Evaluation of Polymers as binder on Coprocess of tablet

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Abstract: Evaluation of polymers as binder on coprocess tablet was prepared with hydroxypropyl methyl cellulose (HPMC), citric acid graft locust bean gum (CAgLBG), locust bean gum (LBG) and polyvinylpirrolidone K-30 (PVP K-30) as binder. Study aims to determine the physical quality of coprocess granules, tablets, and dissolution studies. Wet granulation method was used to create granules coprocess. Granules were evaluated for flow rate, angle of repose, granul density, tapped density, housemer ratio, and carr’s index. Tablet were evaluated for thickness, hardness, friability, disintergrant time, and dissolution of tablet. All granules coprocesses using variation binder were meet to standard of physical quality of granules and tablets. Tablets using binder LBG have drug release and ED₆₀ are highest.

Keyword : binder, HPMC, CAGLBG, LBG, PVP K-30, coprocess.

Introduction

Coprocess is a combination of two or more excipients by manufacture method precisely. The advantages of coprocess is to create an excipient have better character than the single use of the parent material, for the development of direct compress, reducing the amount of component of tablet production, and the production costs of tablet is lower.¹,² Some methods of create coprocess is granulation, spray dry, melt extrusion, solven evaporation and crystallization. the method used depends on the character of the composition of coprocess.³,⁴

The binder is an excipient to increase the bond strength of interparticulate and plasticity in the tablet.⁵,⁶ Based on the origin of binder of tablet are sugar (sucrose), nature (guar gum), and synthetic / semi-synthetic (polyvinyl pyrrolidone). Based on solubility of binder of tablet are soluble binder (sucrose) and insoluble (microcrystalline cellulose).⁷,⁸ The binder affects the flowability and compactibility of granule, depending on the type, quantity and the way the binder is added (Gunatilake, et al., 2016). In this study, the binder are used HPMC (semi-synthetic cellulose and soluble), CAGLBG (semi-synthetic esterification and low soluble), LBG (natural and soluble), and PVP K-30 (synthetic and soluble).⁹

The novelties of this study are creates coprocess by wet granulation with a variation of the type of binder and lactose monohydrate as filler. Variations binder used HPMC, CAGLBG, LBG and PVP K-30. The advantages of manufacture coprocess are using binders and fillers as constituent components. The aims of this study is determine the physical quality of the granules, tablets, and dissolution.
Experimental

Material

The materials used in this study were HPMC (Methocel K4M CR Premium USP/EP, Colorcon, Singapore), CAgLBG (esterification of citric acid on locust bean gum), LBG (Viscogum, Cargill, France), PVP K-30 (BASF Corp., Germany), lactose monohydrate (Leprino Foods, UDM, USA).

Preparation of coprocess tablet

Coprocess tablet was prepared by HPMC, CAgLBG, LBG and PVP K-30 as binder and lactose monohydrate as filler. Binder (3g) was dispersed in 3 mL of warm water in mortar. After the binder swollen, 27g of lactose monohydrate was added into the mortar, stir and compression of mixture to form a mass of wet granules, sieved by a mesh number 18, and dried at 50 °C until 15 minutes. Dried granules sieved by a mesh number 20 and evaluated the physical quality of the granules. Dried granules was compressed into tablets 200 mg and evaluated physical quality of tablet and dissolution.

The evaluation of dried granules were flow rate, angle of repose, granul density, tapped density, housner ratio, and carr’s index. The evaluation of tablet were thickness,hardness, friability, disintergrant time, dissolution of tablet.

Flow rate and angle of repose

Granules (10 g) was placed in a funnel of flowability tester (Erweka type GTB). The time required flow granular through the tip of the funnel was recorded as the flow time and the weight of granules per time was recorded as the flow rate. The angle of repose (α) is anti tan ratio between height (H) with a half of base diameter (R) of cone. The angle of repose of sample was calculated according to equation 1.

\[ \alpha = \arctan \frac{H}{R} \]  

Bulk density and tapped density

Measuring cylinder (50 mL) was weighed and the weight recorded. The granules filled into the measuring cylinder until volume 50 mL, was weighed and the weight recorded. Place the measuring cylinder on the tapped volume (Erweka SVM 12) and run 500 taps. The granules density and tapped density of sample was calculated according to equation 2 and 3.

\[ \text{Bulk density} = \frac{W_2 - W_1}{V_0} \]  

\[ \text{Tapped density} = \frac{W_2 - W_1}{V_1} \]  

where W_2 is weight of granules on measuring cylinder, W_1 is weight empty of measuring cylinder, V_0 is volume of granules before taps, V_1 is volume of granules after taps.

