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Effect of operating conditions and physico-chemical properties on the wet granulation kinetics in high shear mixer

M. Benali*, V. Gerbaud, M. Hemati

Laboratoire de Génie Chimique, UMR CNRS 5503, 5 rue Paulin Talabot, BP1301, 31106 Toulouse Cedex 01, France

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A B S T R A C T

The wet granulation process is sensitive to changes in product properties and process variables. The optimal process and formulation are based on the knowledge of the granule growth mechanisms and of the effects of product properties and process variables. This paper presents the study of wet granulation of microcrystalline cellulose powder, MCC (Avicel PH101) using high-shear mixer granulator. It aims at understanding the effect of operating parameters (impeller rotational speed, liquid binder flow rate) and of physicochemical properties (viscosity, wettability) of a binder solution on solid particles surfaces, on the agglomeration kinetics. The experiments are carried out with water, aqueous solutions of sodium carboxymethylcellulose, polyvinylpyrrolidone, hydroxypropylmethylcellulose or a non ionic surfactant oxo-C₁₀C₆ at a critical micellar concentration.

Concerning the process variables the experimental results show that an optimal interval of impeller speed operation exists ranging from 150 to 200 rpm for granule growth. Below, an uncontrollable agglomerate size and localised over-wetting occur, and above granule breakage occurs. Increasing the liquid binder flow rate reduces the extension of the non growth regime, but does not affect the granule mean size.

The effect of the physicochemical properties is evaluated using a modified capillary viscous number, Ca' , that we define as the ratio between the viscous forces (μU) and the work of adhesion $W_a = \gamma_L(1 + \cos\theta)$. For $Ca' < 1$, the viscosity of the solution does not significantly affect the granulation process. The dominant forces in the granulation process are the interfacial forces since increasing the work of adhesion enhances the growth kinetics. For $Ca' > 1.6$, the viscous forces predominate and control the granule growth.

1. Introduction

Granulation may be considered as a size-enlargement process where small particles are formed into larger, physically strong agglomerates, in which the original particles can still be identified.

In wet granulation processes, this is performed by spraying a liquid binder onto the particles while they are agitated in a tumbling drum, a fluidized bed, a high shear mixer or similar devices. The main objectives of granulation are to improve the flow properties and compression characteristics of the mix, and to prevent segregation of the constituents. The wet granulation in a high shear mixer is characterized by a short processing time and less liquid binder's consumption compared to fluidized beds or low shear mixer granulators [1–3]. Granulation has been described in three principal mechanisms [4]: *wetting and nucleation*; *consolidation and growth*; *attrition and breakage*. These mechanisms control the obtained granule properties and are influenced by a combination of formulation design (choosing the feed powder, binder, and the liquid properties) and process design (choosing the type of granulator and the operating parameters).

Hence, the growth mechanisms depend on the relative magnitude of:

- the building forces depending on the local phenomena taking place at the solid surface. These phenomena depend on the physico-chemical properties of the solution and of the solid particles.
- the break-up forces depending on the process variables, such as the impeller speed, the bed geometry and the atomization conditions. These variables affect the growth kinetics by modifying the mixing intensity.

According to Rumpf [5], the main cohesive forces that operate during wet agglomeration result from static liquid bridges formed between the solid particles. The strength of agglomerates depends on the surface tension of the liquid, on the wettability of the solid particle with respect to binder solution and on the particle size and shape. During the granulation process, the particles undergo relative displacements with respect to one another. The liquid bridges cannot be regarded as stationary, and the interparticle attractive force depends on the viscosity of the granulating solution in addition to surface tension and binder-particle wettability [6].

Ennis et al. [7] expressed the importance of the viscous force in comparison with the capillary force through the capillary number

* Corresponding author.

E-mail address: Mohammed.Benali@ensiacet.fr (M. Benali).

Table 1
Physical properties of solid particles

True density ρ_s (kg/m ³)	Bulk density (kg/m ³)	BET (m ² /g)	Shape factor ϕ (%)
1540	450	1.36	27

$Ca = \mu_L U / \gamma_L$, where γ_L is the liquid surface tension, μ_L the liquid viscosity and U the velocity (in agitated process $U = \pi ND$, where N is the impeller speed and D the bowl diameter). When the capillary viscous number is greater than a critical value ($Ca > 1$), the cohesion of dynamic liquid bridges becomes greater than that of the static liquid bridges. This is attributed to the additional effect of viscous energy dissipation. Despite numerous applications of granulation in high shear mixers, the dominant force is not pointed out experimentally in the literature.

This work deals with the wet granulation of microcrystalline cellulose powders by aqueous solutions of polymers. It aims at understanding the effect of operating condition and the main forces which lead to the formation of granules in a high shear mixer. The effects of physicochemical properties, such as the viscosity of the solutions and the wettability of the solid by the liquid, on agglomeration kinetics are pointed out.

2. Materials and methods

2.1. Materials

The experiments were conducted using a microcrystalline cellulose powder (MCC) (Avicel PH 101) having the following characteristic diameters: $d_{10} = 10 \mu\text{m}$, weight mean diameter $d_{p0} = 60 \mu\text{m}$ and $d_{90} = 140 \mu\text{m}$, as the starting material. Its physical properties are presented in Table 1. Some experiments were carried out using hydrophobic particles of cellulose microcrystalline. The binder solutions used are water and aqueous solutions of polyvinylpyrrolidone (PVP), non-ionic surfactant (oxo-C10C6) at critical mycell concentration (cmc), sodium carboxymethylcellulose (Na-CMC) or hydroxypropylmethylcellulose (HPMC). Their physicochemical properties are presented in Table 2. The binder solutions viscosities are measured by a Rheometer (CSL2 500 TA Instruments), the surface tension using a tensiometer (3S GBX Instrument) and the density using DMA38 densimeter.

Table 2 shows that the presence of PVP and of non-ionic surfactant reduce the surface tension and does not affect the solution viscosity. The use of non-Newtonian solutions of Na-CMC solutions leads to an increase of the viscosity from 3.6 to 25.4 cP at a velocity gradient of 1500 s^{-1} when the Na-CMC mass concentration ranges from 0.1 to 1%. The surface tensions for these solutions are weakly affected by the concentration. On the other hand, the presence of HPMC reduces the surface tension and increases the viscosity.

Table 2
Characteristics of the binder solutions and liquid–solid contact angle values

Binder solution	ρ_L (kg/m ³)	γ_L (mN/m)	μ_L (cP)
Water	1000	72	1.0
oxo-C ₁₀ C ₆ (cmc)	1000	26	1.0
2 % PVP	1000	62	1.1
3 % PVP	1000	61	1.1
5 % PVP	1003	61	1.5
0.1 % Na-CMC ^a	999	72	3.6
0.3 % Na-CMC ^a	999	72	7.2
1 % Na-CMC ^a	1000	73	25.4
1 % HPMC	1000	53	10.0
2 % HPMC	1000	54	50.0

^a Non-Newtonians solutions.

2.2. Experimental apparatus and procedure

Batch wet granulation was performed with a Zanchetta Roto high-shear mixer (Fig. 1) with a vertical bowl of 10 L capacity, a spraying system and a vacuum system to dry the wet product. The bowl is also equipped with two agitators: one is a three-bladed impeller that is vertically mounted on a central axis on the base of the bowl, and the other is a chopper in a tulip shape. The impeller speed can be adjusted within the range of 40–640 rpm, and the chopper up to 2600 rpm. The chopper was not used in the experiments described here.

