

WET GRANULATION IN HIGH SHEAR MIXER: EFFECT OF PHYSICOCHEMICAL PROPERTIES ON THE GROWTH KINETICS

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Abstract. 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 product properties and process variables effects. This paper presents some results obtained by the study of wet granulation of microcrystalline cellulose powder, MCC (Avicel PH101) using high-shear mixer granulators. It aims at understanding the effect of physicochemical properties, such as the viscosity and the wettability of a binder solution on solid particles surfaces, on the agglomeration kinetics. The experiments are carried out with various liquids having different surface tensions, viscosities, binder concentrations, etc. (water, aqueous solutions of sodium carboxymethylcellulose, polyvinylpyrrolidone, hydroxypropylmethylcellulose or non ionic surfactant oxo-C₁₀C₆ at a critical mycell concentration). The effect of the physicochemical properties is evaluated using a modified capillary viscous number, Ca' , which is defined, in this study, by the ratio between the viscous forces ($\mu_L U$) and the work of adhesion $W_a = \gamma_L (1 + \cos\theta)$. The results show that 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. When Ca' becomes higher than 1.64, the viscous forces predominate and control the granule growth.

Keywords. wet granulation, high shear mixer, wettability, growth kinetics

1. INTRODUCTION

Granulation may be considered as a size-enlargement process wherein 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 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, 2]. Granulation has been described in three principal mechanisms [3]: *wetting and nucleation; consolidation and growth; attrition and breakage*. 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 the solid particles.
- the break-up forces depending on the process variables, such as impeller speed, bed geometry and the atomization conditions. These variables affect the growth kinetics by modifying the mixing intensity.

According to Rumpf [4], 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, the wettability of the solid particle with respect to binder solution and the particle size and shape. During the granulation, the particles undergo various 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 [5]

Ennis *et al.* [6] expressed the importance of the viscous force in comparison with the capillary force through the capillary number $Ca = \mu_L U / \gamma_L$, where γ_L is the liquid surface tension, μ_L the liquid viscosity and U the velocity (in agitated process $U = \pi N D$, 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 become 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, which deals with the wet granulation of microcrystalline cellulose powders by aqueous solutions of polymers, aims at understanding the main forces which lead to the formation of granules in 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. 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- C_{10}C_6) at critical mycell concentration (cmc), sodium carboxymethylcellulose (Na-CMC) or hydroxypropylmethylcellulose (HPMC). Their physicochemical properties are presented in Table 1. It shows that the presence of PVP and of non-ionic surfactant reduce the surface tension and do 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 1 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)	θ (°)
Water	1000	72	1.0	69
oxo- C_{10}C_6 (cmc)	1000	26	1.0	5
2 % PVP	1000	62	1.1	60
3 % PVP	1000	61	1.1	44
5 % PVP	1003	61	1.5	28
0.1 % Na-CMC ¹	999	72	3.6	72
0.3 % Na-CMC ¹	999	72	7.2	74
1 % Na-CMC ¹	1000	73	25.4	76
1 % HPMC	1000	53	10.0	68
2 % HPMC	1000	54	50.0	67

¹ non-Newtonians solutions.

The wettability of the solutions on the MCC powder is characterized by the contact angle. It is obtained by Levine & Neale method [7]. 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:

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

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 1. 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° .

2.2. Experimental apparatus and procedure

Batch wet granulation was performed with a Zanchetta Roto high-shear mixer 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 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 with an angle of jet dispersion of 45° . After granulation, the granules are dried under vacuum by the circulation of hot water in the double jacket of the bowl.

In order to study the growth kinetics during operation, at fixed time intervals, the representative samples of solid are removed from the bed and tray-dried at 60°C during 24h. The sieve analysis allows to determine the size distribution of granules, the weight mean diameter and the growth rate:

$$\text{- Mean diameter: } d_{pm} = \frac{\sum_i f_i d_{pi}}{\sum_i f_i} \quad (2)$$

$$\text{- Growth rate: } X = \frac{d_{pm} - d_{po}}{d_{po}} \quad (3)$$

Where f_i is the particle mass fraction of size interval i , d_{pi} is the mean diameter of size interval i (μm), d_{po} is the initial mean diameter and d_{pm} is the mean diameter at time t . The agglomerates obtained during the granulation are analysed by SEM (Scanning Electron Microscopy).

In order to understand the mechanism of agglomeration, three characteristic particle classes were defined (fine class: diameter less or equal to $140 \mu\text{m}$; intermediate class: diameter between $140 \mu\text{m}$ and $450 \mu\text{m}$; coarse class: diameter greater than $450 \mu\text{m}$).