Housner ratio and carr’s index

Housner ratio is the ratio between tapped density with bulk density. Carr’s index is percentage of ratio between the difference of tapped density and bulk density with tapped density. Housner ratio and carr’s index of sample was calculated according to equation 4 and 5.

\[ \text{Housner ratio} = \frac{\text{tapped density}}{\text{bulk density}} \]  

\[ \text{Carr’s index} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \]
Thickness and hardness

Thickness of tablet from each batch was determined of average 20 tablets using vernier calipers. Hardness of tablet from each batch was determined of average 10 tablets using hardness tester.

Friability

Friability of tablet from each batch was determined of 20 tablets using friability tester (Erweka). The tablet were cleaned, weighed, and rotated 25 rpm until 4 minutes. The tablets were cleaned and reweighed. Percentage of weight loss of sample was calculated according to equation 6.

\[
\text{Friability} = \left( \frac{W_1 - W_2}{W_1} \right) \times 100\%
\]

where \(W_1\) and \(W_2\) are initial and final weight of tablets.\(^{14}\)

Disintegration time

The disintegration time of tablet from each batch was determined of average 6 tablet using disintegration tester (Erweka Z3). The tablets were inserted in the mesh of a vessel containing distilled water 37°C and moves up and down constantly. The time needed until the tablet is not left behind on the mesh was recorded as the disintegration time.

Dissolution

The dissolution study was conducted with the tablet (200 mg) of each coprocess and ketoprofen as the active ingredients model (1:1). Release studies were used dissolution apparatus type II with a paddle. The rotation speed of the stirrer was 50 /min during 60 min, the temperature of the buffer in the bath was 37 ± 1°C, and volume of phosphate buffer pH 6.8 was 900 mL.\(^{15}\) The samples were analyzed using a UV-Vis spectrophotometer (Hitachi U1900) wavelength of 260 nm.

Result and Discussion

Flow rate and angle of repose

Flow rate and angle of repose of granules using variation binder are shown in Table 1. Granules using binder CAgLBG is the best among the others. The granules has flow rate 2.3 g / sec and angle of repose 29\(^\circ\). CAgLBG create strong bond of intraparticle to form granules and granules have low cohesiveness so that when the force of gravity causes the granule can flow freely and it has angle of repose is low. The angle of repose of granules 25-30\(^\circ\) is excellent and 30-35\(^\circ\) is good granules (Well and Aulton, 1988). HPMC, LBG, and PVP K-30 is binder that can withstand moisture and swell when wetted. Although the granules have been dried but be able to withstand the humidity is higher than the granules using a binder CAgLBG. Moisture of granules will inhibit the flowability because the granules have a strong cohesiveness.

Table 1. Evaluation quality of granules

<table>
<thead>
<tr>
<th>binder</th>
<th>flow rate (g/sec)</th>
<th>angle of repose (°)</th>
<th>bulk density (g/mL)</th>
<th>tapped density (g/mL)</th>
<th>Housner ratio (%)</th>
<th>carr's index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>2.4</td>
<td>30.75</td>
<td>44.86</td>
<td>52.16</td>
<td>1.16</td>
<td>13.99</td>
</tr>
<tr>
<td>HPMC</td>
<td>2.3</td>
<td>29.71</td>
<td>39.98</td>
<td>46.49</td>
<td>1.16</td>
<td>14.00</td>
</tr>
<tr>
<td>CAgLBG</td>
<td>3.4</td>
<td>32.28</td>
<td>37.66</td>
<td>45.93</td>
<td>1.21</td>
<td>18.00</td>
</tr>
<tr>
<td>LBG</td>
<td>3.1</td>
<td>31.27</td>
<td>36.00</td>
<td>43.90</td>
<td>1.21</td>
<td>17.99</td>
</tr>
<tr>
<td>PVP-K30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Bulk density and tapped density

Bulk density and tapped density of granules using variation binder are shown in Table 1. The granules using a binder HPMC have bulk density and tapped density is highest. This is shown that the binder can retain intraparticle bonding so when given taps can retain its shape and size of granules. Additionally, the granules can be docked when given taps and reduce of intergranular porosity. The granules with binder CAgLBG, LBG, and PVP K-30 has bulk density and tapped density is lower than granules with a binder HPMC. The granules become brittle when given taps so granule size is reduced, changed of the shape, and decreased of intergranular porosity.

Housner ratio and carr’s index

Housner ratio and carr’s index of granules using variation binder are shown in Table 1. The granules using binder HPMC and CAgLBG have housner ratio and carr's index are better than the granules using binder LBG and PVP K-30. This value is influenced by bulk density values and tapped density. The higher the bulk density and tapped density so housner ratio and Carr's index are low. The value of housner ratio ≤ 1.25 and carr's index ≤ 20% is granules good flow (Well and Aulton, 1988).