The dispersion of binder liquid in the bed can be ensured by two spraying systems: mono and bi fluid. In the first, the liquid is placed in a tank maintained between 4 and 9 bars by compressed air. The spray system includes an air feed circuit compressed to a mono-fluid nozzle. Concerning the bi-fluid system, the binder solution is drawn up by a volumetric pump from a reservoir to an external mixing two-fluid spray nozzle. The atomizing gas flow rate is controlled by a needle valve and measured by a rotameter.

Prior to a granulation experiment, the powder was introduced into the mixer and homogenised during 2 min, with the same mixing conditions used during granulation, before the spraying of the binder solution in powder bed. In order to study the growth kinetics during operation (wetting step), at fixed time intervals, the representative samples of solid are removed from the bed and tray-dried at 60 °C during 24 h to determine the granule size distribution.

The dried granules were sized by shaking in a test sieve shaker (SAULAS NF. X11.501) for 10 min. Size fractions of <80, 80–140, 140–300, 300–450, 450–600, 600–1000, 1000–1250, 1250–1600, 1600–2000 and >2000 μm were collected.

The sieve analysis allows determining the size distribution of granules, the weight mean diameter and the growth rate:

- Mean diameter:

$$d_{pm} = \frac{\sum_i f_i d_{pi}}{\sum_i f_i} \quad (1)$$

- Growth rate:

$$X = \frac{d_{pm} - d_{pmo}}{d_{pmo}} \quad (2)$$

Where f_i is the particle mass fraction of size interval i , d_{pi} is the mean diameter of size interval i (μm), d_{pmo} is the initial mean diameter and d_{pm} is the mean diameter at time t . In addition, the particle size distribution of granules in the fine fraction was measured by a Malvern Mastersizer analyzer using a dry measurement cell.

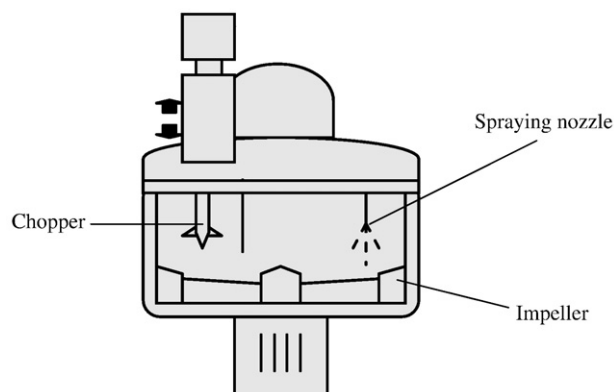


Fig. 1. Schematic view of the Zanchetta Roto high-shear mixer 10 L.

In order to understand the mechanism of agglomeration, three characteristic particle classes were defined: fine (corresponds to feed powder having diameter less or equal to 140 μm), intermediate (diameter between 140 μm and 450 μm) and coarse agglomerate (diameter greater than 450 μm). The intermediate class is characterized by its low strength, and the coarse class is categorized by its high strength granules having a spherical form. In this study, the coarse class corresponds to the marketable product.

2.3. Method

2.3.1. Wettability measurement

The wettability of the solutions on the MCC powder is characterized by the contact angle. It is obtained by Levine and Neale method [8]. This method is based on the determination of the equilibrium height of solutions rising through a fixed bed of particles in a vertical tube due to capillary forces. The value of this contact angle can be evaluated according to the following relation:

$$\cos\theta = \frac{\phi d_p}{6(1-\varepsilon)\gamma_{LV}} \rho_L \varepsilon g h^\infty \quad (3)$$

where ε is the porosity of the fixed bed, ρ_L is the liquid density, g is the gravity, ϕ is the shape factor and h^∞ is the height of liquid in the porous medium at equilibrium. This method is applicable for the Newtonian and non Newtonian binder solutions. The contact angle values are given in Table 3. The contact angle of hydrophobic powder is directly determined using a goniometer (Digidrop, GBX-instrument) which measures the equilibrium contact angle of a liquid droplet deposited on hydrophobic MCC powder bed surface. The contact angle of hydrophobic MCC/water system is about 108°.

2.3.2. Morphological study

The dried agglomerates obtained during the granulation are analysed by LEO 435 VP Scanning Electron Microscopy. The granules were coated with gold using coating apparatus (Edwards Pirani 501) to create electric conductivity on the surface of the samples.

2.3.3. Friability

The dried granule friability was characterized by batch grinding test experiment. It was carried out in a tumbling ball mill, constituted of a stainless steel cylindrical chamber, with a capacity of 1.2 L, rotating around its horizontal axis. Stainless steel balls, with a diameter of 5.5, 9.3 and 17.5 mm in volumes proportion of 1/4, 1/4 and 1/2 respectively, were used as the grinding medium. They occupied 20% of the chamber volume.

The friability test is realised by placing 10 g of the granule having a homogenised size (the majority class of granule obtained) in the bottle (cylindrical chamber) containing the stainless steel balls. The bottle was then placed in the rotating shaker at 70 rpm for 45 min. In the end

Table 3
Wettability of MCC solid particles

Binder solution	$h^\infty(\text{cm})$	θ (°)
Water	45.7	69
oxo-C ₁₀ C ₆ (cmc)	46.5	5
2 % PVP	55.0	60
3 % PVP	78.0	44
5 % PVP	93.9	28
0.1 % Na-CMC ^a	38.0	72
0.3 % Na-CMC ^a	35.0	74
1 % Na-CMC ^a	30.7	76
1 % HPMC	42.0	68
2 % HPMC	38.0	67

^a Non-Newtonians solutions.

Table 4
Operating condition for granulation experiments

Experiments	Binder solution	Powder	Rotational speed N (rpm)	Liquid flow rate (g/min)	Spray nozzle
1	Water	MCC	40	50	Mono-fluid
2			100		
3			150		
4			200		
5			300		
6			400		
7	Water	MCC	400	50	Bi-fluid
8			90		
9	Surfactant	MCC	400	50	Mono-fluid
10				2% PVP	
11				3% PVP	
12				5% PVP	
13				0.1% Na-CMC	
14				0.3% Na-CMC	
15				1% Na-CMC	
16				1% HPMC	
17	2% HPMC				
18	water	Hydrophobic MCC			

of the operation, the abraded samples were sieved and the friability was determined via Eq. (4). The measurements were made in triplicate.

$$\kappa = \frac{|d_{pm} - d_{pm0}|}{d_{pm0}} \times 100 \quad (4)$$

2.3.4. Porosity

Granule porosity (E) was calculated from the apparent particle density of the MCC powder (ρ_a) and the effective particle density of the pellets (ρ_e) using Eq. (5) [9]. The apparent particle density of the MCC particles was determined using a helium pycnometer (ACCUPIY 1330 Micromeritics). The effective pellet density of the pellets was determined by mercury porosimetry (Autopore IV 9500, Micromeritics Instrument Co.). Effective density was calculated from the sample weight and the sample volume at the initial mercury filling pressure:

$$E = \left(1 - \frac{\rho_e}{\rho_a}\right) \times 100 \quad (5)$$

3. Results and discussion

The operating conditions for the experiment carried out in this study are summarized in Table 4. All the experiments were carried

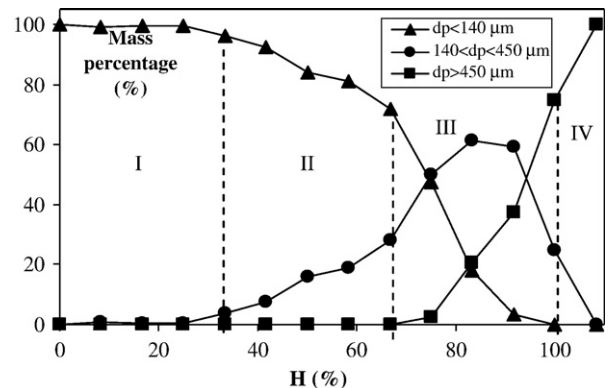


Fig. 2. Evolution of fines, intermediate and coarse mass percentage during liquid addition (experiment 11).

