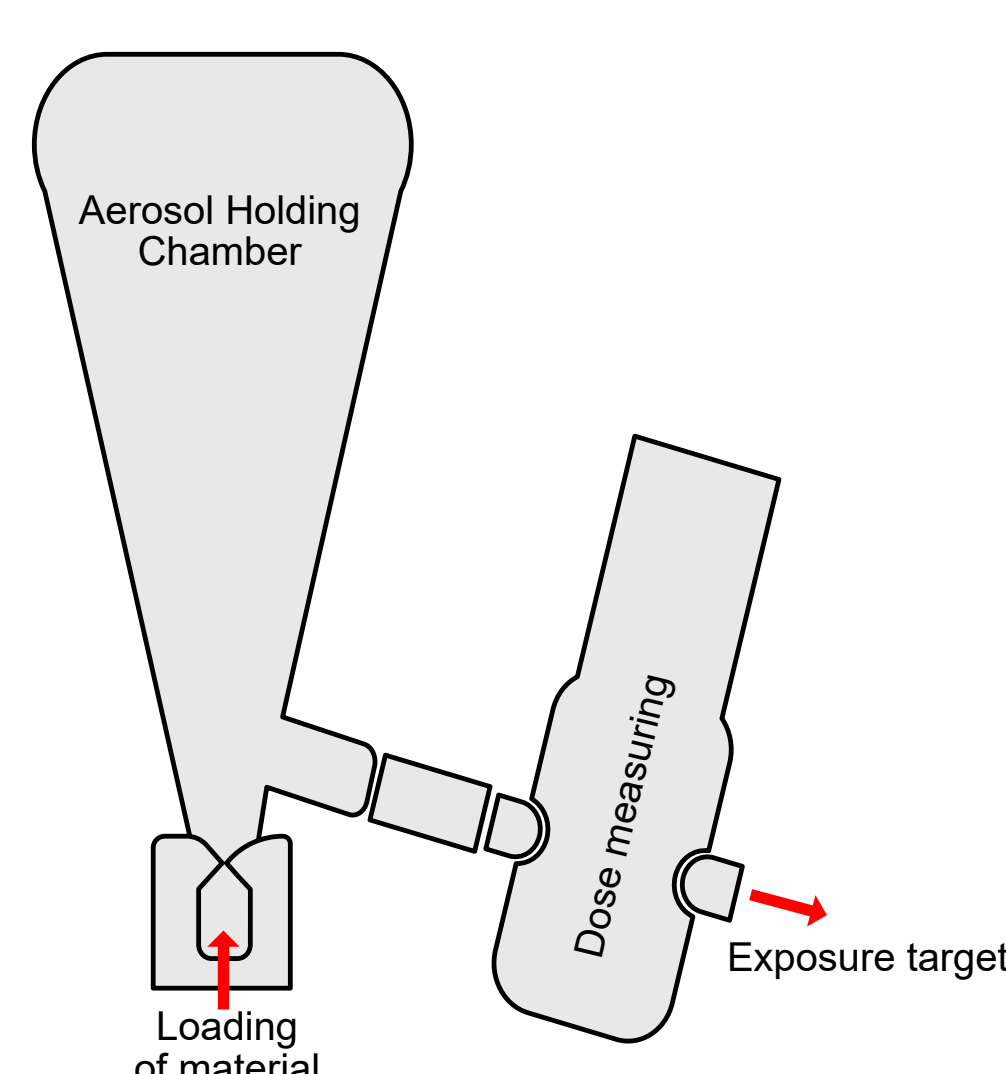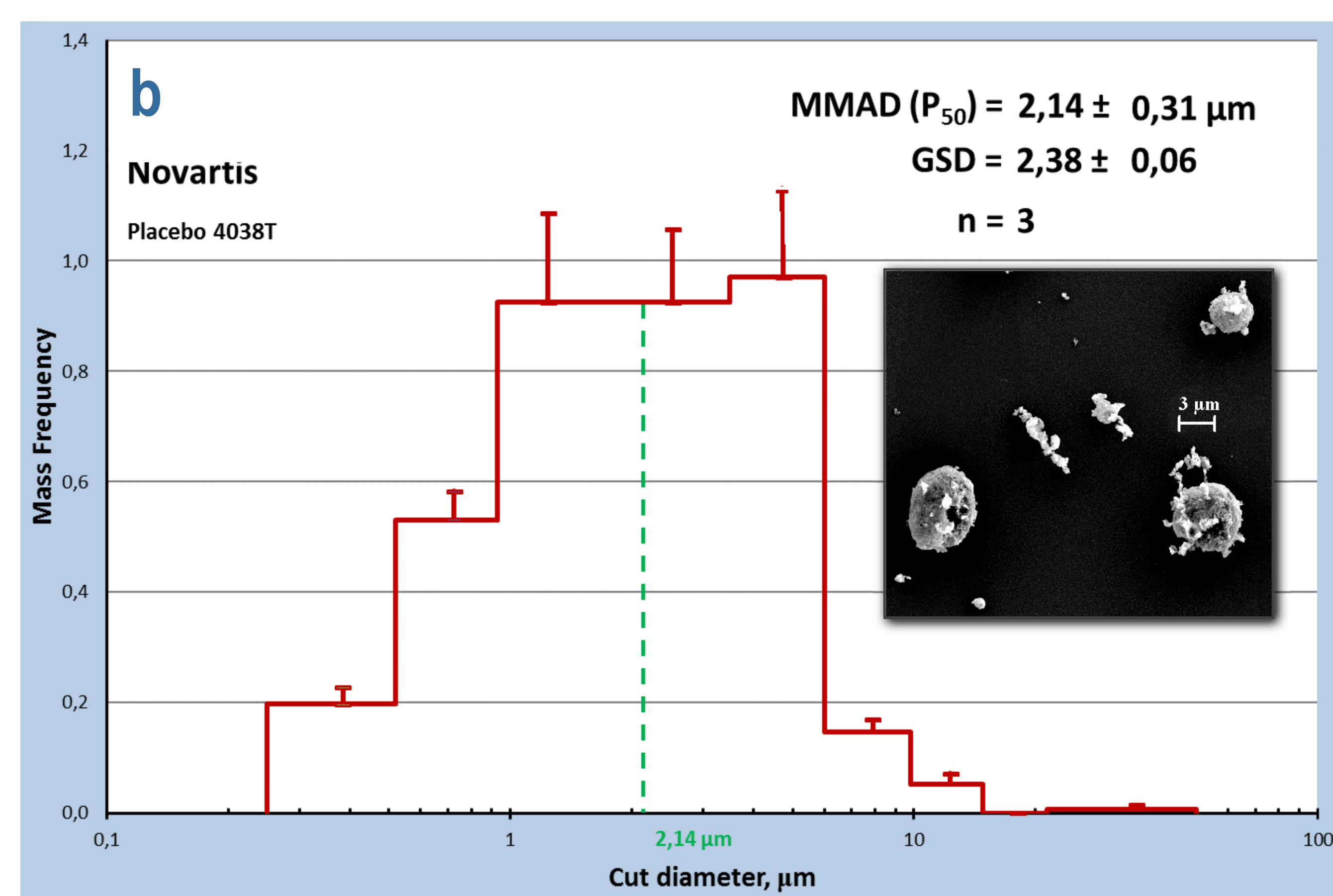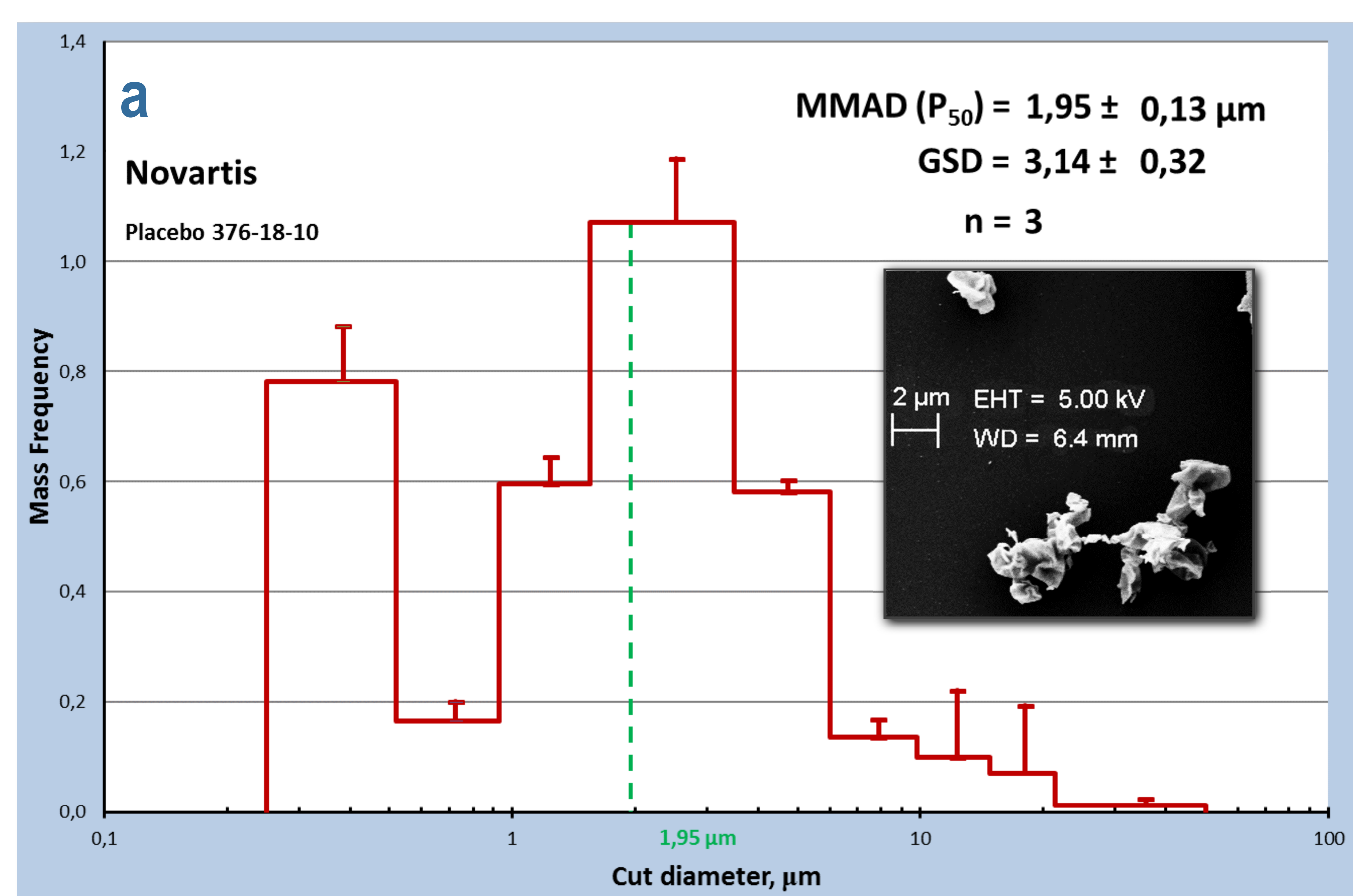

Figure 2. MMAD results and SEM images of a) PulmoSol and b) PulmoSphere particles. For PulmoSol, there is a fraction of fine material, despite using generation pressure in the low range.

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