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THE INFLUENCE OF THE MOISTURE CONTENT OF MICROCRYSTALLINE CELLULOSE ON THE COATING PROCESS IN A FLUIDIZED BED

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Abstract - The objective of this work was to study the coating of microcrystalline cellulose with a polymeric suspension in a fluidized bed. The coating operation was carried out using a fluidized bed with top spraying by a double-fluid nozzle. The fluidized bed consists of a cylindrical column made of plexiglass with a height of 0.6 m and an inner diameter of 0.14 m. The polymeric coating suspension was formulated using Eudragit® as the basic component. As the quality of the coating product is greatly affected by the spraying characteristics, the influence of the flow rate of the coating suspension and the moisture content of the particles on the agglomeration index and efficiency of the process of coating microcrystalline cellulose was analyzed.
Keywords: coating, fluidization, moisture content, microcrystalline cellulose.

INTRODUCTION

The process of particles coating has been widely employed in food, dye, fertilizer, agricultural and specially in pharmaceutical industries. The main objectives of coating solid particles are to obtain a product with controlled release of active components, to protect the particle from external conditions, to mask taste and odor and to provide physical and chemical protection to a specified component. The principle of operation of a fluidized bed coater consists in passing a preheated gas through the particles to be coated with a velocity higher than the minimum fluidization velocity. The particles are intensively mixed and the energy for drying the coated product is available. The coating material can be fed by spray nozzle as a solution, dispersion, suspension or melt in the form of tiny droplets. It can be injected into the fluidized bed at the top, side or bottom.

The literature presents works concerning the process of granule coating in the pharmaceutical area in fluid-dynamically active equipment, like the Glatt and Wurster process (Fukumori *et al*., 1991; Ichikawa *et al*., 1993; Heng et al., 1996 and Altaf *et al*., 1998), aiming mainly at analyzing the product in terms of formulation, additives and efficiency of the release kinetics. However, it's necessary to study the effect of operational variables aiming at process optimization. Knowledge of the process allows design of the fluidized bed equipment to operate under optimized conditions. Microcrystalline cellulose in solid formulations of oral dosage is the main excipient used in the pharmaceutical industry due to its low reactivity with the active ingredients. In this work, two ranges of particle sizes were used: -0.420 + 0.300 mm for experiments 1 to 3 and -0.420 + 0.210 mm for experiments 4 and 5, with mean diameters of 0.330 and 0.308 mm, respectively. The objective of this work was to study the coating of

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microcrystalline cellulose with polymeric suspension in a fluidized bed and to analyze the efficiency of the process, the relative growth of particles, the agglomeration index and the effect of the moisture content of the particles before the bed collapsed.

MATERIALS AND METHODS

Materials

To study the fluid dynamics and coating in the fluidized bed, microcrystalline cellulose – MICROCEL, with a bulk density of 0.98 g/cm^3 and a sphericity of 0.62, obtained for both sizes of particles, 0.330 and 0.308 mm was used.

Development of the coating suspension aimed at achieving an uniform and smooth coating surface. An aqueous polymeric suspension with a solids weight concentration of 12 % was utilized. The polymer applied was Eudragit® and the formulation included a pigment suspension of talc, titanium dioxide, magnesium stearate and lake colorant. This suspension had been used previously in polymer coating of urea in a spouted bed (Donida and Rocha, 2000). Table 1 shows the composition of this suspension.

The polymeric suspension, having Eudragit® as its basic component, is atomized on the of particles bed by a double-fluid nozzle. Preceding the coating experiments, the effects of the atomization air on the fluid-dynamic behavior of particles of microcrystalline cellulose in the fluidized bed were analyzed under different operational conditions of pressure and atomization air flow rate. Visual observations of the bed dynamics were made during the experiments, before collapse of the fluidized regime. In this stage, temperature, bed pressure drop and the moisture content of the particles were measured in order to identify the causes of bed collapse.