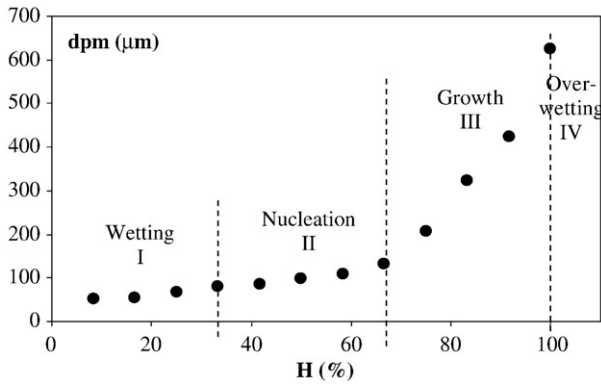


Fig. 3. Evolution of mean granule size during liquid addition (experiment 11).

out with 600 g of MCC particles and the amount of binder solution is fixed at 600 g in the most of them to avoid the powder bed over-wetting. The growth evolution is expressed versus the liquid/solid ratio, H , which is defined as the mass ratio between the introduced granulating liquid and the initial dry powder in percentage.

3.1. Granulation profile

In order to understand the MCC granule growth mechanisms, an experiment was considered using the 3% PVP aqueous solution (experiment 11). The evolution of the three characteristic classes and the mean granule size versus the liquid/solid ratio is presented on Figs. 2 and 3. These figures show the existence of four regimes which

were observed in all experiments regardless of the nature of the binder liquid and the operating conditions:

- a first regime I ($H < 33.3\%$): the percentages of fine particles and intermediate agglomerates are not modified. This regime corresponds to the no growth phase or the wetting phase which is characterized by the absence of liquid bridge,
- a second regime II ($33.3 < H < 66.6\%$): the proportion of fine particles decreases and the percentage of intermediate agglomerates increases gradually. In this regime the percentage of coarse agglomerates is negligible and the collision between small particles produces either intermediate particles (Fig. 4a) or new nuclei. This phenomenon leads to a slight increase of the mean granule size.
- a third regime III ($66.6 < H < 100\%$): regular increase of the coarse agglomerates mass percentage and a rapid decrease of the fine particles mass percentage. The evolution trend of the intermediate particles mass percentage in bell form indicates that the growth mechanism corresponds to small and intermediate particles colliding with intermediate ones to produce larger granules, rather than larger sizes colliding and coalescing together (Fig. 4b). As the growth proceeds, the mass percentage of small (fine) particles continues to decline but at a reducing rate. The large (coarse) granules mass percentage increases as the intermediate and larger granules mop-up the remaining small particles in the bed. This process results in the intermediate granules passing through a maximum mass percentage. At the end of the operation, the fines fraction tends towards zero, the intermediate class percentage also declines and spherical granules are formed (Fig. 4c).

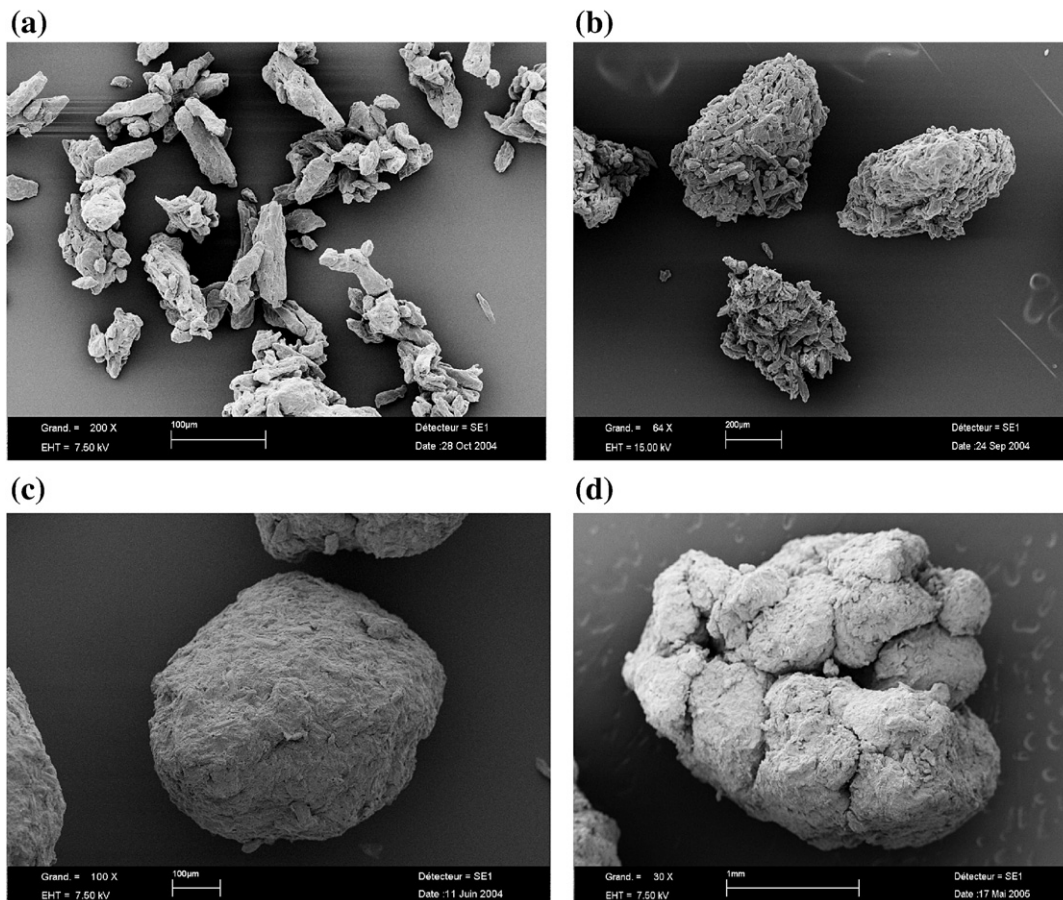


Fig. 4. SEM images of granules obtained at different liquid to solid ratio H ; (a) nuclei; (b) coarse granule; (c) spherical granule; (d) granule formed by over-wetting (experiment 11).

