



# The water holding ability of powder masses: Characterization and influence on the preparation of pellets via extrusion/spheronization



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## ABSTRACT

The water holding ability of powder masses greatly influences their extrusion/spheronization performance during pellets preparation. To quantify this ability and explore its influence on pellets preparation, two characterized parameters were proposed. One was the maximum water content that could be retained by the mass ( $WHA_{max}$ ), the other was the remaining water content in the mass subjected to certain extrusion force ( $WHA_{extrusion}$ ). The methods to determine WHA were established by centrifugation. MCC,  $\kappa$ -carrageenan, mannitol were employed to investigate the relationship between WHA and their extrusion/spheronization performance. The results showed that the  $WHA_{max}$  and  $WHA_{extrusion}$  of MCC were 1.0 g/g and 0.85 g/g, which were less than that of  $\kappa$ -carrageenan ( $WHA_{max} > 6.0$  g/g,  $WHA_{extrusion} = 3.0$  g/g), accordingly. Since mannitol had the lowest parameter values ( $WHA_{max} = 0.3$  g/g,  $WHA_{extrusion} = 0.25$  g/g), it was hard to be extruded. Therefore,  $\kappa$ -carrageenan ( $\geq 10\%$ ) or mannitol ( $\geq 30\%$ ) were added to prepare satisfactory pellets by increasing the WHA values ( $\geq 0.53$  g/g) of the mixed masses. In addition, the WHA of mixed masses could be predicted based on WHA of each mass. To obtain enough extrudates and non-agglomerated pellets, the water content added in the mass should be equal with  $WHA_{max}$ . In conclusion, the established two parameters were useful to predict the extrusion/spheronization performance of masses, therefore, selecting the potential pelletization aids and determining the optimal water content.

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## 1. Introduction

Extrusion/spheronization is one of the most-commonly used pelletization technique in pharmaceutical industry [1]. This process mainly involves two major steps: firstly, the pre-mixed dry powder masses were wetted with granulation liquid to form a homogeneous wet mass, which is then pressed through dies to obtain cylindrical extrudates. Secondly, the extrudates are broken up and spheronized to form pellets by a spheronizer. During this process, the mass must possess good fluidity to pass through dies successfully. Besides, the resulting extrudates should be resilient yet brittle enough to break up into small pieces and subsequently plasticized and rounded into spherical pellets [2,3].

The granulation liquid (often water) plays an important role to acquire these properties mentioned above [4]. It moves faster than the solids under extrusion stress and exists at the surface of particles as a lubricant, reducing the shear forces of extrusion and assisting in the formation of cylindrical extrudates from the wetted mass. Meanwhile the remaining liquid inside the extrudates acts as a plasticizer to allows the extrudates to be less structurally rigid during spheronization [5]. However, when the phase separation is excessive, this process fails

due to shark-shinned extrudates or agglomerated pellets [6]. Therefore, researches have been done to understand the water movement during extrusion, and it is founded that this movement can be affected by process parameters such as extruder geometry, extrusion rate, extrusion pressure and so on [7–9]. In addition, the influence factors coming from solids also determine the rheology of pastes [10], and among them the water holding ability is the most important one [11].

For excipients intended to produce pellets via extrusion-spheronisation, a large water absorption and retention capacity is an essential property [12]. One of the reasons why MCC is a common excipient used in formulation of extrusion/spheronization is its ability to hold water strongly [6]. MCC can retain a large amount of water to provide the mass with desired fluidity, viscosity and plasticity during extrusion/spheronization. Moreover, by controlling the water movement, it is possible to prevent phase separation during extrusion [12]. Nevertheless, it is still unclear how the water holding ability of masses impact their performance in the preparation of pellets by extrusion/spheronization.

In this research, an attempt was made to explain this problem by two characterized parameters. One was the maximum water content that could be retained by the mass ( $WHA_{max}$ ), the other was the remaining water content in the mass subjected to certain extrusion force ( $WHA_{extrusion}$ ). They were proposed to characterize the water holding ability of wet masses during extrusion/spheronization and

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certain centrifugal conditions were established to determine these parameters. Three kinds of power masses (mannitol, MCC,  $\kappa$ -carrageenan) were involved in this study. Among them, MCC and  $\kappa$ -carrageenan were common pelletization aids in extrusion/spheronisation [13] while mannitol was chosen as a model component for it was unable to be extruded in the preliminary experiment. The water holding ability of them was all evaluated by determining their  $WHA_{max}$  and  $WHA_{extrusion}$ . Then MCC and  $\kappa$ -carrageenan were separately added to mannitol to prepare mannitol pellets, and the change of corresponding parameter values after adding pelletization aids was monitored at the same time. Besides, the influence of parameter values on the optimal water content for pellets preparation, the consumption of pelletization aids and the extent of water movement during extrusion were all investigated in this paper.

## 2. Materials and methods

### 2.1. Materials

Microcrystalline cellulose (Avicel PH101, Jiangsu Hengrui, China), pigment tartrazine (Shanghai Institute of dye, China), mannitol (Pearlitol® 200SD, Roquette Freres, France),  $\kappa$ -carrageenan (Green Fresh Food stuff Co., Ltd., China), Nanosep® MF Centrifugal Devices (Pall Corporation, East Hills, NY), deionized water was used as the granulation liquid.

