Preparation of Orally Disintegrating Tablets Containing Taste-Masked Coated Pellets

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ABSTRACT SUMMARY
Orally disintegrating tablets containing taste-masked coated Acetaminophen pellets were prepared and evaluated. The taste-mask coating was performed using a combination of Hypromellose Acetate Succinate (HPMCAS) and Methylcellulose (MC). A co-processed compound SmartEx® was used as filler excipient for ODT. The resulted finished ODT product showed a good performance with respect to sensory test and drug release.

INTRODUCTION
Orally disintegrating tablets (ODT) are getting more popular dosage form especially for geriatric patients. In this study, ODTs containing taste-masked pellets were prepared and evaluated.

EXPERIMENTAL METHODS
Acetaminophen (APAP) was used as the model drug. The drug was layered on spheres of microcrystalline cellulose (Celphere® CP-102, Asahi-Kasei, Japan), using a fluid-bed coating equipment (MP-01 SPC, Paurex, Japan).

Taste-mask coating to the pellets was performed using the same fluid-bed equipment. The coating formulations consisted of two polymers Hypromellose Acetate Succinate (HPMCAS, Shin-Etsu AQOAT®, Type AS-MG, Shin-Etsu Chemical Co., Ltd., Japan) and Methylcellulose (MC, Metolose® Type SM-4, Shin-Etsu Chemical Co., Ltd., Japan). Four formulations with different ratio of HPMCAS/MC were tested. The coating level was 3 % as the weight gain of the core pellets. The coating formulations are shown in Table 1.

<table>
<thead>
<tr>
<th>Coating Formulation</th>
<th>HPMCAS / MC Ratio</th>
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<tbody>
<tr>
<td></td>
<td>10/0</td>
</tr>
<tr>
<td>HPMCAS</td>
<td>6</td>
</tr>
<tr>
<td>MC</td>
<td>0</td>
</tr>
<tr>
<td>Talc</td>
<td>1.8</td>
</tr>
<tr>
<td>NH₃</td>
<td>1.9 % with regard to HPMCAS</td>
</tr>
<tr>
<td>Colorant</td>
<td>0.01</td>
</tr>
<tr>
<td>Water</td>
<td>q.s.</td>
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</tbody>
</table>

For preparation of ODT, a newly-developed co-processed excipient (SmartEx®, Shin-Etsu Chemical, Japan) was used. The ODTs were prepared by direct compression of the blend of SmartEx® and the coated pellets, using a rotary tablet press (Virgo®, Kikusui, Japan). The tablet dimension was 8 mm in diameter and 12 mm in radius, and the weight was 200 mg per tablet.

The dissolution test (in water, paddle speed: 100 rpm) and disintegration test (in water) were performed based on USP. A sensory test was also carried out by eight healthy volunteers.

RESULTS AND DISCUSSION
The results for dissolution test of the coated pellets are shown in Figure 1. When the ratio of HPMCAS / MC was 9:1, the drug release was optimum for both taste-masking effect and drug release rate. Therefore, the coated pellets of this polymer ratio were chosen for the further ODT preparation.

Figure 2 shows tablet hardness and disintegration time of the ODT tablets in various ratio of the filler compound and coated pellets.
When the pellets were 30 % in tablet, the ODT showed a sufficient tablet hardness (higher than 50 N at 10 kN-compression force). However at more than 40 % pallet, the tablet hardness was lower than the optimum level. Disintegration time was not significantly affected by the pellet content, and this was rather influenced by compression force.

Figure 3 shows the dissolution profile of APAP from the ODT formulation in comparison with the original pellet formulation. Influence of compression was not significantly affected on the release of APAP.

Figure 4 shows the results of sensory test by volunteers. This indicates that the taste-mask coating using HPMCAS and MC (9:1) was effective in vivo.

CONCLUSIONS
The combination of HPMCAS and MC for pellet coating was effective for taste masking. In this study, HPMCAS / MC with a ratio of 9:1 showed the best results.

The taste-masked pellets were able to be included into ODT at 30 %. There was no coating damage, and the performance of taste masking and drug release were maintained.