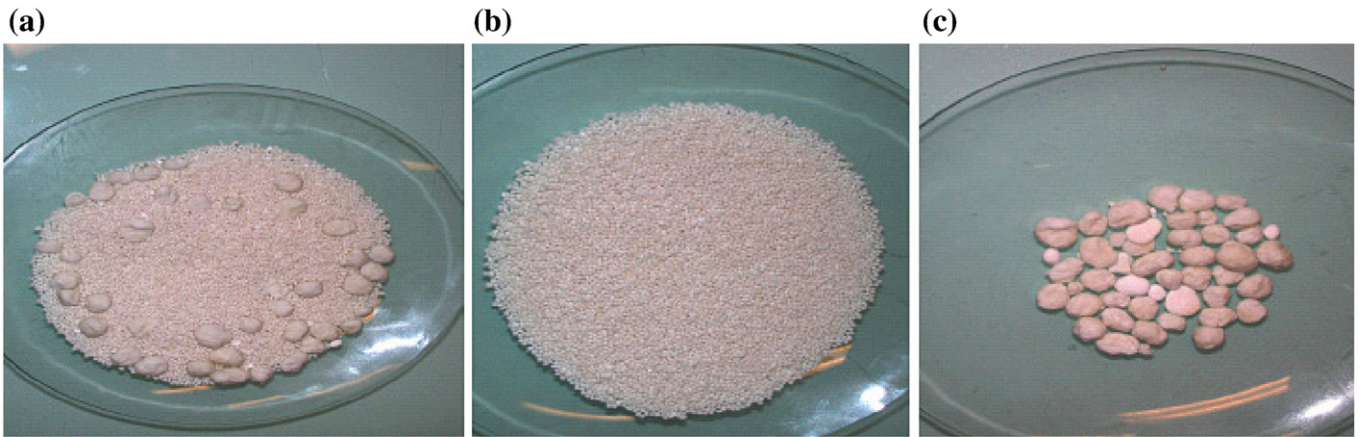


Fig. 5. Pictures of the granulation product: (a) product obtained; (b) spherical granule; (c) lumps having a size > 5 mm (experiment 11).

- a fourth regime IV: the liquid to solid ratio becomes higher than 100% (w/w). Large granules having a size diameter higher than 2500 μm are formed (Fig. 4d). These huge granules are generated by over-wetting phenomenon which leads to uncontrolled granules growth.

Let us note that, the evolutions of the three characteristic size classes versus the liquid/solid ratio in the second and the third regimes are similar with those of first order consecutive chemical reactions $A \rightarrow B \rightarrow C$. So, an overall growth kinetic constant K has been defined by replacing the concentration of A by the percentage of the fine particles, x_{fines} , and the time by the liquid to solid ratio H in the chemical kinetic law:

$$K = \frac{d}{dH} \ln \left(\frac{x_{\text{fines}}^0}{x_{\text{fines}}} \right) \quad (6)$$

This constant is determined using the slope of the evolution of $\ln(x_{\text{fines}}^0/x_{\text{fines}})$ versus H during the second and the third regimes.

3.2. Influence of the operating parameters

There are several process variables that control the granule growth. The most important are impeller rotational speed and binder solution flow rate. These process parameters are interdependent and can produce a desirable product if this interdependency is understood.

The influence of these operating parameters was studied by the granulation of the microcrystalline cellulose with the water. The

principal comparison criteria are the mean diameter of granule formed, the size distribution of the granule formed, the evolution of the particle mean diameter and the evolutions of the three characteristic classes (fine, intermediate and large). Other criteria such as the friability or the physical properties of the granule also help to understand the growth phenomena.

3.2.1. Impeller rotation speed effect

The impeller rotational speed plays a major role in the granulation operation. It affects the quality of the mixing between the powder and the binder fluid, and the collisions between the particles or between the particles and equipment. Increasing the impeller speed leads to granule compaction and good binder dispersion which infers uniform wetting and controlled granulation. A bad mixing between the powder and the binder solution by decreasing the agitation intensity creates local-wetting and preferential growth leading to uncontrolled granulation.

This section presents the influence of impeller speed on the dry granule characteristics and on the growth kinetics. Five experiments are performed at different impeller speeds from 40 to 400 rpm (experiments 1 to 6), and the amount of binder solution is fixed at 600 g.

Fig. 5 presents the pictures of the product obtained at the end of the operation. It shows the presence of two agglomerate populations: the spherical granule and the lumps larger than 5 mm. Lumps were considered as the agglomerates obtained by localized over-wetting.

The evolution of the lumps mass percentage obtained in the end of the operation versus impeller speed is presented in Fig. 6. It

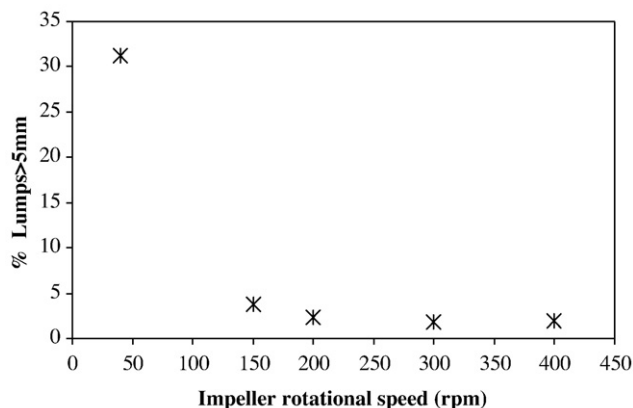


Fig. 6. Impeller rotational speed effect on the amount of the lumps (experiments 1 to 6).

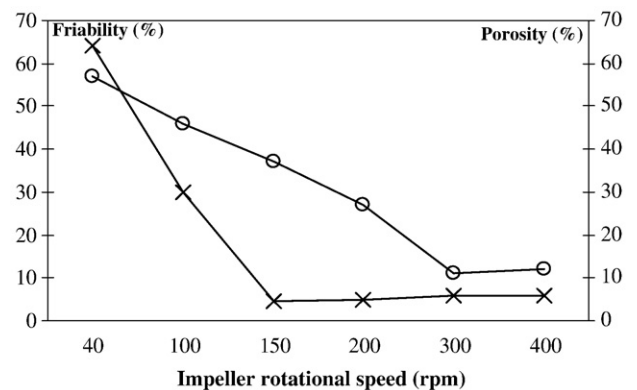


Fig. 7. The properties of the granule obtained versus rotational impeller speed (experiments 1 to 6).

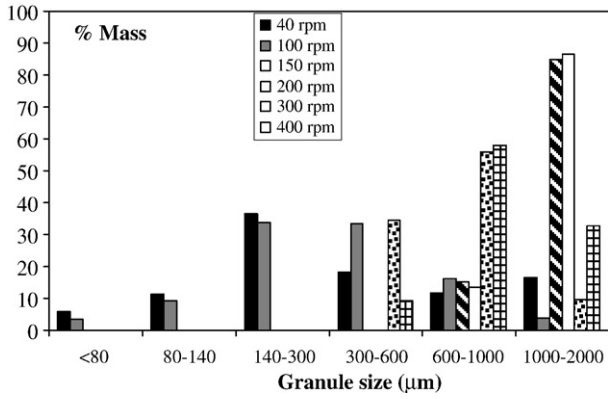


Fig. 8. The granule size distribution versus rotational impeller speed (experiments 1 to 6).

shows that the increase of the impeller speed between 40 and 150 rpm leads a rapid decrease of the lumps mass percentage from 30 to 3%. It remains constant beyond 150 rpm.