### 2.2. Theoretical basis for characterized parameters

In order to quantify the water holding ability of powder masses in extrusion/spheronization, two characterized parameters were proposed, which were  $WHA_{max}$  and  $WHA_{extrusion}$  respectively.  $WHA_{max}$  represented the maximum water content the mass can hold after granulation while  $WHA_{extrusion}$  was the amount of water retained in the mass under extrusion stress. The proposition of  $WHA_{max}$  was based on the liquid saturation model [14] because the optimum water content in pellet formulation is usually obtained when the mass is in a capillary state [15]. When the liquid saturation is  $>1$ , the mass would be in drop-let or suspension state, leading to excessive water movement in extrusion/spheronization [4]. As a result, the water content added should be less than  $WHA_{max}$ . But if the water added is too little, there is not enough free water available to soften and lubricate the mass through the extruder [8]. Therefore,  $WHA_{extrusion}$  was put forward to determine the minimum water content required by the mass for extrusion.

### 2.3. The determination of characterized parameters

#### 2.3.1. Centrifugal device

Centrifugation was used to assess the water holding ability of wet masses [16] and the experimental arrangement was placed in a commercial Nanosep® MF centrifugal device. According to Fig. 1, the centrifugal device consists of a centrifuge tube with a filter device inside. There

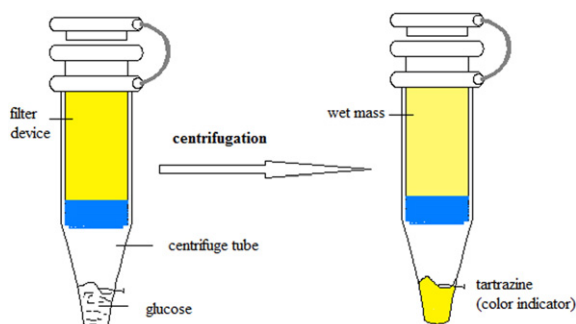


Fig. 1. The structure of centrifuge device.

is a membrane filter at the base of the filter device to prevent any particles from passing into the drained liquid.

The filter device was filled with wet mass before centrifugation and a small amount of glucose powder was added at the bottom of centrifuge tube for balancing. During centrifugation, the water containing tartrazine as color indicator would flow to the bottom of centrifuge tube and be absorbed by glucose, therefore the color change of glucose can be observed at the same time. The amount of water drained ( $W_1$ ) was obtained by weighing the centrifuge tube before and after centrifugation, and the water held in wet mass after centrifugation expressed as  $WHA$  was then calculated by the following equation:

$$WHA = (W_2 - W_1) / W_3 \quad (1)$$

where  $W_2$  is the weight of water added in dry powder mass,  $W_1$  is the water collected at the centrifuge tube and  $W_3$  is the weight of the dry powder mass. All the values of  $WHA$  were expressed as g/g.

#### 2.3.2. Measurement condition for $WHA_{max}$

The selection of centrifugal condition to determine  $WHA_{max}$  was based on the water distribution in MCC powder masses reported in literature [11,17]. There are four distinct fractions of water (nonfreezing, freezing bound, free, and bulk water) in MCC (Avicel® PH-101) wet masses, and the water distribution is influenced by granulation [17]. For granulated MCC, no bulk water exists outside the particles when the water content reaches its saturation point (1 g/g). But, if the mass is ungranulated, 50% bulk water would exist. Due to this difference, centrifugal speeds and duration were selected to separate bulk water in the determination of  $WHA_{max}$ .

First, granulated MCC masses were prepared by mixing the solid and water for 10 min. The water content added was 1.0 g/g to reach saturation. In this case, the total bound water content is 0.75 g/g and there is no bulk water. Ungranulated masses were prepared by adding the same amount of water except mixing. The bulk water inside is nearly half of the amount of water added. Then they were allowed to equilibrate overnight in plastic bags before centrifugation. Afterwards, these masses were centrifuged (Hence H1850R, Hunan Xiangyi Laboratory Instrument Development Co., Ltd., China) at various conditions to make sure that the bulk water was separated while other kinds of water were retained, and this condition was called  $C_{WHA_{max}}$ .

To evaluate the accuracy and reliability of the measuring condition, the  $WHA$  values of granulated MCC masses with different initial water content (0.9, 1.1, 1.2, 1.3 g/g) were also determined under  $C_{WHA_{max}}$  to see whether the  $WHA$  values were influenced by the water content added in the wet masses [6,11].

#### 2.3.3. Measurement condition for $WHA_{extrusion}$

To determine the centrifugal condition for  $WHA_{extrusion}$ , the water movement of MCC pastes with three levels of water content (0.8, 1.0, 1.3 g/g) were researched. Each batch was extruded at a speed of 20–22 rpm in an axial single-screw extruder (Fig. 2) equipped with a die of 0.1 cm diameter circular holes (JBZ-300, New Drug Research Institute of Liaoning Yilian, China). The extrudates were then collected and dried to constant weight to calculate the water content per gramme of dry mass. Because the last extrudate fractions are normally drier than the former one [8], the water content of the final extrudates was defined as  $WHA_{extrusion}$ . Afterwards, the wet powder masses were centrifuged at different speeds until the same values were obtained and this condition was called  $C_{WHA_{extrusion}}$  to simulate the extrusion force.

#### 2.3.4. The $WHA_{max}$ and $WHA_{extrusion}$ of powder masses

The powder masses involved in this study were MCC,  $\kappa$ -carrageenan and mannitol. The  $WHA_{max}$  and  $WHA_{extrusion}$  of MCC can be obtained in Sections 2.3.2 and 2.3.3, only the other two components were studied in this section. 5 g of each component was accurately weighed and mixed with different water contents using a pestle and mortar for 10 min. Then

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