



Prediction of solid–binder affinity in dry and aqueous systems: Work of adhesion approach vs. ideal tensile strength approach



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ARTICLE INFO

Article history:

Received 2 July 2014

Received in revised form 27 October 2014

Accepted 1 November 2014

Available online 8 November 2014

Keywords:

Agglomeration

Pharmaceutical products

Solubility parameter

Work of adhesion

Tensile strength

Coating

ABSTRACT

Wet granulation process requires the addition of a coating agent or binder, typically composed of surfactants such as hydroxypropyl-methylcellulose (HPMC), water and a small amount of filler such as stearic acid (SA). In dry granulation however, the coating agent is added to the system in the form of fine solid particles. In both cases, a successful granulation requires good affinity between host and guest particles. In this study, we compare two approaches to predict the binder–substrate affinity in dry and in aqueous media, one based on the work of adhesion and the other based on the ideal tensile strength (Rowe, 1988). The novelties of this paper are four folds. First, the equations used in both approaches are generalized and rewritten as a function of the Hildebrand solubility parameter δ . δ is obtained from molecular simulations or predicted from HSPiP group contribution method. Secondly, a correlation between δ and the experimental surface tension γ is established for cellulose derivative (such as HPMC and ethyl cellulose). Thirdly, the concept of ideal tensile strength, originally formalized by Gardon (1967) for binary systems, is extended to ternary systems and applied for granulation in aqueous media. Fourthly, the approaches are tested for various systems and compared to experimental observations. For dry binary systems, predicted adhesive and cohesive properties agree with literature experimental observations, but the work of adhesion approach performs better than the ideal tensile strength approach. Both approaches predict that HPMC is a good binder for microcrystalline cellulose (MCC). The results also indicate that polyethylene glycol 400 (PEG400) has a good affinity with HPMC and stearic acid. For ternary aqueous systems, the results fully agree with the observations of Labouffie et al. (2013).

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1. Introduction

Granulation is a size-enlargement process during which small particles are formed into larger and physically strong agglomerates [1]. In wet granulation processes (Fig. 1), this is performed by spraying a liquid binder onto the particles as they are agitated in tumbling drum, fluidized bed, high shear mixer or similar device [2,3].

Coating is a process which allows to deposit on the surface of particles a thin film layer which can be of different nature: polymers, salts, sugars, etc. (Fig. 1).

These two operations confer on powder's new properties for customers, such as hydrophobicity, masking bitterness, reducing the risks of explosion, avoiding the segregation of the constituents, improving the flow properties and the compression characteristics of the mix.

Processes of size enlargement involve the coupling of two classes of parameters. The first class corresponds to the local physico-chemical

parameters dependent on the nature of the solutions and powders. The second class corresponds to the parameters of the processes which are the constraints exercised by the process equipment on the bed of powder, such as the temperature and the flow rates. The quality of the end product depends on the control of the coupling between these two families of parameters which exist in different scales. At present, the optimization of these parameters, notably the choice of solvent and binders is based on an empirical, by nature long and expensive approach.

The three principal mechanisms of wet granulation are as follows: wetting and nucleation; consolidation and growth; and attrition and breakage [4]. Inspired by Ennis' work [5,6], Benali et al. [7] proposed the modified capillary number Ca' to evaluate the importance of the viscous force with respect to the adhesion work. When the $Ca' > 1$, the cohesion of dynamic liquid bridges during nucleation and growth becomes greater than that of the static liquid bridges. This is attributed to the effect of viscous energy dissipation. When the $Ca' < 1$, the effect of the adhesion force is dominant.

Mastering granule processing under the $Ca' > 1$ regime is routine for laboratory and industrial practitioners. Mastering the $Ca' < 1$ regime

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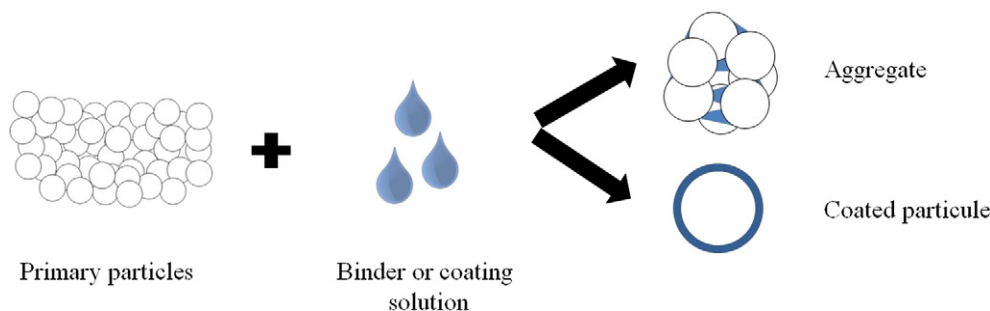


Fig. 1. Wet particle growth mechanisms.

requires to select binders adequately. Formulating the optimum binder or coating is essential even if suitable operating conditions may bring enough mechanical energy to obtain rigid granules.