Below, only the results of granule having a size lower than 5 mm are analyzed and discussed.

3.2.1.1. Impeller rotation speed effect on the properties of granule formed. The Fig. 7 presents the evolution of the porosity and the friability of obtained product. It shows two trends:

- The first one is observed for the impeller rotational speed between 40 and 150 rpm. The increase of the shear reduces in the granule friability from 62 to 2% and porosity from 57 to 37%. These results show that the increase on the impeller speed, inducing good mixing between the liquid binder and the powder, enables the reduction of the preferential growth and the formation of rigid granule.
- The second trend, corresponding to the impeller rotational speed higher than 150 rpm. The increase of the agitation intensity doesn't have a significantly effect on the friability, but leads to granule compaction and densification. The porosity of granule decreases from 37 to 12 %.

These results show that the impeller rotational speed plays a major role on the product characteristics. For the moderated agitation intensity between 150 and 200 rpm, the formed agglomerate is porous and easily dispersible and compressible, whereas beyond 200 rpm, the dense and strongly rigid product is formed. These results can be explained by the fact that the increase of the impeller speed leads to a

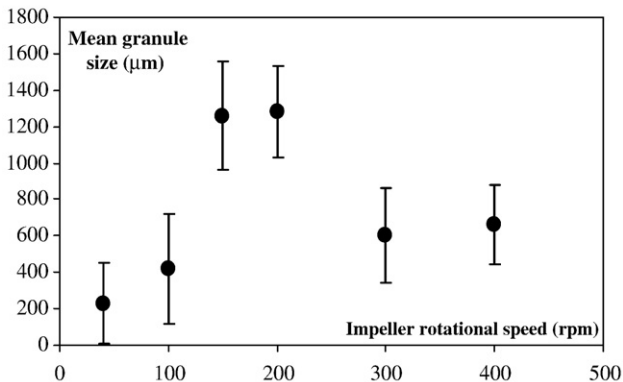


Fig. 9. Evolution of the mean granule diameter versus the rotational impeller speed (experiments 1 to 6).

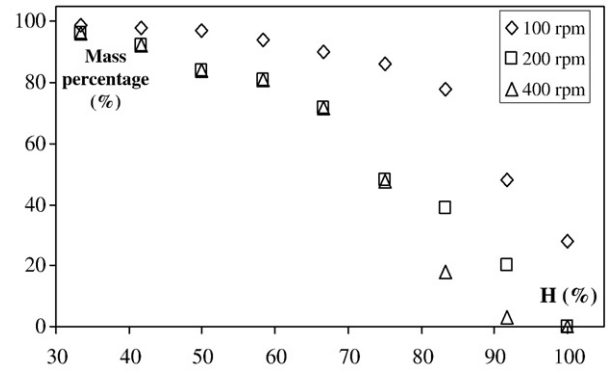


Fig. 10. Evolution of fine particle mass percentage: effect of impeller rotation speed (experiments 2, 4 and 6).

well dispersion of the binder liquid on the powder bed by reducing the localised over-wetting.

The existence of these two regimes is confirmed in Figs. 8 and 9 which show that:

- between 40 and 150 rpm, the fine particles (size <140 µm) mass percentage and that of intermediate agglomerate (between 140 and 300 µm) decrease in the mean while the mean granule diameters increases.
- beyond 200 rpm, middle size granules between 300 and 600 µm appear while the mean granule size decreases. This can be explained by the fact that the mechanism of granule breakage occurs when stress due to mechanical agitation is important.

The aspect of mixture in the mechanically agitated granulator depends on the competition between the gravity force ($F_g = mg$) and the centrifugal force ($F_c = m(\pi ND)^2 / (D/2)$). The equilibrium between these forces occurs when the impeller speed is equal to a critical impeller speed N_c :

$$N_c = \left(\frac{g}{2\pi^2 D} \right)^{1/2} \quad (7)$$

where g is the acceleration due to gravity, D the diameter of the bowl (0,28 m).

In our conditions, $N_c = 85$ rpm. At an impeller rotational speed lower than 85 rpm, bad mixing between the binder liquid and the powder creates local wetting. In this case, agglomerates don't have equal amount of liquid, the preferential growth occurs, causing the formation of lumps and the production of porous and more friable

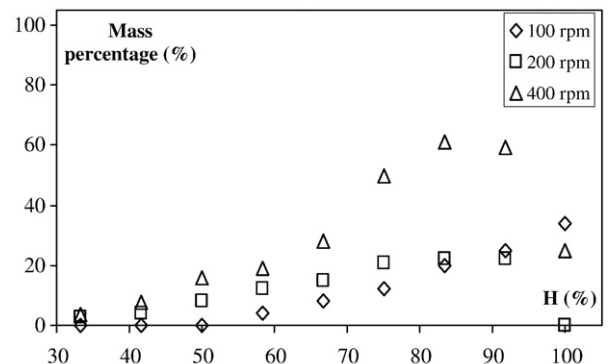


Fig. 11. Evolution of intermediate particle mass percentage: effect of impeller rotation speed (experiments 2, 4 and 6).

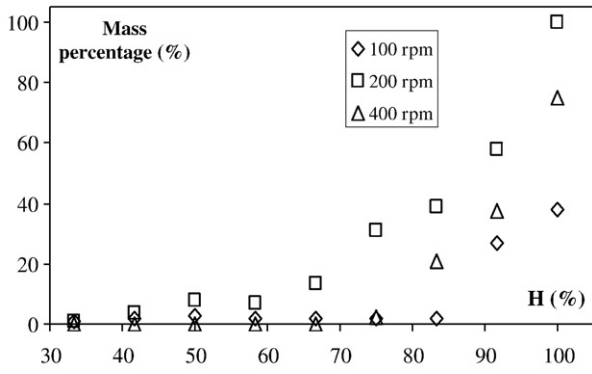


Fig. 12. Evolution of coarse particle mass percentage: effect of impeller rotation speed (experiments 2, 4 and 6).

granules. For the impeller rotational speed higher than N_c , the granular bed becomes well mixed and moves in a fluidised manner which leads to a homogenised granulation. Results show that good granulation is achieved for the impeller rotational speed higher than $2N_c$.

The breakage of granules can be explained by comparing two strengths: the static tensile strength of granules and the impact pressure. The tensile strength of the nuclei can be estimated with the formula of Rumpf for the static tensile strength:

$$\sigma_t = CS \frac{1-\varepsilon}{\varepsilon} \frac{\gamma_L}{d_{po}} \cos\theta \quad (8)$$

where C is a material constant (for uniform spheres $C=6$), ε is the granule porosity, d_{po} the initial particle diameter, γ_L liquid surface tension, θ is the liquid–solid contact angle and S is the liquid pore saturation given by:

$$S = H \frac{1-\varepsilon \rho_s}{\varepsilon \rho_l}$$

Where H is the liquid to solid ratio and ρ_s , ρ_l are respectively the true density of the powder and the density of the binder solution.