Table 1: Composition of coating suspension

Reactants	(%) weight
Eudragit L30-D55	16.7
PEG 6000	0.75
Talc	2.75
Magnesium stearate	1.00
Titanium dioxide	1.40
Lake colorant	0.60
Triethyl citrate	0.50
Water	76.30

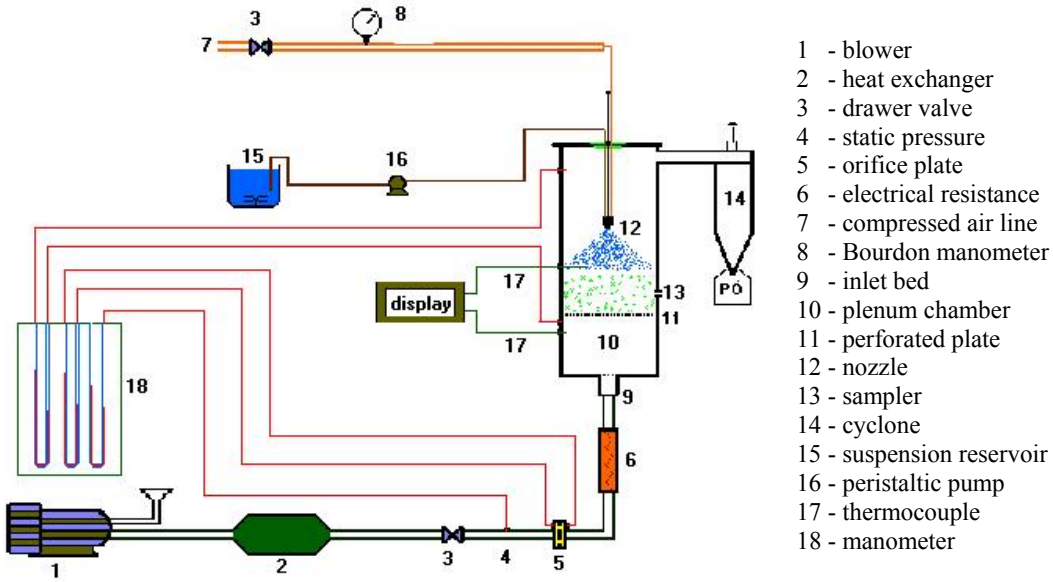

Figure 1: Sketch of the experimental fluidized bed

Experimental Setup

The experimental setup used in this study is shown schematically in Figure 1. The fluidization column was constructed of plexiglass having an inner diameter of 0.14 m and a height of 0.6 m. A 0.2 m high plenum chamber (10) is placed to the lower end of the column. The air distributor is a stainless-steel perforated plate with a free area of 5 %. Before entering the bed, the air is preheated by an electrical heater and the fluidizing air flow rate is measured by an orifice plate. The elutriated particles are collected at the column outlet by a cyclone. The nozzle atomizer (12) was supplied by a compressed air line (7) and the coating suspension was conveyed by a peristaltic pump (16).

a) Measuring Flow Rate of the Fluidization Air

The airflow rate is controlled by a drawer valve. There is an orifice plate on this line, where differential pressure is measured in a flange connected to the plate by a U-tube differential manometer whose manometric fluid has a density of 0.75 g/cm^3.

Through the calibration equation for the orifice plate, the airflow rate is calculated as a function of the differential pressure on the plate. This equation was developed based on Ower and Pankhurst (1977):

$$Q = 0.718\left[\frac{\Delta P}{273.15+T}\right]^{0.5} - \left[\frac{0.22}{P_{sta}}.\frac{(\Delta P)^{1.5}}{(273.15+T)^{0.5}}\right] \quad (1)$$

where ΔP is the bed pressure drop, T is gas temperature and P_{sta} is the absolute static pressure in the bed.

The mean velocity of the air in the bed is calculated by the following ratio:

$$U = \frac{Q}{\rho_g . A_t} \quad (2)$$

where ρ_g is gas density and A_t is the cross-sectional area of the bed.

The operational velocity, U_{op}, was of 15 cm/s, corresponding to 2.6 times the minimum fluidization velocity, U_{mf}. In this work, U_{mf} was determined by Richardson's classic method (Richardson, 1971).

Atomization System

The atomization air is supplied by a blower of 10 cv, displacement of 1.1 m^3/min and maximum pressure of 175 psi. The line of compressed air has an inner diameter of one inch. The coating suspension is in 2,000 mL container under magnetic stirring.

The top spraying was done by a double-fluid nozzle, supplied with compressed air and the coating suspension conveyed by a *Masterflex* peristaltic pump.