Thickness and hardness

Thickness and hardness of tablets using variation binder are shown in Table 2. Tablets using binder CAgLBG have thickness and hardness are high. Tablets are elastically deformed. At the time of tablet compression, granules being compressible to form a tablet but granules stretchable after compress is removed. Tablets using the binder PVP K-30 has high hardness and thickness lower than tablet using binder CAgLBG. Tablets are formed from strong interlocking granules. PVP K-30 is a hygroscopic binder sensitive to temperature and humidity so it can form strong bonds between the granules. Tablets using binder HPMC and LBG have a lower hardness and thickness of the tablet using binder CAgLBG. Tablets are plastically deformed. At the time of tablet compression, granules can retain the shape though compress is removed.

Friability

Friability of tablets using variation binder are shown in Table 2. Tablets using binder CAgLBG has friability is high (0.72 %). The tablet has a high porosity between granules and interlocking between the granules are not strong. This condition is caused by the elastic deformation during tablet compression. Tablets using LBG binder has a friability 0.47%. Tablets have interlocking between the granules are not strong. Tablets using binders HPMC and PVP K-30 has a low Friability (0.20% and 0.27%). The tablet has a low porosity between granules and interlocking between granules are strong.

Table 2. Evaluation quality of tablet

<table>
<thead>
<tr>
<th>binder</th>
<th>thickness</th>
<th>hardness</th>
<th>friability</th>
<th>disintegration time</th>
<th>drug release</th>
<th>ED₆₀</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(mm)</td>
<td>(kgf)</td>
<td>(%)</td>
<td>(min : sec)</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPMC</td>
<td>3.60 ± 0.05</td>
<td>9.94 ± 0.47</td>
<td>0.20</td>
<td>23:44</td>
<td>54.11 ± 0.13</td>
<td>25.43 ± 0.11</td>
</tr>
<tr>
<td>CAgLBG</td>
<td>3.84 ± 0.02</td>
<td>10.12 ± 0.94</td>
<td>0.72</td>
<td>8:50</td>
<td>54.29 ± 0.23</td>
<td>27.69 ± 0.17</td>
</tr>
<tr>
<td>LBG</td>
<td>3.63 ± 0.09</td>
<td>8.83 ± 1.22</td>
<td>0.47</td>
<td>29:50</td>
<td>78.52 ± 0.39</td>
<td>48.16 ± 0.27</td>
</tr>
<tr>
<td>PVP-K30</td>
<td>3.64 ± 0.04</td>
<td>10.15 ± 0.96</td>
<td>0.27</td>
<td>20:55</td>
<td>67.61 ± 0.32</td>
<td>33.32 ± 0.23</td>
</tr>
</tbody>
</table>

Disintegration time

Disintegration time of tablets using variation binder are shown in Table 2. Tablet using a binder CAgLBG has the most rapid disintegration time (8:50). High porosity accelerate wetting and influx of media in the tablet. The presence of media in tablet, accelerate disintegration tablet into granules and the granules into...
powder. Tablets using binder HPMC and PVP K-30 have disintegration time of 23:44 and 20:55. The tablet has a compactibility high and low of porosity so little space of the influx of media. Tablets using binder LBG has the longest disintegration time (29:50). Disintegrating tablets by mechanism LBG swell and pushing particles in the surrounding to disintegrasi. LBG can swelling when wetted media, thus need for a longer time.

Dissolution

The percentage, efficiency dissolution (ED₆₀), and profil drug release of tablets using variation binder are shown in Table 2 and Figure 1. Tablet using a binder LBG has of drug release and ED₆₀ are 67.61 % and 33.32 %. Although the tablet has high hardness, low friability, and long of disintegration time but PVP K-30 is a hydrophilic binder and serves also as a solubilizer so it is accelerate the release of ketoprofen. Tablet using a binder CAgLBG has of drug release and ED₆₀ are 54.29 % and 27.69 %. CAgLBG is poorly soluble so it is inhibited of wetting and release of ketoprofen though the tablet has high friability and a long of disintegration time. Tablet using a binder HPMC has of drug release and ED₆₀ are 54.11 % and 25.43 %. The tablet has high hardness, low friability, and a long of disintegration time so their are inhibited the release of ketoprofen.

Conclusions

All granules coprocesses using variation binder were meet to standard of physical quality of granules and tablets. Tablets using LBG binder have drug release and ED₆₀ are highest.

Figure 1. Profil of release of ketoprofen of tablets using variation binder

References


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