The swelling property and the shape of MCC make the use of the tensile strength formula of Rumpf somewhat questionable. Because this formula is developed for spherical particles and the swelling of the solid in the liquid is not included in the liquid saturation model. Nevertheless, the order of magnitude of the tensile strength is used to compare the tensile strength of the granule with the impact of the impeller.

The impact pressure characterises the attrition and the breakage phenomenon rupture caused by the impact of the impeller with a

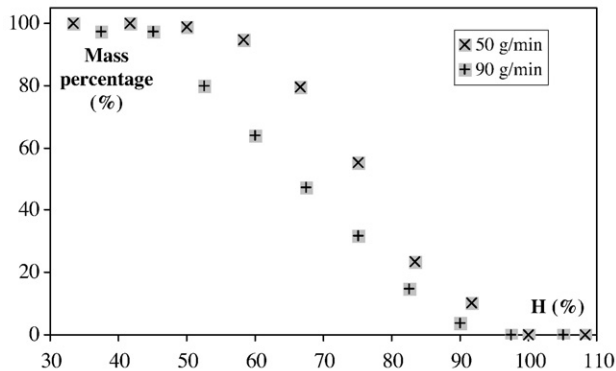


Fig. 13. Evolution of fine particle mass fraction: liquid flow rate effect (experiments 7 and 8).

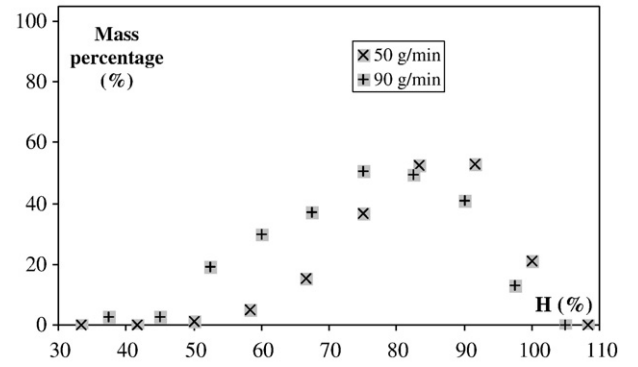


Fig. 14. Evolution of intermediate particle mass fraction: liquid flow rate effect (experiments 7 and 8).

granule. According to Vonk et al. and Thornton et al. [10,11], the impact pressure (σ_{impact} , kPa) is given by Eq. (9).

$$\sigma_{\text{impact}} = \frac{2}{3} \rho_a U^2 \quad (9)$$

with $U^2 = \pi N D$ (m/s).

In this expression, ρ_a is the density of the agglomerate, D the bowl diameter, N impeller rotation speed and U the tip velocity.

The breakage is much more important as the value of σ_{impact} is higher. The application of this relation to our operating conditions leads to values of 0.4, 9.4 and 37.5 kPa respectively for impeller speeds of 40, 200 and 400 rpm. The estimation of the static tensile force of the granule for, $\theta=0^\circ$, $C=6$ and for two values of particles porosity, 0.5 and 0.71 shows that it ranges from 1.8 and 11.1 kPa. These results show that for the impeller speed higher than 200 rpm, the pressure of impact can exceed the cohesion strength of the formed granules, causing their fragmentation.

3.2.1.2. Impeller rotation speed effect on the granule growth. The effect of impeller rotation speed on growth kinetics has been investigated in experiments 2, 4 and 6 realised at different impeller rotational speed: 100, 200 and 400 rpm. The evolutions of the three characteristic particle classes, fine, intermediate and coarse particles, versus the liquid to solid ratio are respectively presented on Figs. 10, 11 and 12.

The results show clearly that the three granulation regime profile, wetting, nucleation and growth, is conserved for all experiments. However, the transitions between the regimes depend on the impeller rotation speed. The increase of the rotational speed reduces the liquid amount requirement to enhance the transition between the regimes and accelerates the wetting and nucleation kinetics ($H < 66.6\%$) (Figs. 10 and 11). This is mainly due to the increase of the collision frequency between wetted particles with increasing the impeller rotation speed.

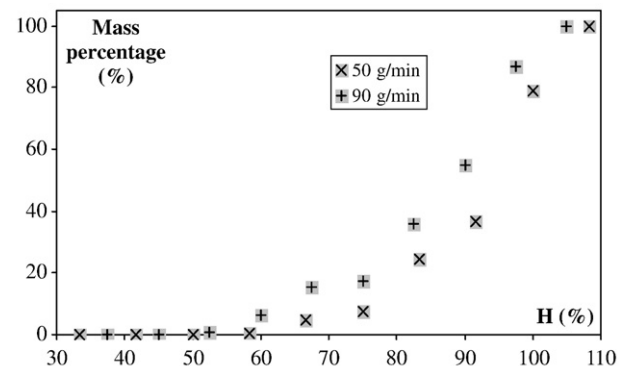


Fig. 15. Evolution of coarse particle mass fraction: liquid flow rate effect (experiments 7 and 8).

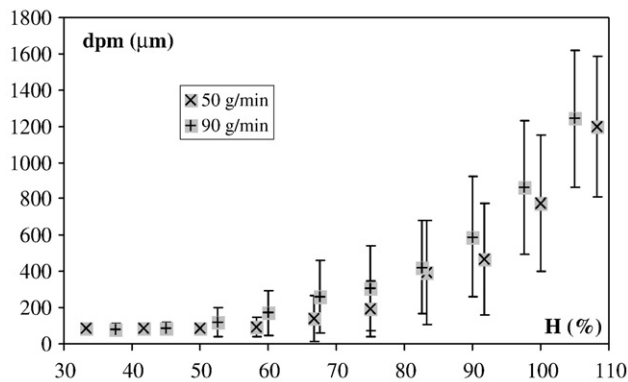


Fig. 16. Evolution of mean granule diameter: liquid flow rate effect (experiments 7 and 8).

Concerning the granule growth kinetics ($H > 66.6$), Fig. 12 confirms the presence of attrition and breakage phenomenon for the impeller rotation speed higher than 200 rpm. We noted that the mass percentage of coarse particles is more important for 200 rpm than 400 rpm.

3.2.2. Influence of the binder solution flow rate

The effect of binder liquid flow rate (F_L) was investigated between 50 and 90 g/min (experiment 7 and 8). The increase of F_L leads to a reduction of the operation time from 14 to 8.7 min. The pulverisation of water in the powder bed is done using a spray nozzle bi-fluid. Generally this system generates small liquid droplet and good dispersion of liquid binder in the bed compared to a mono-fluid system. Note, the use of bi-fluid system increases the liquid amount needed to reach the wetting regime from 33.34 to 58.34%, but does not affect the extension of the nucleation and growth [12].

Fig. 13 shows that, increasing F_L reduces the extension of the non growth regime, in other words, the liquid to solid ratio corresponding to the beginning of the nucleation period. This critical wetting ratio is 58.34% for a flow rate of 50 g/min whereas it is 45% for 90 g/min. Concerning the nucleation regime, increasing F_L enhances the intermediate class formation (Fig. 14). Indeed, for similar liquid to solid ratios the intermediate fraction is smaller at the lower liquid flow rate. In the growth regime, increasing F_L accelerates the granulation kinetic (Fig. 15), but doesn't affect significantly the mean diameter of granule formed (Fig. 16). This growth mechanism can be explained by the fact that for a given liquid to solid ratio, H , the attrition phenomena take place over a longer time as F_L decreases.