Fluid Dynamics of the Bed

Before the coating experiments, preliminary tests were conducted with microcrystalline cellulose, aiming to establish appropriate fluidization conditions, based on observation of bed dynamics, related to operational velocity. A fluidization run was carried out during 2 h to verify the occurrence of particle damage by friction in the bed. After 0, 1 and 2 h samples of 50 g were collected to verify the breakage of particles by screen analysis with sieving and also with photos of the particles obtained by microscopy. This experiment was carried out with the load that had the best conditions for the fluidization regime, 0.7 kg of MICROCEL (Silva and Rocha, 2002).

Continuous Feeding of Coating Suspension

The process begins with air fluidization supplied by a blower of 2 cv with an empty bed. The air is heated to the desired temperature (60^{o}C) by a group of four resistances in the fluidization air line.

After stabilizing bed temperature, the valve for air fluidization is closed and a load of 0.7 kg of MICROCEL is introduced into the bed. Soon after, the valve is opened and adjusted to the operational velocity, defined previously as 15 cm/s, to provide a good movement of the particles into the bed. The choice of load and of operational velocity was based on preliminary tests and by the limiting conditions of the equipment (Silva and Rocha., 2002).

The next step is atomization of the coating suspension, as described in the section on atomization system. When the coating suspension reaches the nozzle, it comes in contact with the compressed air and produces a spray on the particles bed.

After coating, the peristaltic pump is turned off and the particles are fluidized during 15 minutes, so that the moisture content of the particles can be reduced, preventing bed packing and facilitating withdrawal of the particles from the bed. The final product is removed from the bed and weighed.

a) Process Condition

The operational conditions were defined in preliminary experiments and are given in Table 2, where Ws is the suspension flow rate and P_{at} is the atomization pressure. The inlet air temperature was maintained at 60 ^{o}C and the load in the bed at 0.7 kg for all the experiments. The pressure drop in the bed ranged from 490 to 505 Pa, in agreement with the resistance that the bed offers during the coating process.

Coating with Intermittent Feeding of Suspension

For the experiments using a coating suspension flow rate higter than 6 g/min with an atomization pressure of 20 and 30 psi, it was necessary to conduct the coating process with intermittent feeding of suspension due to the tendency of the bed to collapse. At each interruption of the coating suspension, a sample of particles was collected from inside the bed. Bed temperature and pressure drop were measured and the fluid-dynamic behavior of the particles in the bed was observed. Also, the moisture content of the particles was determined three times by the Karl Fischer's method and then averaged.

Atomization of the coating suspension was restarted when the bed showed a good movement of particles until the need for a new interruption, which was visually verified by the occurrence of dead zones and a reduction in particle movement.

Table 2: Operational conditions

Variables	Experiments				
	Intermittent			Continuous	
	1	2	3	4	5
W_s (g/min)	8.9	13.4	15.9	5.4	5.5
P_{at} (psi)	20	30	20	10	20

Determination of Coating Efficiency, the Agglomeration Index and Particle Growth

In the fluidized-bed coating process, MICROCEL granules grow by a layering mechanism. Each time the solids pass through the spray zone, a thin liquid layer is added to the granules and quickly solidifies. For evaluation of coating efficiency, η, the definition used by various researchers (Kucharski and Kmiéc, 1988; Oliveira, 1992; Ayub, 1993; Silva and Rocha, 2002), as in Equation 5, was adapted.

$$\eta = \frac{\text{mass of solid adhering to particles}}{\text{total mass of solid supplied to the bed}} = \frac{M_f - M_i}{W_s C_s t_p} \quad (5)$$

where M_f is the final load of particles, M_o is the initial load of particles, W_s is the suspension flow rate, C_s is the suspension concentration and t_p is the process time.

After they were sieved a small quantity of the coated particles had a diameter larger than 0.42 mm. These particles were defined as agglomerated and an agglomeration index was determined by Equation 6.

$$Agl = \frac{M_{agl}}{M_t} 100 \quad (6)$$

where M_{agl} is the total weight of agglomerates and M_t is the total mass of the product.

The mass relative growth was calculated by Equation 7.

$$\delta = \frac{M_f - M_i}{M_i} 100 \quad (7)$$

The moisture content of the particles during the coating process was determined by the Karl Fischer method.

RESULTS AND DISCUSSION

Fluid Dynamics and Coating

As reported by Silva and Rocha (2002), the friction between particles during the fluidization

does not cause significant breakage. However, it was verified that around 2 % of the material had a diameter smaller than 0.100 mm in the two ranges of particle size studied. The two size ranges of particle sizes used in this work showed similar behavior and adequate solids movement during fluidization.

