Effect of moisture sorption on the performance of crospovidone

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ABSTRACT

Crospovidone is a commonly used tablet disintegrant. However, the synthetic disintegrant has been known to be hygroscopic and high moisture content in crospovidone used could exert deleterious effects on tablets formulated with it. The objective of this study was to elicit a better understanding between crospovidone-water interaction and its effect on disintegrant performance. Moisture sorption and desorption isotherms were obtained together with the enthalpy of immersion. Crospovidone samples stored at four relative humidities were used to formulate tablets and the resultant tablets were evaluated for their mechanical, dimensional and disintegratability attributes. Analyses of the moisture sorption isotherms indicated that externally adsorbed moisture accounted for the bulk of the total moisture content in crospovidone, with minimal amount of moisture absorbed intramolecularly. Enthalpy of immersion became less exothermic with crospovidone samples stored at increasing storage humidity. Correspondingly, improvement in disintegration time became less pronounced. This was postulated to be a consequence of premature wetting of the particle surfaces by externally adsorbed moisture. High humidity was also detrimental to tablet hardness and thickness. In conclusion, the impact of moisture sorption during storage by excipients such as crospovidone could be better understood by the appreciation of crospovidone-water interaction and its consequence on tablet quality.

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1. Introduction

Disintegrants are essential excipients in immediate release tablet formulations because they facilitate tablet matrix breakdown in aqueous environment, thus increasing the effective surface area available for dissolution and absorption of the active pharmaceutical ingredients (Alderborn, 2007; Hersen-Delesalle et al., 2007; Moreton, 2008).

Disintegrants act by overcoming the cohesive strength of tablets due to the particle-particle bonds formed during compaction. Different disintegrants have different mechanisms of action, by swelling force such as sodium starch glycolate (Moreton, 2008; Quodbach et al., 2014), capillary force or wicking like microcrystalline cellulose (Moreton, 2008) and strain recovery for crospovidone (Desai et al., 2012).

Crospovidone is a synthetic cross-linked homopolymer of N-vinyl-2-pyrrolidinone (Fig. 1) (Augsburger et al., 2006; Bühler, 2005; Haaf et al., 1985). It is a water-insoluble tablet disintegrant that can be used in wet- and dry-granulation or direct compression (Kornblum and Stoopak, 1973; Rudnic et al., 1980). Crospovidone is usually added in small amounts of 1–5% in tablet formulations (Rudnic et al., 1980). There are a variety of commercial crospovidone grades, prepared by different methods, with different mean particle sizes, and it has been reported that coarser crospovidone grades are more effective in terms of disintegration and dissolution (Rudnic et al., 1980).

While crospovidone has been used extensively in tablet formulations, it has been known as a hygroscopic excipient and therefore, care has to be taken to ensure that it is not exposed to high humidity conditions. Besides affecting the disintegration time (Zhao and Augsburger, 2006), moisture was also shown to decrease the hardness of tablets containing crospovidone (Hersen-Delesalle et al., 2007; Sheen and Kim, 1989) and cause a slight increase in tablet thickness (Gordon et al., 1993). All these changes in addition to drug stability issues as a result of exposure of moisture could

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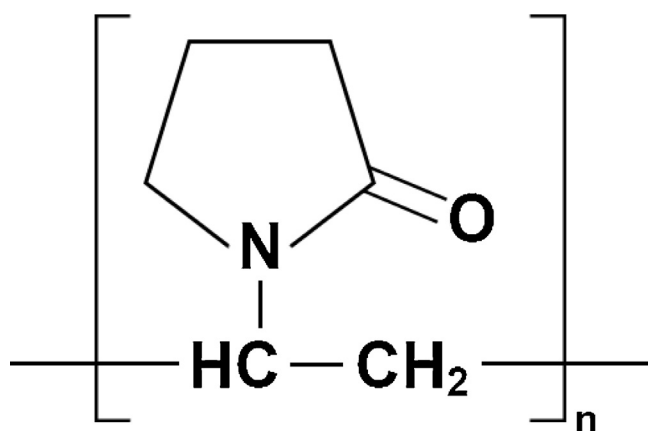 E-mail address: phapaulh@nus.edu.sg (P.W.S. Heng).

Fig. 1. Structural formula of crospovidone.

affect the overall quality of the tablets. It is therefore imperative to evaluate the relationship between increasing ambient humidity and moisture uptake of crospovidone, which will provide insights into the mode and impact of crospovidone-water interaction.