3.3. Influence of the physicochemical properties

During the wet agglomeration process, wetting, mixing and coalescence take place simultaneously in the same apparatus. The most important physicochemical variables that affect these elementary processes are the viscosity of solutions and the wettability of the liquid on the solid particles. The interdependency between the effects of these

Table 5
Adhesion work and capillary viscous number values; Ca' is calculated at $N=400$ rpm

Binder solution/particles	W_a (mN/m)	Ca'
Water/MCC	98	0.06
Water/MCC hydrophobic	50	0.12
Surfactant/MCC	52	0.11
2% PVP/MCC	93	0.07
5% PVP/MCC	115	0.08
0.1% Na-CMC/MCC	94	0.22
0.3% Na-CMC/MCC	92	0.46
1% Na-CMC/MCC	91	1.64
1% HPMC/MCC	73	0.80
2% HPMC/MCC	75	3.90

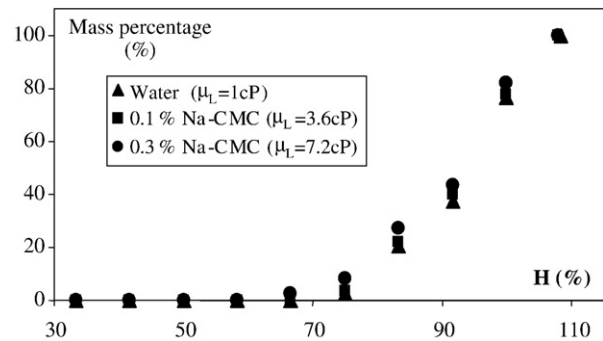


Fig. 17. Evolution of coarse agglomerates ($d_p > 450 \mu\text{m}$) percentage: viscosity effect ($Ca' < 1$) (experiments 6, 13 and 14).

variables makes difficult the analysis of the influence of each one on the growth kinetics. For this purpose, the influence of physicochemical properties was investigated considering the values of a modified capillary viscous number Ca' . This adimensional number is defined by the ratio between the viscous forces ($\mu_L U$) and the static forces. Our experimental results show that the static forces are depended on the work of adhesion W_a . So, a modified capillary viscous number is defined by the ratio between the viscous forces and the work of adhesion:

$$Ca' = \frac{\mu_L U}{W_a} \quad \text{with } W_a = \gamma_L (1 + \cos \theta) \quad \text{and } U = \pi N D \quad (10)$$

The values of the adhesion work and the capillary viscous number determined for different couple binder/MCC are given in Table 5. The use of these liquid/solid systems enables to realize the experiment in a wide range of capillary viscous number (between 0.06 and 3.9) and consequently to study the influence of the viscous forces and the work of adhesion on granule growth.

3.3.1. The effect of the work of adhesion: $Ca' < 1$

The effect of the liquid viscosity is investigated using water and aqueous solutions of Na-CMC at 0.1 and 0.3% as binding solutions (experiments 13 and 15). An increase in the Na-CMC mass percentage leads to an increase of the solution viscosity but does not affect significantly the work of adhesion (Tables 2 and 5). The evolution of the coarse agglomerates percentage (Fig. 17) shows that the growth is also not affected by an increase of the solution viscosity. This result shows that the increase of the viscosity cannot be responsible for the granule growth for weak values of the capillary viscous number.

Concerning the effect of adhesion work, an experiment was carried out using hydrophobic MCC particles and water as binder (experiments 6 and 18). In this case, the work of adhesion is decreased by a factor of 2 compared to the granulation of non hydrophobic MCC. The experimental data presented in Fig. 18 show that the amount of

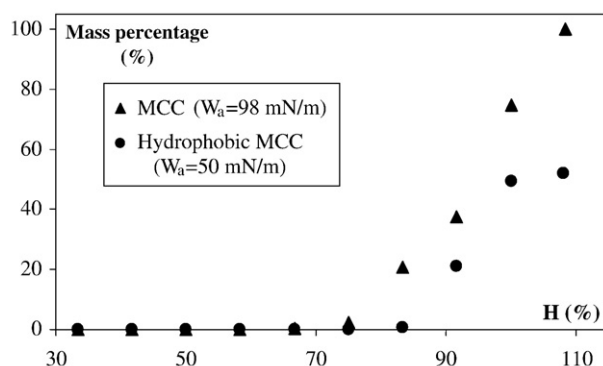


Fig. 18. Evolution of coarse agglomerates ($d_p > 450 \mu\text{m}$) percentage: effect of the work of adhesion ($Ca' < 1$) (experiments 6 and 18).

Table 6
Granule properties: work of adhesion effect ($Ca' < 1$)

Binder solution/particles	W_a (mN/m)	Porosity (%)	Friability (%)
Water/MCC hydrophobic	50	56.0	20.6
Surfactant/MCC	52	50.4	12.4
2% PVP/MCC	93	13.3	5.8
Water/MCC	98	12.0	5.0
5% PVP/MCC	115	9.3	6.9

liquid required to achieve granule growth depends on the work of adhesion. The increase of W_a leads to a faster appearance of the coarse agglomerates and a smaller amount of liquid binder required to enhance the growth, while it reduces the granule friability from 20.6 to 5% and its porosity from 56 to 12% (Table 6). This is confirmed by the experimental results concerning the granulation of MCC with the aqueous solutions of PVP at 2% and 5% and of non-ionic surfactant (Fig. 19).

All these results show that the work of adhesion determines the growth kinetics for $Ca' < 1$. Fig. 20 represents the evolution of the overall growth kinetic constant K versus the work of adhesion for different experiments where $Ca' < 1$. This figure shows that the kinetic constant is directly related to the work of adhesion, whatever the liquid surface tension values, the contact angle values or the binder nature.

3.3.2. The influence of the viscosity: $Ca' \geq 1$

The effects of viscosity on the granule growth were investigated by granulation of MCC with aqueous solutions of HPMC at 1 and 2% (w/w) and of Na-CMC at 1% (w/w) (experiments 15 to 17). The viscosities of the solutions range from 10 to 50 cP and the work of adhesion varies from 73 to 91 mN/m.

Figs. 21 and 22 show an increase of the growth rate by a factor of 2, while the solution viscosity increases from 10 to 50 cP, a decrease of the amount of liquid to achieve agglomerate growth and the reduction of the granule porosity and friability (Table 7).

These results can be explained by the effect of the viscosity on the time, t_p necessary for liquid penetration in the pores of the granule which can be estimated from the model of the parallel capillary beam:

$$t_p = \frac{2a^2\mu_L}{r_{\text{pore}}\gamma_L \cos\theta} \quad (11)$$

where a is the pore length equivalent to the radius particle multiplied by the tortuosity factor and r_{pore} represents the pore radius.