It was verified during the experiments that most of these fine particles were picked up in the initial instants of fluidization, evidencing that they were still linked to the larger particles (dp = 0.300 mm) by electrostatic forces. More than 60 % of the fines picked up by the cyclone contain particles smaller than 0.075 mm. This result indicates that the particles are quite cohesive in this size range (dp < 0.100 mm). When they are attached to the large particles, it is difficult to separate them by sieving. Thus, to continue this study, the total particle load is fluidized for five minutes before starting the coating process.

Figure 2 shows photos of the particles (40X magnified). In photo (a), particles of MICROCEL before fluidization can be observed; in (b), particles submitted to fluidization for 2 h are seen; in (c), the coated particles are shown and in (d), the formation of agglomerate during the coating process can be observed.

The formation of undesirable agglomerates indicates a shift in coating regime from layering to coalescence. It´s possible to observe the result of this behavior in Figure 2d. The range of the agglomeration index attained was from 0.4 to 4 %.

Five experiments on coating of MICROCEL were carried out using an Eudragit® polymeric suspension. After the experiments, the size distribution of these coated particles by sieving was analyzed. The distribution histograms are presented in Figures 3 and 4, were the experiments are identified with numbers from 1 to 5. In runs 1 to 3, the uncoated particles used are in the following size range: -0.420+0.300 mm. For experiments 4 and 5, this range was enlarged to -0.420+0.210 mm. The number "0" in Figures 3 and 4 represents the distribution of the uncoated particles of MICROCEL, having mean diameters of 0.330 and 0.308 mm, respectively. In Table 3 the mean diameters of the particles are presented for the two size ranges, before and after coating.

In the size distribution shown in Figures 3 and 4, it can be observed that an accentuated relative growth occurred for the mean range of particle sizes of around 0.355 mm independent of the size range used. Comparing the graphic behavior of these size distributions with the values in Table 3, it can be observed that this result contributed towards obtaining high values for the mean diameter of the particles, as in experiments 1, 3 and 4.

For coatings using the -0.420 + 0.210 mm range of particle sizes, runs 3 and 4, a larger amount of fine powder was collected by the cyclone (2.2 and 3.75 %) than for to the -0.420 + 0.300 mm range of particle sizes which had values lower than 0.5 %, for runs 1, 2 and 3.

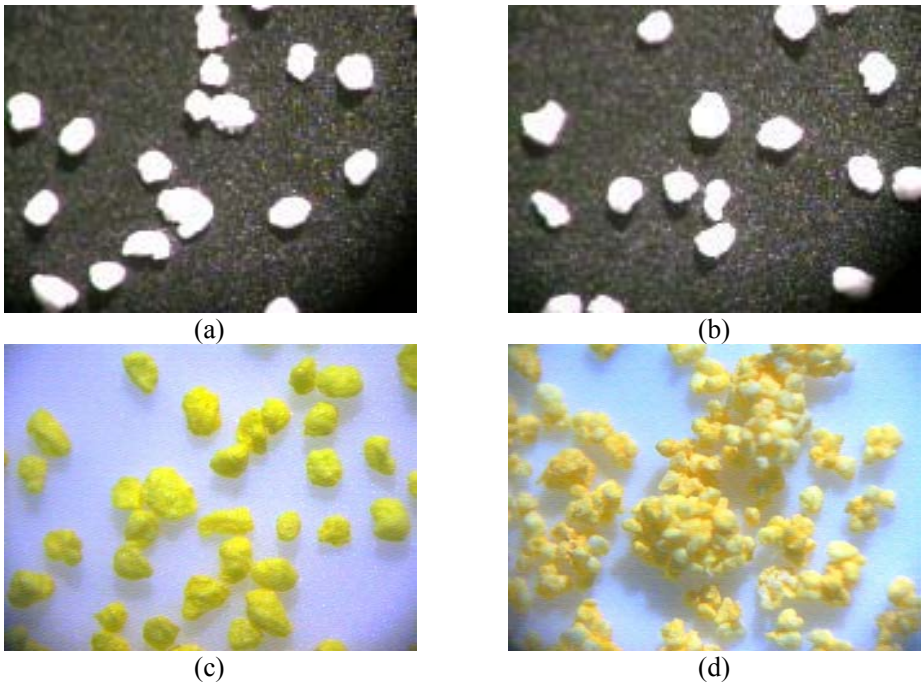

Figure 2: Photos of the MICROCEL particles. (a) before fluidization; (b) fluidization for 2 h; (c) after coating and (d) agglomerated particles.

