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Short communication

Method optimization and validation for particle size distribution for Ibuprofen S380 using Malvern Mastersizer 3000

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Introduction

Particle size distribution (PSD) is a critical physicochemical attribute that characterizes the dimensional heterogeneity of particulate systems by quantifying the relative proportions of particles within defined size intervals. In pharmaceutical applications, PSD plays a pivotal role in governing key quality attributes, including dissolution kinetics, content uniformity, physical stability, and overall product performance. Variations in particle size directly influence surface area, interparticle interactions, and mass transfer processes, which in turn affect drug release and bioavailability.

Even subtle shifts in PSD can lead to significant changes in processing behavior, such as powder flowability, compressibility, and blend homogeneity, thereby impacting manufacturing robustness and batch-to-batch consistency. Consequently, precise and reproducible measurement of PSD is essential across all stages of the product lifecycle, from early formulation development to routine quality control.

Robust control of PSD is therefore fundamental to ensuring consistent product quality, regulatory compliance, and therapeutic efficacy.

Materials and methods

The Malvern Mastersizer 3000 is a laser diffraction-based particle size analyzer capable of measuring particle size distributions from approximately 10 nm to 3.5 mm. Instrument uses an advanced optical system with a wide detection range, ensuring accurate measurements across diverse particle sizes. The Hydro MV dispersion unit enables analysis of small sample volumes, reducing the consumption of costly dispersants, while the Aero S dry dispersion unit allows efficient and reproducible measurement of dry powders through controlled air dispersion.

The system provides automated control of dispersion processes, including pumping, stirring, sonication, and cleaning. The software supports SOP-driven workflows, data analysis, and reporting.

This study presents the optimization and validation of a laser diffraction–based analytical method for the determination of particle size distribution (PSD) of Ibuprofen S380 using the Malvern Mastersizer 3000 (EDQM, 2026; ISO 13320:2020) .

The primary objective was to enhance the robustness, accuracy, and reproducibility of the method under controlled laboratory conditions, thereby ensuring reliable and consistent

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measurement outcomes. Particular emphasis was placed on optimizing critical method parameters, including dispersion conditions, obscuration levels, and measurement settings (hopper gap of the sample tray, air pressure and ect.) in order to minimize variability and improve data quality. The assessment also considered the influence of sample preparation and instrumental factors on PSD results (ICH, 2005. ICH Q14).

Results and discussion

Method performance was evaluated through a comprehensive set of validation parameters:

Precision – Degree of closeness between individual results from replicate determinations of the same homogeneous sample take from the same material.

- Repeatability – refers to determination of precision of the method under the same conditions over a short period of time. In this study, repeatability was assessed using six replicate measurements.
- Intermediate precision – Intermediate precision refers to the evaluation of precision within the same laboratory under varying conditions, such as different days, analysts, or instruments. In this study, the assessment was performed using the same instrument and analyst, with measurements conducted on different days, with 6 replicate measurements for each day.

Robustness – systematically evaluated by introducing small, deliberate variations in key operational parameters, in order to assess the method's sensitivity and stability under slightly altered conditions (tests was assessed ussing 6 replications for each variation):

- Hopper gap ± 2 mm
- Air pressure ± 0.2 bar

All validation parameters were concluded with acceptance criteria for RSD values to not exceed 10% for D50 and 15% for D10, D90 and D4.3 while twofold acceptance criteria were applied to particle fractions below 10 µm to account for increased variability in finer particles (ICH, 2005. ICH Q2(R2); ICH, 2005. ICH Q14).

Conclusion

The method demonstrated high reproducibility, with relative standard deviation (RSD) values remaining within predefined acceptance limits. The findings confirm that the validated method is robust, reliable, and suitable for routine application, enabling accurate and controlled determination of particle size distribution in pharmaceutical analysis.

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