During wet granulation, interaction between wet particles leads to nuclei formation. The elementary particles are held together by liquid bridges. This phase is nearly independent on viscosity and primarily dependent on the agitation intensity. Once the nuclei are formed, the distribution liquid inside the granules depends on the viscosity. For

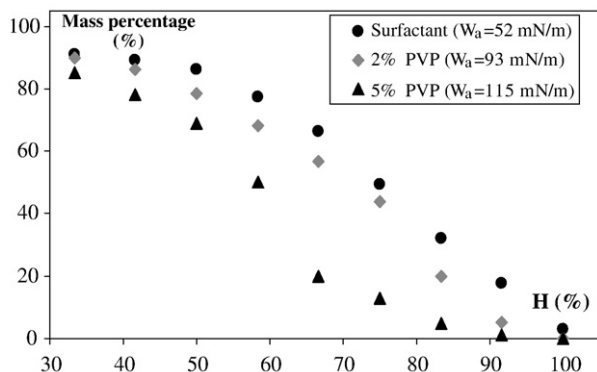


Fig. 19. Evolution of fines particles ($d_p < 140 \mu\text{m}$) percentage: effect of the work of adhesion ($Ca' < 1$) (experiments 9, 10 and 12).

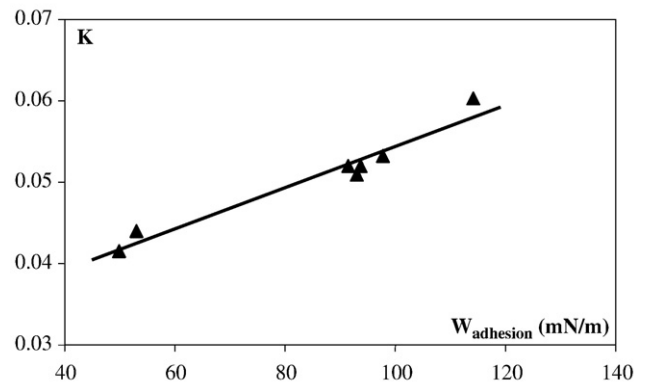


Fig. 20. Evolution of kinetic constant versus the work of adhesion ($Ca' < 1$) (Experiments 6, 9, 10, 12, 13, 14 and 18).

low liquid viscosities, the time of penetration of the solution in the nuclei is short and the growth takes place only when the liquid content in the medium becomes sufficient to ensure the non-elastic collision between the particles. In this case, our experiments show that the viscosity has no significant influence on the granule growth. When a high viscous liquid is used, the high value of the penetration time, t_p , leads to the formation of a sticky liquid layer at the surface of the granules. In this case, the agglomeration is controlled by the viscous dissipation forces. These results are in agreement with those obtained by Ennis et al. [6] which show that the viscous force becomes dominant for values of $Ca > 1$.

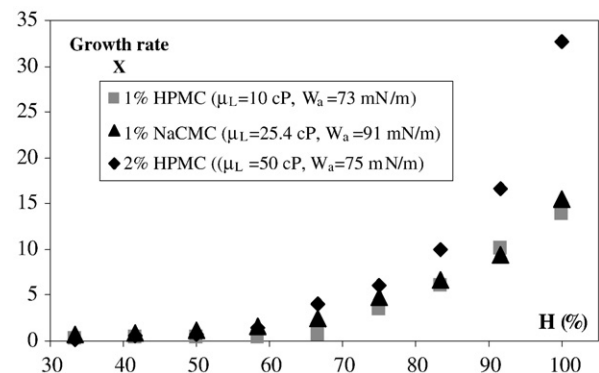


Fig. 21. Evolution of granule growth rate: viscosity effect ($Ca' \geq 1$) (experiments 15, 16 and 17).

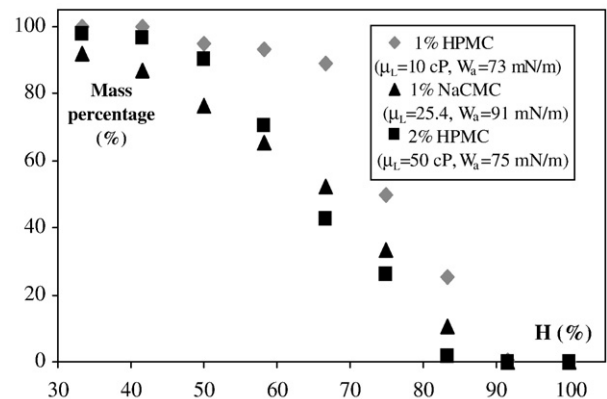


Fig. 22. Evolution of fines particles ($d_p < 140 \mu\text{m}$) percentage: viscosity effect ($Ca' \geq 1$) (experiments 15 to 17).

Table 7
Granule properties: effect of the viscosity ($Ca' \geq 1$)

Binder solution	μ_L (cP)	Porosity (%)	Friability (%)
1 % HPMC	10.0	37.6	7.5
1 % Na-CMC	25.4	17.7	4.4
2 % HPMC	50.0	15.9	3.1

4. Conclusion

The effects of the operating condition and of the liquid binder physicochemical properties on the kinetics of agglomeration of microcrystalline cellulose in a high shear mixer are investigated. The results point out that concerning the process variables the experimental results show that the impeller rotational speed has a great importance on granule growth. An optimal interval of impeller speed operation exists ranging from 150 to 200 rpm. Low shear granulation (40 and 100 rpm) leads to uncontrollable agglomerate size and localised over-wetting, and for impeller speed higher than 200 rpm, the mechanism of the granule breakage occurs. The result shows that the increase in the liquid binder flow rate leads to a reduction of the extension of the non growth regime, but does not affect the granule mean size.

Concerning the physicochemical parameters, the viscosity of the solution has no significant effect on the granulation process for a capillary number lower than 1. In these conditions, the dominant forces in the granulation process are the capillary and/or interfacial forces. Increasing the work of adhesion enhances the growth kinetics. For a capillary viscous number higher than 1.6, the granule growth is controlled by the viscous dissipation forces.

List of symbol

a	pore length m
C	material constant (for uniform sphere $C=6$) (-)
d_p	primary particle diameter m
d_{pi}	mean diameter of size interval i m
d_{pmo}	initial mean diameters m
d_{pm}	mean diameters at time t m
D	bowl diameter or agitator diameter m
E	granule porosity %
F_c	centrifugal force N
F_g	gravity force N
F_i	particle mass fraction of size interval i % w/w
F_L	liquid flow rate g/min
g	gravity kg/m
h^∞	height of liquid in the porous medium m
H	liquid to solid ratio % (g/g)
K	growth kinetic constant (-)
N	impeller rotational speed rpm
N_c	critical impeller speed rpm
r_{pore}	pore radius Å
S	liquid pore saturation %
t_p	time penetration s

U	velocity m/s
W_a	adhesion work N/m
X_{fines}	mass percentage of fine particle at liquid to solid ration H %
X_{fines}^0	initial masse percentage of fine particle (=100%) %
X	growth rate (-)

Greek symbol

γ_{LV}	liquid surface tension N/m
ε	porosity of fixed bed %
θ	contact angle radian
μ_L	liquid viscosity Pa.s
ρ_S	solid density kg/m ³
ρ_L	liquid density kg/m ³
ρ_a	apparent particle density kg/m ³
ρ_e	effective particle density of the granule kg/m ³
ϕ	shape factor %
κ	friability
σ_{impact}	impact pressure Pa
σ_T	tensile strength Pa

Adimensionally number

Ca'	modified capillary viscous number
Ca	capillary viscous number

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