3. RESULTS AND DISCUSSION

The experiments were carried out with 600 g of MCC particles. It has been show in the previous work [1] that the optimum operating conditions which improve the granulation of MCC are the following: impeller speed equal to 400 rpm and binder solutions flow rate equal to 50 g/min . 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 realised using the 3% PVP aqueous solution. The evolution of the three characteristic classes and the mean granule size versus the liquid/solid ratio is presented on figures 1 and 2. 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. 3a) 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. 3b). 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 intermediates 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. 3c).
- a fourth regime IV: the liquid to solid ratio becomes higher than 100% (w/w). Large granules having a size diameter higher than $2500 \mu\text{m}$ are formed (Fig. 3d). 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:

$$K = \frac{d}{dH} \ln\left(\frac{x_{fines}^0}{x_{fines}}\right) \quad (4)$$

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

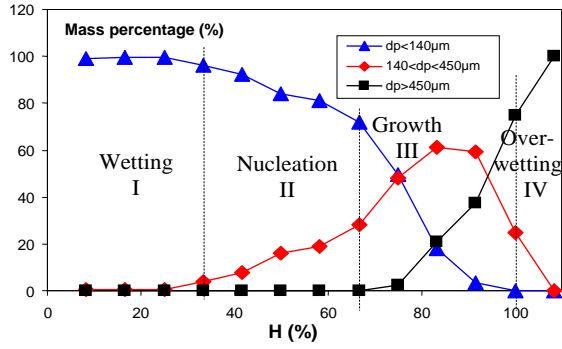


Fig. 1: Evolution of fines, intermediate and coarse percentage during liquid addition

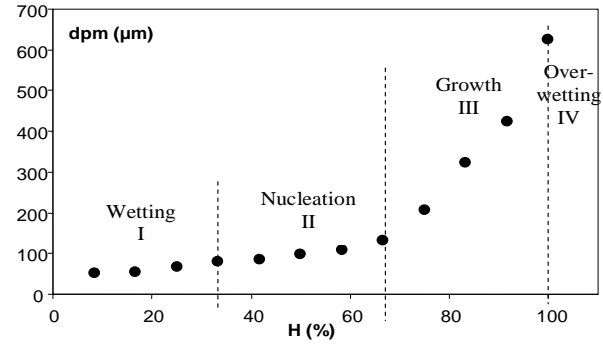
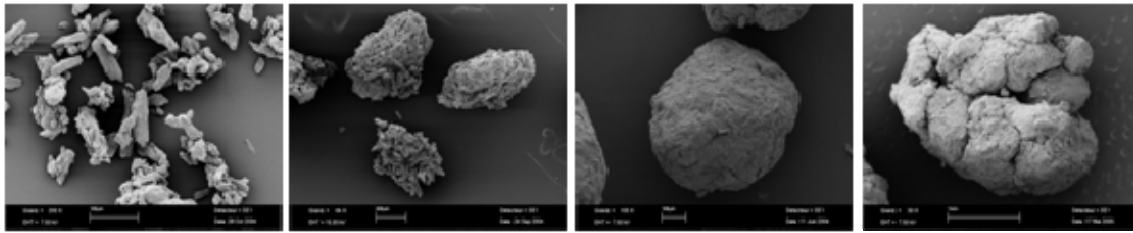


Fig. 2: Evolution of mean granule size during liquid addition



(a) (b) (c) (d)
Fig. 3: SEM images of granules obtained at different liquid to solid ratio H

3.2. Influence of the physicochemical properties

During 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 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 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:

$$Ca' = \frac{\mu_L U}{W_a} \quad \text{with} \quad W_a = \gamma_L (1 + \cos \theta) \quad \text{and} \quad U = \pi N D \quad (5)$$

Table 2 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
3% PVP/MCC	104	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

The values of the adhesion work and the capillary viscous number determined for different couple binder/MCC are given in Table 2. The use of these liquid/solid systems permits 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.

3.2.1. 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. 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. The evolution of the coarse agglomerates percentage (Fig. 4) 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. 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 figure 5 show that the amount of liquid required to achieve granule growth depends on the work of adhesion. The increase of this parameter leads to a faster appearance of the coarse agglomerates and a smaller amount of liquid binder required to enhance the growth. 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. 6). All these results show that the work of adhesion determines the growth kinetics for $Ca' < 1$. Figure 7 represents the evolution of the overall growth kinetic constant K versus the work of adhesion for different experiments. 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.

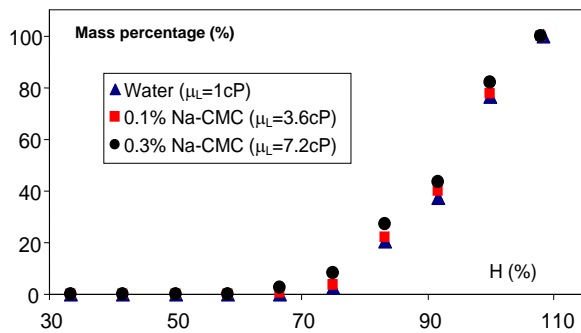


Fig. 4: Evolution of coarse agglomerates ($dp > 450 \mu m$) percentage: viscosity effect ($Ca' < 1$)