Table 3: Particle-size distributions of MICROCEL before and after the coating process

Figure	Number	dp (mm)
3	**0**	**0.330**
	1	0.351
	2	0.344
	3	0.351
4	**0**	**0.308**
	4	0.321
	5	0.311

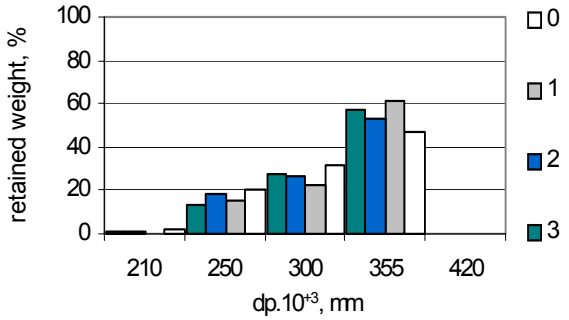

Figure 3: Particle-size distributions of MICROCEL for experiments 1, 2 and 3.

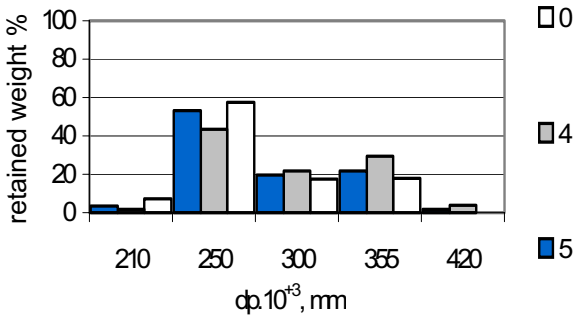

Figure 4: Particle-size distributions of MICROCEL for experiments 4 and 5.

Determination of Moisture Content the Particles Before Collapse of the Bed

The experimental results point out that the suspension flow rate, associated with atomization pressure, has an important influence on the coating process. Packing of the bed was observed for the runs conducted with high coating suspension flow rates: 8.9; 13.4 and 15.9 g/min. This evidence was preceeded by the following effects:

1) a reduction in particle movement into the bed;
2) a decrease in temperature in the atomization region;
3) a small increase in bed pressure drop;
4) channeling.

In all experiments, moisture content of the particles was measured at each interruption of the atomization suspension, before collapse of the bed. In Figures 5 and 6, the effects of moisture content are shown, together with bed pressure drop and temperature versus time of coating. Pressure drop and temperature in the bed showed smaller variations than moisture content of the particles. We can observe that moisture content increases until reaching three times the initial condition of the particles, evidencing its strong influence at the moment that the bed approaches collapse. Thus, variations in the bed pressure drop and temperature can not be used as parameters to identify the moment at which the bed tends to pack. On the other hand, moisture content of the particles was shown as a decisive factor in identifying this moment at which it increases and the movement of particles decreases. The critical value for moisture content, at which bed collapse occurs, is 22 %.

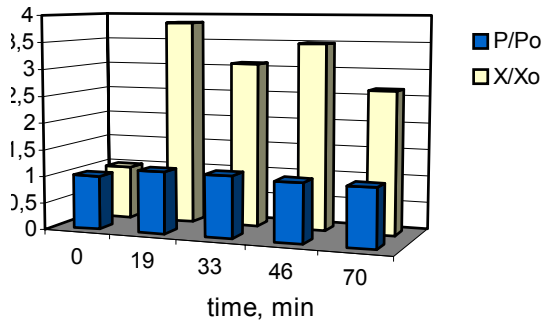

Figure 5: The influence of bed temperature and moisture content of the particle versus process time. P_o = 495Pa and X_o = 8 %.

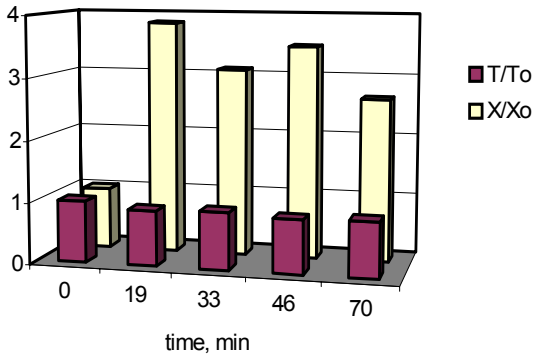

Figure 6: The influence of bed temperature and moisture content of the particle versus process time. T_o = 34°C and X_o = 8 %.

