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Multivariate modelling for investigating the impact of raw materials and process variability on high drug load immediate release tablets obtained through wet granulation

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The batch-wise wet granulation, drying and tableting are ones of the most widely used technologies in the pharmaceutical industry, with potential impact on both product quality and processability in subsequent steps.

Multivariate data analysis by means of Principal Component Analysis and Projection to Latent Structures models can cope with the highly inter-correlated variables of interest from these processes.

In this study, the multivariate modelling approach was challenged using a historical dataset from 95 industrial-scale batches. This increases the level on inter-correlation even more as the available data are not the result of a planned study.

Batch level models show a good correlation between raw material properties and the evolution of torque values during wet granulation, with 70 % of the Y-variability explained by the model and showing a decent predictability ($Q^2 = 0,7$). The evolution of torque values during wet granulation and the raw material properties are correlated with differences observed in the granulate particle size and disintegration time of core tablets.

Expected correlations were confirmed by this modelling exercise (eg. the influence of active product ingredient particle size), but also new insights were gained regarding the influence of different excipient batches. Despite the relatively tight specification ranges applicable for excipients, the multivariate influence of all raw materials is a good starting point to consider for systematic optimization of disintegration time and tableting performance.