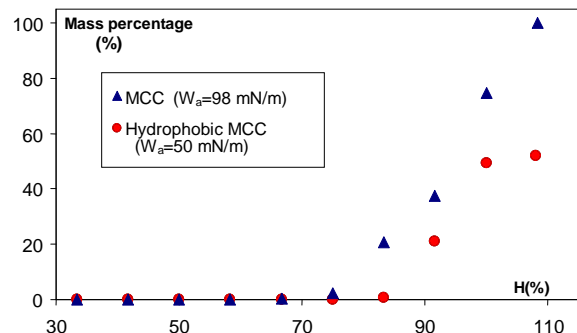


Fig. 5: Evolution of coarse agglomerates ($dp > 450 \mu m$) percentage: effect of the work of adhesion ($Ca' < 1$)

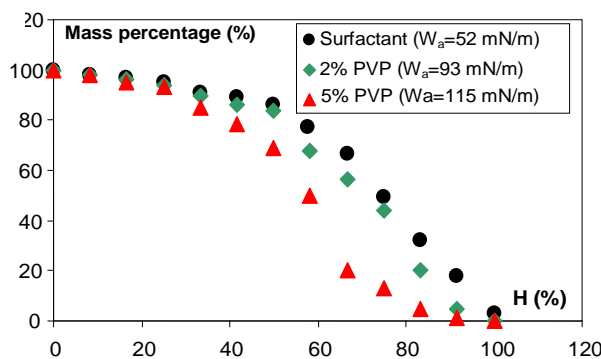


Fig. 6: Evolution of fines particles ($dp < 140 \mu m$) percentage: effect of the work of adhesion ($Ca' < 1$)

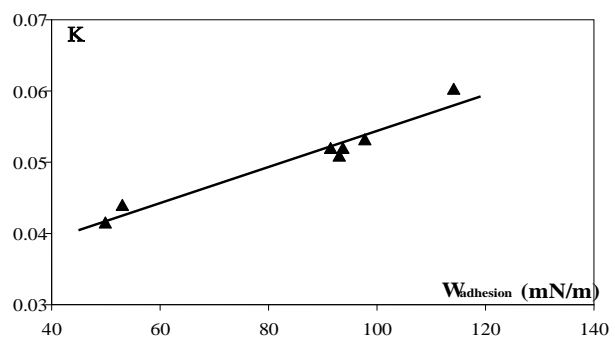


Fig. 7: Evolution of kinetic constant versus the work of adhesion ($Ca' < 1$)

3.2.2. 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). The viscosities of the solutions range from 10 to 50 cP and the work of adhesion varies from 73 to 91 mN/m. Figures 8 and 9 show an increase of the growth rate by a factor of 2 while the solution viscosity increases from 10 to 50 cP, and a decrease of the amount of liquid to achieve agglomerate growth.

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:

$$t_p = \frac{2a^2 \mu_L}{r_{pore} \gamma_L \cos \theta} \quad (6)$$

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 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 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 $Ca > 1$.

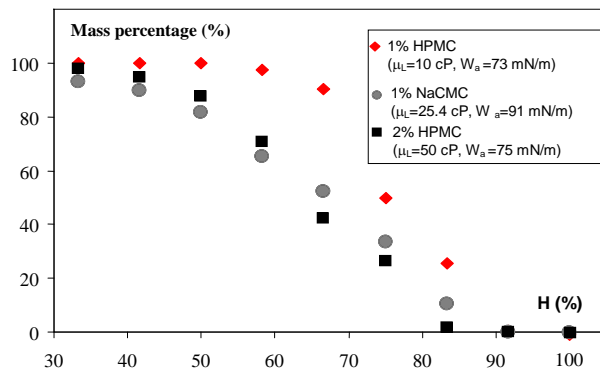


Fig. 8: Evolution of fines particles ($dp < 140 \mu m$) percentage: viscosity effect ($Ca \geq 1$)

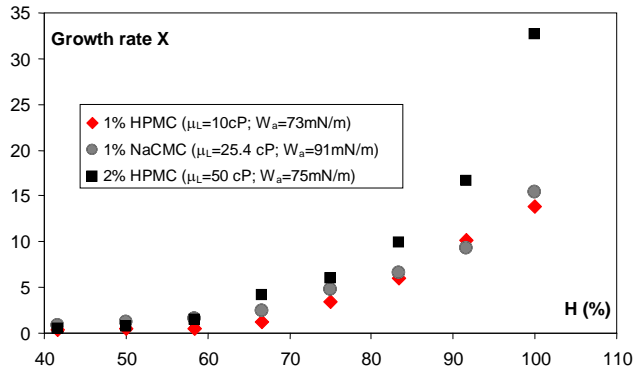


Fig. 9: Evolution of granule growth rate: viscosity effect ($Ca \geq 1$)

4. CONCLUSION

The effects 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 the viscosity of the solution has no significantly effect on the granulation process for a capillary number lower than 1.64. In these conditions, the dominant forces in the granulation process are the capillary and/or interfacial forces and increasing the work of adhesion enhances the growth kinetics. For a capillary viscous number higher than 1.64, the granule growth is controlled by the viscous dissipation forces.

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