Analysis of Efficiency, Growth and the Agglomeration Index

The results of the coating experiments are presented according to the experimental procedure used for the feeding of the coating suspension: intermittent or continuous.

a) Intermittent Feeding of the Coating Suspension

The results of coating experiments 1, 2 and 5 are shown in Table 4. It can be observed that run 5 had high efficiency, high relative growth and a high agglomeration index, as this run was carried out with a size distribution with a large number of small particles, a high coating suspension flow rate and a long process time. A larger number of fine particles was collected by the cyclone (3.75 %) than in runs 1 and 2, which produced a percentage of agglomeration lower than 0.5 %.

b) Continuous Feeding of Suspension

The results obtained for coating runs 3 and 4 are presented in Table 5. The results indicate that when the -0.420 + 0.210 mm range of particle sizes is used one can obtain higher efficiency, higher relative growth and a higher agglomeration index. Similar behavior was found for the experiments conducted with feeding of the coating suspension in an intermittent way.

With the results presented here it is not possible to guarantee that the film formed during the coating process has the same thickness for all the particles. However, analyzing the colored surface of the particles by optical microscope, one can verify an uniform film involving the whole particle surface. It is also observed that there is not any particle without coating in the product, indicating the process viability.

Table 4: Experimental results

RUN	1	2	5
W_S (g/min)	8.9	13.4	15.9
P_{at} (psi)	20	30	20
t_p (min)	40	35	70
T_l (°C)	32	27	29
η (%)	80.3	78.2	86.4
δ (%)	4.4	5.6	17.5
Agl (%)	0.3	0.1	2.0

Table 5: Experimental results

RUN	3	4
W_S (g/min)	5.5	5.4
P_{at} (psi)	20	10
t_p (min)	70	110
T_l (^oC)	31	29
η (%)	55.6	69.4
δ (%)	3.3	7.1
Agl (%)	0.4	4.0

CONCLUSIONS

From the results presented and analyzed here, the following conclusions can be drawn:

1) the two ranges of particle sizes used in this work showed similar behavior and adequate solids movement during the fluidization;

2) the relative growth of particles was evidenced more for a particle diameter of 0.355 mm, as shown by the retained weight versus particle diameter histogram, independent of the initial size range used;

3) the utilization of suspension flow rates higher than 6 g/min was possible only with intermittent feeding;

4) the coating experiments using the -0.420 + 0.210 mm range of particle sizes had a larger number of agglomerates (4 and 2 %), a larger number of fines collected by the cyclone (2.2 and 3.7 %) and a greater relative growth of particles, while another distribution (-0.420 + 0.300 mm) had amounts smaller than 0.5 % for all the parameters;

5) the moisture content of the particles during coating was the most important factor in identifying the beginning of collapse of the bed;

6) satisfactory values were obtained for coating efficiency, up to 86 % were obtained for two operational conditions when the suspension was fed in an intermittent way with W_s = 8.9 and 15.9 g/min, P_{at} = 20 psi, T = 60 ^oC;

7) It's possible to carry out the coating process with this range of particle sizes in a fluidized bed only with intermittent feeding of the suspension. To understand the influence of operational variables in the process, it's necessary to study it by experimental design.

NOMENCLATURE

Agl	Agglomeration index	%
A_t	Cross-sectional area of the bed	cm^2
C_S	Suspension concentration	g/min
dp	Particle diameter	mm
M_{agl}	Total weight of agglomerates	g
Mo	Initial load of particles	g
M_f	Final load of particles	g
M_t	Total mass of product	g
P_{at}	Atomization pressure	psi
$P_{está}$	Static pressure drop in air line	cm H_2O
Q	Airflow rate	kg/min
t_p	Process time	min
T_g	Gas temperature	^oC
T_l	Bed temperature	^oC
U	Gas superficial velocity	cm/s
U_{op}	Operational velocity	cm/s
Ws	Suspension flow rate	g/min
ΔP	Pressure drop	Pa
δ	Relative growth %	
ΔP	Pressure drop on the orifice plate	cm H_2O
ρ_g	Gas density	g/cm^3

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