This work has for objective to develop predictive methodologies and theoretical tools of investigation allowing to choose the adequate binder or to formulate the right coating solution to assure the customer's requested properties of the end product. As such, we explore two theoretical approaches for predicting substrate–binder interactions, one based on the work of adhesion, and the other based on the ideal tensile strength. We extend the approaches to ternary systems so as to study the interactions between compounds mixed in a solvent such as hydroxypropyl-methylcellulose (HPMC) and stearic acid (SA) mixed in water. The background section gives an overview of binders and coatings commonly used in granulation processes. It also reviews some theoretical models for binary mixtures. Then, we derive the tensile strength model for ternary mixtures. The last section concerns the model testing. First, we discuss the selection of the model core data, either coming from group contribution method or from molecular simulations, and we compare them with experimental data. Second, a relationship between the surface free energy and solubility parameter is proposed for cellulose derivatives. Third, it is used next for the prediction of the interactions in binary and ternary mixtures. The predictions obtained through the tensile strength approach and the work of adhesion approach are compared and discussed.

2. Background

2.1. Binder and coating compounds

Cellulose derivatives such as hydroxypropyl methylcellulose (HPMC) and microcrystalline cellulose (MCC) are often used in granulation processes. Generally, HPMC is used as a protective colloid by coating hydrophobic particles with multimolecular layer and promote wetting [8]. MCC is frequently used in pharmaceuticals as a binder/diluent in oral tablet and capsule formulations [9]. Fatty acids such as stearic acid (SA) are often added to the cellulose derivatives to enhance specific properties. For example, adding SA to HPMC leads to a decrease in the water affinity due to SA hydrophobic properties caused by its content of long-chains [10]. Stearic acid is also widely used in oral formulations as a tablet and capsule lubricant [11]. Another additive is the polyethylene glycol (PEG), which can be used in various polymerization grades. Their main advantage over fatty acids is their physical and thermal stability on storage. However, they are chemically more reactive than fats [12] and have only limited binding action when used alone. PEG are often used as plasticizers [13] or added to pharmaceutical mixtures to improve their mechanical properties [14].

2.2. Theoretical models and equations

In order to predict the affinity between the different compounds, we need to calculate the work of adhesion and the ideal tensile strength. These quantities can be obtained using the Hildebrand [15] solubility

parameter δ which can be estimated by experimental methods or by using molecular simulation.

2.2.1. Hildebrand solubility parameter δ

As Barton [16] asserted in his handbook of solubility parameters, many properties of polymers can be related to the Hildebrand solubility parameter δ which is proportional to the square root of the cohesive energy density e_{coh} . This parameter describes the intra- and intermolecular forces of a substance. It can also be expressed in terms of the individual Hildebrand parameters describing two contributions to the cohesive energy, namely, the non-polar Van der Waals dispersion forces δ_d , and the polar interactions (electrostatic) δ_p . Hydrogen bonding interactions δ_h are included here in the polar contribution:

$$\delta = \sqrt{\delta_d + \delta_p}. \quad (1)$$

Experimentally, there are numerous methods for Hildebrand solubility parameter determination such as the homomorph method [16], the maximum-in-swelling method often used for the determination of solubility parameters of crosslinked polymers [17], and inverse gas chromatography [18]. Many scientists including Hansen [19], Van Krevelen [20], Hoy [21] and Small [22] and recently Yamamoto (HSPiP [23]) have proposed correlations and lists of contributions for various chemical groups.

In molecular simulation, the Hildebrand solubility parameter can be calculated from the pair potential by summing the pairwise interactions [24]. The cohesive energy density is equal to minus the intermolecular energy, i.e. the intramolecular energy minus the total energy:

$$\delta_k^2 = \frac{\langle \sum_{i=1}^n E_i^k - E_c^k \rangle}{N_{av} \langle V_{cell} \rangle}. \quad (2)$$

With n the number of molecules in the simulation cell, N_{av} the Avogadro number, and $k = 1, 2$, are the van der Waals energy (dispersion) and the coulombian energy (polar) respectively. " $\langle \rangle$ " denotes a time average over the duration of the dynamics in the canonical ensemble NVT, V_{cell} the cell volume, the index "i" refers to the intramolecular energy of the molecule i , and the index "c" represents the total energy of the cell. Calculation of the Hildebrand solubility parameter will permit us to estimate the work of adhesion and the ideal tensile strength.

2.2.2. The work of adhesion and cohesion

The energy required to separate unit areas of two surfaces A and B from contact is referred to as the work of adhesion (W_{AB}), and for surfaces of the same material, this is called the work of cohesion (W_{AA}). Girifalco and Good [25] have expressed the work of adhesion in terms of the surface free energy of the pure phases by:

$$W_{AB} = 2\phi_1\phi_V(\gamma_A\gamma_B)^{1/2}. \quad (3)$$

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