One method to investigate the interaction between water and crospovidone is to study its moisture sorption and desorption profiles, which can be graphically represented in the form of moisture sorption isotherms that illustrate the equilibrium moisture content as a function of water activity (a_w). Moisture sorption isotherm of a sample can be determined by subjecting it to different equilibrium moisture contents and the water activities determined, at a constant temperature. Moisture sorption isotherms can be prepared either through the wetting of sample starting from a dry state (sorption curve), or drying of sample from its hydrated state (desorption curve).

The sorption and desorption isotherms can be modeled using equations to derive useful parameters such as the monolayer moisture content, which is the amount of moisture required to form a saturated monolayer on powder surfaces. Besides, moisture sorption and desorption data encompasses the complete range of water activities (from 0 to 0.95), which makes it invaluable when interpreting changes in water-solid interaction at low, intermediate and high water activities. Mathematical models with two or more parameters have been used to fit the moisture sorption data. Among these, the most commonly encountered are the Brunauer-Emmett-Teller (BET; Brunauer et al., 1938) and Guggenheim-Anderson-de Boer (GAB; Anderson, 1946; Anderson and Hall, 1948; de Boer, 1968; Guggenheim, 1966) models. In addition, the Young and Nelson equations (Young and Nelson, 1967a; Young and Nelson, 1967b) capitalize on the sorption and desorption isotherms to elucidate the three states of moisture associated with a polymer-like material, monolayer moisture, externally adsorbed moisture condensed on the monolayer, and bound moisture. While the BET, GAB and Young and Nelson models have been used to analyze crospovidone samples (Malamataris et al., 1991; Roškar and Kmetec, 2005; Saripella et al., 2014b), no study was directed at the effect of crospovidone-water interaction on the disintegrant's performance in a tablet dosage form.

The objective of this study was to elicit the relationship between crospovidone and moisture and the effect of any interaction on the performance of the disintegrant as a tableting excipient. Moisture sorption and desorption isotherms were generated using the dynamic vapor sorption mode on the vapor sorption analyzer. Crospovidone samples were stored at four different relative humidities and used to produce tablets for evaluation of disintegration time, thickness and hardness. The

enthalpy of immersion for the disintegrants was also determined using a solution calorimeter.

2. Materials and methods

2.1. Materials

Crospovidone (Kollidon CL-SF, BASF, Germany) was the disintegrant used in this study. Dibasic calcium phosphate (DCP; Emcompress, JRS Pharma, Germany) and magnesium stearate (MgSt; M-125, Productos Metalest, Spain) were used as the diluent and lubricant, respectively. Materials were used as received and percentage concentrations given, unless otherwise mentioned, were calculated based on percentage weight by weight (%, w/w) basis. All inorganic salts were of analytical reagent grade obtained from Merck Chemicals, Germany.

2.2. Dynamic vapor sorption analysis

Moisture sorption and desorption isotherms were generated at 25 °C using a vapor sorption analyzer (VSA; AquaLab Vapor Sorption Analyzer, Decagon Devices, USA). The VSA is equipped with a microbalance and a dew point hygrometer for the measurement of weight change and water activity, respectively. The instrument was calibrated using 13.40 mol/kg LiCl and 2.33 mol/kg NaCl solutions, which correspond to 0.25 ± 0.003 and 0.92 ± 0.003 a_w, respectively. A step of 0.1 a_w increment was used to generate the sorption isotherm from 0.1 to 0.9 a_w and at each water activity, a weight change of not more than 0.001%/h was considered as equilibrium was reached. The desorption isotherm was generated by decreasing the water activity from 0.9 to 0.1.

2.2.1. GAB modeling

Nonlinear regression analysis of the GAB equation was used to analyze the sorption and desorption isotherms from 0.1 to 0.9 a_w and the monolayer moisture content, M_m obtained.

The GAB equation is written as:

$$M_w = \frac{M_m C K a_w}{(1 - K a_w)(1 - K a_w + C K a_w)} \tag{1}$$

where a_w is the water activity, M_w is the equilibrium moisture content of the sample, M_m is the GAB monolayer moisture content, and

$$C = k' e^{[(H_1 - H_M)/RT]} \tag{2}$$

and

$$K = k'' e^{[(H_L - H_M)/RT]} \tag{3}$$

where k' and k'' are constants, R is the ideal gas constant, T is the absolute temperature, H_M is the heat of sorption for vapor in the intermediate state, while H_1 and H_L are heat of sorption to the solid sample and heat of liquefaction (condensation) of water, respectively.

2.2.2. Young and Nelson equations fitting

The Young and Nelson equations were used to identify the locations of bound (monolayer) moisture, bound absorbed moisture and condensed moisture.

The Young and Nelson equations are as follows:

$$\theta = \frac{RH}{RH + (1 - RH)E} \tag{4}$$

$$\varphi = \theta RH \tag{5}$$