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QUALITY BY DESIGN AND PARTICLE ENGINEERING VIA SPRAY DRYING

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Particle Engineering is a young discipline that combines elements of microbiology, chemistry, formulation science, colloid and interface science, heat and mass transfer, solid state physics, aerosol and powder science, and nanotechnology

The development of **pulmonary therapeutics** that have been intensified in the last decade, comes followed by efforts to understand and control particle formation processes (2,3)

The process that drives **particle formation** is not fully understood yet due to the interaction among many parameters. Therefore, the prediction of the final size, morphology and solid state is complicate requiring a deeper understanding.

The main aim of this project is to investigate which parameters play a key role in the particle formation process and how these properties (parameters) can be model in order to predict the final optimal particles with the desired characteristics. This systematic evaluation allows the detection of interaction between factors and to construct prediction models with the aim of finding rapidly the global optimal conditions. The application of design of experiments to particle formation via spray drying using different model compounds is also studied.

METHOD: spray drying has been the first selected of the among particle engineering strategies (Figure 1). A traditional spray dryer is used to convert liquids into dry powders. This is achieved by mixing a heated gas with an atomized (sprayed) fluid of high surface-to-mass ratio droplets, ideally of equal size, within a vessel (drying chamber), causing the solvent to evaporate uniformly and quickly through direct contact and allowing the dry particles to flow through the cyclone and be deposited in the collector vessel (Figure 1). In order for solvent evaporation to be effective, the temperature of the process must be above the boiling point of the solvent. The process is very rapid, allowing the drying of even temperature-sensitive materials without further degradation [4]. The powder is generally generated as a matrix system in the form of crystalline and amorphous microparticles [5]. The solid-state is critical as determines the apparent solubility of the material

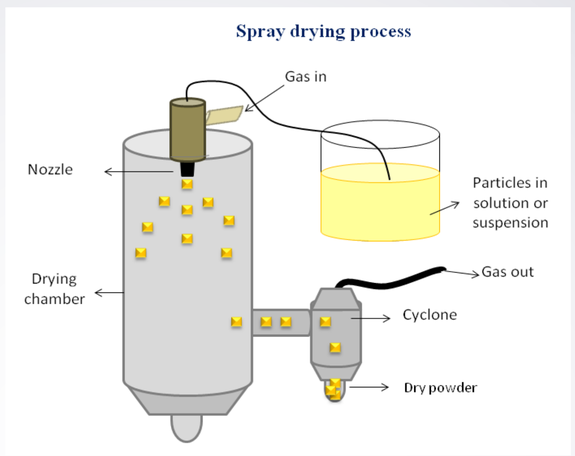

Figure 1. Set up of spray drying instrument (modified from (4).

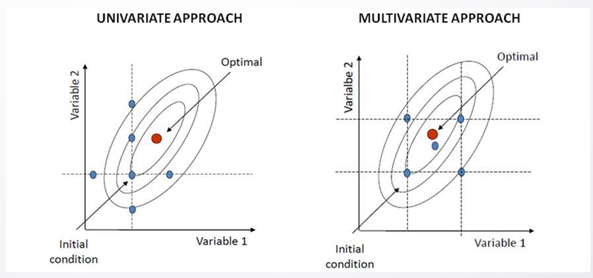

Figure 2. Experimental design: univariate vs multivariate approach

The parameters have been selected to understand their effect in the final dry particles obtained in the process:
-**Feed rate** (ml/min) and preparation (particles can be dissolved or be suspended in the medium).
-**Atomization** (transforming the feed into droplets): Most critical step in the process. The degree of atomization controls the drying rate and therefore the dryer size. The two parameters that can be controlled are: i) pressure nozzle atomization (spray created by forcing the fluid through an orifice which is an energy efficient method which offers the narrowest particle size distribution) and ii) two-fluid nozzle atomization (spray created by mixing the feed with a compressed gas being useful for making extremely fine particles).
-**Temperature** that will determine the residual moisture in the dry powder collected.
Complex structured microparticles are difficult to design using an empirical univariate approach alone because of the many process and formulation variables that need to be tuned correctly to achieve the desired result (requiring quality by design). In the univariate approach (try and error method), one parameter is changed at a time and then the experimental domain is formed by lines but it is not a systematic evaluation because the optimal condition will never be reached and interaction between factors cannot be detected easily (Figure 2).

In order to do a Design of Experiment of how different spray dryer parameters affect to the pulmonary delivery formulation in which the Geometric and Aerodynamic Particle Size are important characteristic to study (Chart 1). The air flow and the aspirator have the most significant effect in the final particle size of the formulation. The components of the formulations are also studied as a parameters (chart 2 and 3).

SD. PARAMETERS	Aspirator	Spray Rate	Air Flow	Inlet (Temperature)
Aerodymanic Particle Size (MMAD)	↓	↓	↑	↑
Geometric Particle Size (PSD-D50)	↓	↓	↑	↑

Chart 1. How The Spray Dryer Parameters should be to reach the minimal particle size

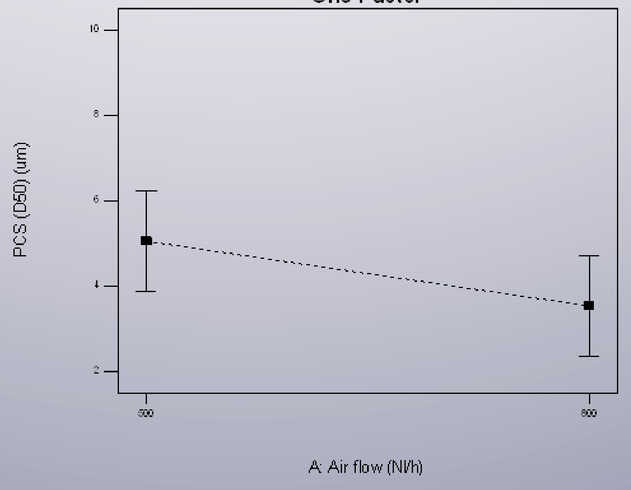

Chart 2. The Air Flow Parameter has significant effect in the PSD of the final formulation.

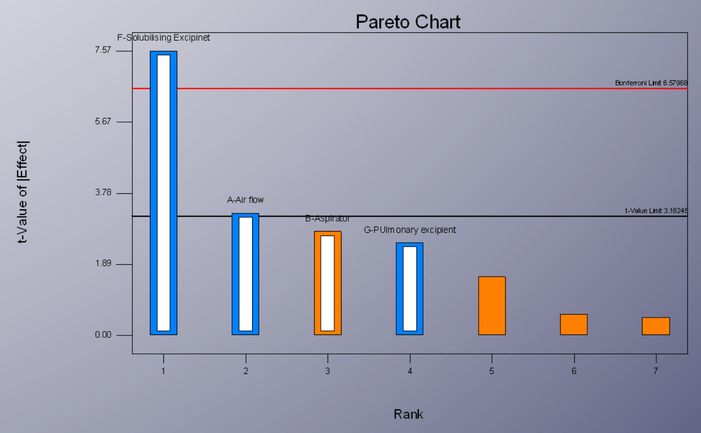

Chart 3. Parameters that affect to the PSD

FUTURE PERSPECTIVE: The potential use of this basic research could be applied in to multiple disciplines and industries such as food and pharmaceutical industries

References

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