DOE Modelling and Optimization of Tangential Spray Rotogranulation Mechanism

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Abstract

The production of the pellets in the pharmaceutical industry generally involves multi-step processing: 1 mixing, 2 wet granulation 3 spheranization 4 drying. Tangential spray rotogranulation is now being considered as an alternative since it combines number of steps into one processing unit thus reduces processing time. This work aimed to development and doe analysis of GPCG125 and optimization using factorial design. The factors consider were 1-Disc Velocity 2-Feeder rate 3-Air Flow Rate 4-Atm Pressure. The pellets were characterized for their physical properties like drug content. The results indicated that Disc velocity has negative effect on drug content while the feeder rate has positive effect.

Keywords: Pellets, rotogranulation, drug, properties, processing time

I. INTRODUCTION

In the process involving a fluid-bed, particles are suspended in a fluid-like state using gas introduced at the bottom of the bed. The gas is normally preheated before it is pumped to the bed where it acts as both heat and momentum carrier. The coating material is sprayed directly into or onto the particles. There are a number of possible processes that can take place inside the bed depending on the bed’s conditions, seed particle characteristics and the coating material used. Once the coating solution is atomized in the nozzle, the resulting droplets can be successful or unsuccessful in reaching and attaching themselves to a particle surface. The coating solution that does not attach itself to a particle is spray dried and may be elutriated out of the bed if it is light or remain in the bed if it is sufficiently heavier. The fines that remain in the bed can be joined with other spray-dried fines resulting in fines agglomeration or they can be captured by larger particles resulting in ‘snow ball’ growth.

A. Disc Velocity:

A helicoidally flow pattern is a characteristic of FBRG which is essential for an efficient spheranization of the agglomerates and an adequate liquid distribution on the bed particles. At low disc velocity, this motion profile disappears and the excessive agglomeration that follows can induce the formation of lumps and material deposition on the processor walls. At high disc velocity, Particle-Particle and particle-wall contacts increases as the bed turnover also increases. It creates a chaotic flow pattern in the bed and yields to increased particle breakage, which can compromise granulation and dosage uniformity of a pharmaceutical product.

B. Feeder Rate:

To obtain a product that is similar at small and large scales, the bed moisture content has to be monitored correctly. Binder flow rate journal affect the bed moisture content. The bed mass can also affect the bed moisture content. It must be conveniently scaled from the small to the large-scale units.

C. Air Flow Rate:

In wet granulation system that use fluid beds, the exhaust air and product temperature reach an equilibrium state. This equilibrium state is directly associated to an adiabatic saturation of the air as it passes through the bed of wet particles. This means that water injected in the bed with the binder solution is completely removed by evaporation.[4]

II. MATERIAL AND METHOD

A. Process Parameter:

There are two phenomena that mainly affect the rotogranulation the solid flow pattern that influences the particle collision velocity and frequency, and the moisture content that plays a role in the particle cohesion through capillary forces and breakage mechanisms. The low inlet air temperature used allows operating in a more sensitive zone of the drying air capacity which promotes net process responses to inlet air temperature and moisture content adjustments thus providing more flexibility on scale-up. It also mimics processing conditions encountered with heat sensitive drugs.
B. Equipment and formulation:

Instrumented tangential spray rotoprocessors GPCG125 were used for this study. The statistical analysis and process optimization were carried out with GPCG125

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td>Disc Velocity</td>
<td>500-1000 rpm</td>
</tr>
<tr>
<td>Feeder Rate</td>
<td>2-3.3 gm/min</td>
</tr>
<tr>
<td>Air Flow Rate</td>
<td>150-180 m³/hr</td>
</tr>
<tr>
<td>Atm Pressure</td>
<td>140-210 kpa</td>
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</table>

C. Experimental Design:

A 2^4 fractional factorial design was prepared to statistically analyse the final product properties mentioned above. Sixteen experiments were carried out, which correspond to two levels for the five process parameters.

III. RESULTS AND DISCUSSION

A. Statistical Analysis

The statistical analysis was carried out by design expert software

<table>
<thead>
<tr>
<th>Run</th>
<th>Disc Velocity (rpm)</th>
<th>Feeder Rate (gm/min)</th>
<th>Air Flow rate (m³/hr)</th>
<th>Atm Pressure (kpa)</th>
<th>Drug Content (%)</th>
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<tbody>
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<td>210</td>
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</tr>
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</table>

B. Priority Analysis:

For getting an idea about the positive and negative effect of the parameter which is affecting on coating efficiency of the pellets, pareto Chart analysis is done from the results it’s clear that disc velocity is negatively affecting the coating while the factors like atm pressure, Feeder rate and air flow rate has positive effect on coating.
C. DOE Equation:
DOE equation has been generated for getting an idea about how should be the values of the parameter for maximum results following figure shows the doe equation

D. Drug Content Result:
By selecting the actual parameters which having the direct impact on coating on pellets i.e air flow rate 165 and atm pressure 175


**E. Response Surface Model:**

It is described as the assembly of mathematical and statistical methods for forming and analysing difficulties according the response that is affected by the involved variables aiming at the optimization of this response. If a response is plotted against the levels of the factors, it is usually represented as a response surface for visualizing its shape, a contour plot is used additionally. Each contour plot resembles to a specific type of response surface.

A low-order polynomial is used in the region of interest of the independent variables; if a linear function is efficient for modelling the response, a first-order model is being employed. If a curvature is found, it is advantageous to use a second-order model. It is obvious that these models are only working for a limited region of interest.

**F. Optimization:**

Optimization of the parameters value in there range is calculated by design expert Insertion of the optimization criteria it possible to obtain the optimal process parameter values for a given set of final product properties. An experiment was carried out using this set of optimal process parameter condition the measured final product properties of the experiments compared with the statistical model prediction. The drug content assay reveals that the optimized product is within the desired criteria.
The maximum deviation observed is 4%, which indicates that the model is efficient for predicting the granular properties as a function of the process parameters. Also, all characteristic values comply with the desired product criteria.

IV. CONCLUSION

This work studied the rotogranulation final product properties with respect to four process parameters (1) disc velocity, (2) Air flow rate, (3) Binder flow rate and (4) atomization pressure. A statistical linear regression model first allowed the determination of an optimized set of operating conditions in order to obtain a high quality final product. The statistical model was experimentally validated, with observed Variations between predicted and measured properties below 4%.

REFERENCES

[4] Optimization and scale-up of a fluid bed tangential spray rotogranulation process J. Bouffard a, H. Dumonb,*, F. Bertrand a, R. Legros a