High tablettability and good disintegration of novel poly(vinylalcohol-acrylic acid-methylmethacrylate) (POVACOAT®) as a granulation binder

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Abstract
Purpose: POVACOAT is a newly developed aqueous polymer which is poly (vinyl alcohol) derivative grafted with acrylic acid and methyl methacrylate. POVACOAT is applied to coating film, granulation binder and solid dispersion carrier etc. This study was focused on the applicability as a granulation binder. **Methods:** In order to elucidate the wet granulation tendency of POVACOAT, the solid-liquid-air packing states of wet massing were evaluated by a mixer torque rheometer (MTR). Hydroxypropylcellulose (HPC-L) was used for comparison. In the next step, the granules obtained with varying the binder liquid amounts were evaluated with regard to tablettability and disintegration. **Results:** Torque profiles by a MTR suggested that the amounts of POVACOAT as a binder liquid for obtaining the optimized tabletting granules were smaller than that of HPC-L. The tablettability which is defined as tablet hardness against tablet density with varying tabletting pressures was found to be superior in POVACOAT against HPC-L. The disintegration times of tablets were rather faster than that of HPC-L in spite of the higher tablet hardness. These results demonstrated that POVACOAT has an excellent performance as a wet granulation binder with a good balance between the tablettability and disintegration
Keywords: POVACOAT, pharmaceutical excipient, granulation binder, tablettability, disintegration

1. Introduction

POVACOAT [1)] is a newly developed aqueous polymer which is poly (vinyl alcohol) derivative grafted with acrylic acid and methyl methacrylate. The chemical structure is shown in Fig.1. POVACOAT is applied to coating film[2)], granulation binder[2,3)], solid dispersion carrier[4,5)] and so on. POVACOAT was registered to Drug Master Files of US as DMF18033, and Master Files of Japan as 219MF20003.

Recently, various oral disintegration (OD) tablets have been developed[6)] and the concept of Design Space (DS) was introduced in pharmaceutical formulation design technology. The granulation binder is well-known as taking an important role for the quality of tablet.

This study was focused on the applicability of novel POVACOAT as a wet granulation binder.

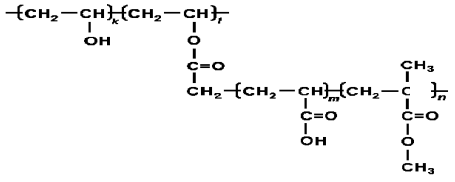

Fig.1 Chemical structure of POVACOAT

2. Materials and methods

2.1. Materials

POVACOAT (Type F and Type MP (D50; 125μm), Daido Chemical Corp., Japan), hydroxypropyl cellulose (HPC-L, Nippon Soda, Japan), lactose (200M, DMV, Japan), and corn starch (Nippon Starch Chemical, Japan.) were used.

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2.2. Equipments

Granulating torque measurement

A mixer torque rheometer (MTR; Caleva, UK) was used.

Kneading

Forty grams of granules with varying the amounts of binder liquid were prepared with kneading by a MTR.

Tabletting

A rotary press (8mmφ 7R, 200mg tablet, Kikusui Seisakusho, Japan) was used.

2.3. Evaluation methods

Powder properties as a tabletting granule

Mean particle size (D_{50}) and geometric standard deviation (σg) as a sharpness of particle size distribution and compression index (CI) as a flowability of powder were measured.

Tablet hardness and disintegration

Tablet hardness was measured by Schleuniger hardness tester. Disintegration time was measured according to JP16 disintegration test method (37°C, 900mL of purified water, non-disk).

3. Results and discussion

3.1. Solid-liquid-air packing (SLA) state

Lactose/corn starch with the weight ratio of 7/3 which is well-known as a standard formulation in Japan was used as a model formulation. An aqueous POVACOAT solution (6 w/v %) and an aqueous HPC-L solution (6 w/v %) were used as a binder liquid.

In Fig. 2, SLA result of the case of using POVACOAT was compared with that of HPC-L. SLA measurement by a MTR was fast; it can be achieved for *ca.* 15 min. The amount of binder liquid which denotes torque maximum is very important value, the so-called “a plasticity limit value (PL)”.

The PL of POVACOAT was 21.0 wt% which was 26% smaller than that of HPC-L, *i.e.*, 28.6 wt%.

