

# Spray-dried Indomethacin Microparticles Designed for Asthma Inhalatory Treatments <sup>†</sup>

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**Abstract:** Indomethacin (IN) has demonstrated usefulness for treating bronchial inflammatory asthma responses. In the dry powder inhaler development frame, IN microparticles (MP<sub>IN</sub>) were produced by spray-drying. The study aim was: (a) to evaluate the effect of spray-drying operating variables on MP<sub>IN</sub> aerodynamic properties and (b) to measure the effect of MP<sub>IN</sub> administration in Calu-3 cell-line interleukins IL-6 and IL-8 production. IN dissolved in ethanol (1 % W/V) was processed in lab-scale equipment using a high-performance cyclone to collect MP<sub>IN</sub>. Liquid feed flow rate (Q<sub>li</sub>, 1.5 and 3 mL/min), atomization air flow rate (Q<sub>aa</sub>, 450 and 742 L/h), and aspiration (A, 90 and 100 %) varied to assess their impact on aerodynamic parameters, which were studied in a cascade impactor, using a high-resistant inhaler. For cell culture studies, different MP<sub>IN</sub> concentrations (20 and 50 mM) were added to the Calu-3 cell line. The highest fine particle fraction for particles with aerodynamic diameters <5 µm (35.82 %) and the lowest mass median aerodynamic diameter (3.60 µm) values were found for Q<sub>aa</sub>: 450 L/h; A: 90 % and Q<sub>li</sub>: 3 mL/min spray-drying operating variables. MP<sub>IN</sub> significantly reduced IL-6 and IL-8 production in Calu-3 cells. No statistically significant differences were found between concentrations assayed. MP<sub>IN</sub> produced under the selected spray-drying conditions is a promising system for asthma inhalatory treatments.

**Keywords:** indomethacin; spray-drying; mass median aerodynamic diameter; fine particle fraction; cell culture.

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## **Conflicts of Interest**

The authors declare no conflict of interest.