ABSTRACT

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The conventional process for developing new medicines involves selecting combinations of various types of factors that impact numerous properties of the final dosage form. This scenario is well-suited for using methods from the statistical field of design of experiments (DoE). Currently, the latest publications on pharmaceutical technology related to the development of new dosage forms are increasingly beginning to incorporate experimental design techniques, which are the subject of study in this work.

This interdisciplinary dissertation thesis is an annotated summary of the publication and research activities of the author and aims to explore the DoE approaches focusing on their practical applications within the realm of pharmaceutical technology; to apply the selected techniques in actual processes of pharmaceutical technology; and to present a review of the most useful techniques of DoE for implementation in pharmaceutical technology scientific area.

In a first published paper, we conducted a retrospective analysis of the data obtained to investigate the flow properties of four fractions of pharmaceutical sorbitol excipient, widely used in pharmaceutical technology. We explored the influence of factors such as orifice diameter and particle size, as well as their interaction, on the mass flow rate of the powder. To assess the obtained data, we utilized a model-fitting technique, constructing and evaluating a total of fifteen models. Our primary conclusions are as follows: (1) for models demonstrating satisfactory precision of flow rate prediction across a broad range of sorbitol particle sizes (0,1 to 0,346 mm), both orifice diameter and particle size need to be included as factors in the regression analysis; (2) for highly precise prediction of mass flow rate, a fully quadratic model is necessary; (3) we identified a statistically significant interaction between orifice diameter

and particle size. This study, which focused on the model excipient sorbitol for direct compression, illustrated the utility of analyzing and modeling flow rate.

In the second publication, we applied a central composite design (CCD) to determine the optimal conditions for milling excipients using a planetary ball mill, one of the most effective techniques for improving the solubility of poorly soluble drugs. After selecting the five most suitable from twenty-four samples of various materials used in pharmaceutical technology, a CCD was proposed for two factors (milling speed and milling time), each of which had five levels for each size of milling balls, with two responses (particle size, particle size distribution). For all ten factor combinations and each ball size, a quadratic response surface model was used to predict the response variable, particle size. For three substances out of five, the best results were achieved using five-mm balls. The approach achieved in this study was found to be useful and is expected to help in selecting the desired conditions of the material processing by dry milling to achieve the required particle size.

The last publication was related to the development of liquisolid delivery systems, representing an innovative approach to enhancing the dissolution of poorly soluble drugs. Four commercially available colloidal silica types were used as coating materials in nine different R values (the ratio of the mass of liquid to the mass of carrier in the range from 5 to 100), to evaluate the compressibility properties of liquisolid powder and the compact obtained. The results of PCA suggest 1) a strong positive correlation between the outcomes of the angle of slide and tablet friability, which can be considered the most sensitive outcomes; 2) the fact that the coating material does have an influence on the output.