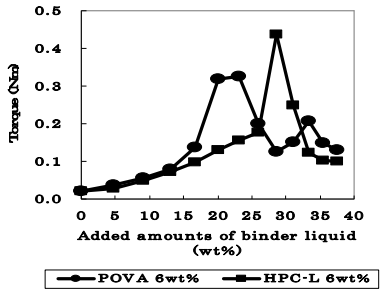

Fig.2 Comparison of torque pattern

3.2. Granulation growth according to Ig

For comparison among various granulation, normalized Ig defined as an arbitrary binder liquid amount vs. PL is well used as a parameter, and granulation growth is said to effectively occur in the range of 0.5~0.85 of Ig[7]. The results of Fig. 2 suggest that the granulation growth of POVACOAT might occur in a smaller amount of binder liquid than HPC-L. In Fig. 3a), mean particle sizes (D_{50}) of the granules obtained with varying the amounts of binder liquid are plotted against Ig, *i.e.*, normalized amount of binder liquid.

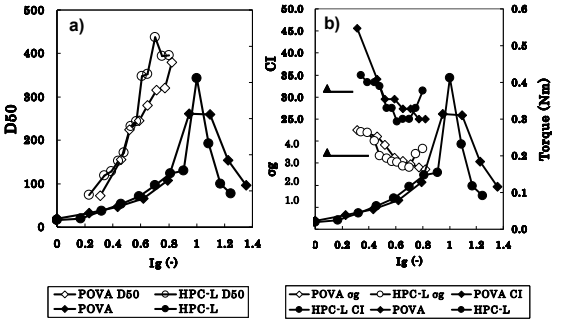

Fig.3 Plots of D_{50} and torque pattern (a) and plots of σg, CI and torque pattern (b) as a function of Ig

In both cases, D_{50} sharply increased around 0.55 of Ig (Fig. 3a) and smaller σg or CI that denotes the appropriate property as a tabletting granule was found to be obtained in the same Ig region (Fig. 3b). From these results, the liquid amount required for obtaining the optimized granules of POVACOAT can be said to be smaller than those of HPC-L. This lesser liquid amount might be due the better wettability of POVACOAT.

3.3. Tablet hardness (TH) and disintegration

The obtained granules with varying Ig were tabletted under various pressures. In this study, the tablettability was discussed not by the plot of TH vs. tabletting pressure but the plot of TH vs. tablet density[8] (ρ; g/cm^3) for the sake of quantitative description of tablettability. TH against ρ with varying tabletting pressures was found to show a linear relationship (data not shown).

TH and disintegration time (DT) at various ρ against Ig is plotted in Fig. 4 for the results of POVACOAT (a) and that of HPC-L (b). The ρ values of 1.36, 1.38, 1.40 and 1.42 correspond to the tabletting pressures (kN) of 7.1, 8.2, 9.4 and 10.6, respectively. From Fig. 4, it can be seen that apparently the higher TH was obtained at near 0.6 of Ig as similar to the case of powder properties. This might be very interesting insight that the amounts of binder liquid for obtaining an optimized tabletting powder and TH exist in almost the same Ig.

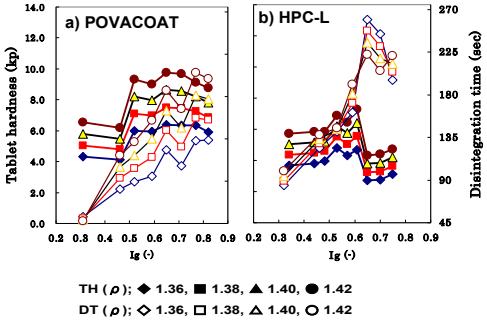

Fig.4 Tablet hardness and disintegration time

As shown in Fig. 4, TH of POVACOAT was found to be larger than that of HPC-L, and its Ig range giving higher TH was broad over 0.5~0.7. Disintegration time of tablet with POVACOAT was gradually increased with increasing Ig, while that with HPC-L showed a sharp increase beyond 0.6 of Ig. In spite of the higher TH, the DT of POVACOAT tablet was shorter than that of HPC-L tablet.

4. Conclusions

1) Binder liquid amount for obtaining the optimized tabletting granules using POVACOAT is smaller and broader than that of HPC-L.
2) POVACOAT has a higher tablettabilty and good disintegration tendency; a good balance between them can be obtained in the broad range of Ig.
3) POVACOAT as wet granulation binder is expected to take a valuable role in dosage form design.

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