Preparation of Taste Mask MUPS (multiple unit particles system) ODT

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ABSTRACT SUMMARY

MUPS orally dispersible tablet (ODT) was prepared by using microparticles including Celphere™ CP-102 and preliminary granulated mixture of 30% microcrystalline cellulose Ceolus™ KG-1000 and 70% Erythritol. It showed sufficient tablet hardness and friability, and fast disintegration. Besides, taste masking profiles unchanged before and after tableting because highly flexible film containing Eudragit NE30D and anti-tacking agents (Ethylcellulose aqueous dispersion and titanium dioxide) absorbed damage during compaction.

INTRODUCTION

Recently, an advanced fine particle coating technology is developed for preparation of the specialty product such as taste-masked preparation and ODT, and then, it is becoming important not only for QOL improvement to patients, but also for product life-cycle management of pharmaceutical products.

Conventionally, coating technology had been used mainly for capsules, but nowadays, fine particles coating devices which could produce stable products and availability of fine seed core enables us to prepare a tablet containing coated pellets. Particularly, ODT with coated pellets can be taken without feeling roughness in oral cavity by microparticulating coated particles. 4)

Tableting mixture of coated microparticles and other excipients is very challenging in terms of segregation, film damage by compression force and tableting problem. Particularly, ODT with coated pellets is developed for preparation of the specialty product such as ODT with coated pellets. 4)

Table-1 General properties of Celphere™

<table>
<thead>
<tr>
<th></th>
<th>CP-102</th>
<th>CP-203</th>
<th>CP-305</th>
<th>CP-507</th>
<th>CP-708</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particle size range [μm]</td>
<td>10-212</td>
<td>150-200</td>
<td>300-500</td>
<td>500-710</td>
<td>710-850</td>
</tr>
<tr>
<td>Bulk density [g/cm³]</td>
<td>0.93</td>
<td>0.87</td>
<td>0.87</td>
<td>0.93</td>
<td>0.93</td>
</tr>
<tr>
<td>Friability [%]</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Water absorption [%]</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>70</td>
<td>85</td>
</tr>
</tbody>
</table>

EXPERIMENTAL METHODS

1) Materials

Seed core

- Celphere™ CP-102 (D50; 146μm)

Drug substance

- Caffeine (CAF; Solubility 20g/L; 20°C)

Excipients

PVP-K30, HPMC, Aquacoat ECD, Titanium dioxide (TiO₂), Eudragit NE30D, Ceolus KG-802, KG-1000, UF-711, Magnesium Stearate (Mg-St), Trehalose, POVACOAT (PVA), Swelstar PD-1, Triethyl citrate, Talc, CaHPO₄, Erythritol

2) Procedure

2-1) Drug layering

Drug layering was performed using caffeine as a model drug for its bitter taste and titanium dioxide as an anti-tacking agent. HPMC seal coating was carried out to prevent caffeine sublimation.

Drug layering (Caffeine)
2-2) Taste-mask coating

Taste-mask coating was performed using ethylcellulose aqueous dispersion (ECD) as a control release agent. Triethyl citrate is a plasticizer of ECD. NE30D is used as a control release and stretchable agent. Titanium dioxide is anti-tacking agent to reduce NE30D’s tackiness. PVA has low tackiness because it is insoluble in water. Therefore it acts as an anti-tacking agent during coating process.

**Taste mask coating**

![Diagram of Taste mask coating process]

2-3) Tablet compaction

Erythritol and KG-1000 were used as excipients. 70% Erythritol and 30% KG-1000 were granulated by fluidized bet granulator. Combination of Erythritol and KG-1000 showed good disintegration and mouth feeling.

**Taste Mask MUPS ODT Compaction**

![Diagram of Taste Mask MUPS ODT Compaction process]

### Table-3 Tablet properties

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Unit</th>
<th>Result</th>
<th>RSD</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness</td>
<td>N</td>
<td>60N</td>
<td>64.0</td>
<td>67.9</td>
</tr>
<tr>
<td>Friability</td>
<td>%</td>
<td>2%</td>
<td>0.156</td>
<td>0.118</td>
</tr>
<tr>
<td>Tablet Weight</td>
<td>mg</td>
<td>379.8</td>
<td>382.6</td>
<td>383.8</td>
</tr>
<tr>
<td>Tablet Thickness</td>
<td>mm</td>
<td>5.154</td>
<td>5.154</td>
<td>5.163</td>
</tr>
<tr>
<td>Compression Force</td>
<td>kN</td>
<td>6.77</td>
<td>6.9</td>
<td>6.9</td>
</tr>
<tr>
<td>Disintegration Time</td>
<td>sec</td>
<td>29.0</td>
<td>30.8</td>
<td>30.5</td>
</tr>
<tr>
<td>Dissolution Media</td>
<td>pH</td>
<td>1.2</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Dissolution Test</td>
<td>Method</td>
<td>2</td>
<td>Paddle method.</td>
<td></td>
</tr>
</tbody>
</table>

Obtained table showed taste masked drug release profiles. (Fig.1) This means that there was little film damage due to high flexibility of NE30D.

### Fig.1 Dissolution profile

![Dissolution profile diagram]

**CONCLUSION**

Formulation of films and excipients were examined for MUPS ODT. Film coated pellets with little agglomeration were obtained because of low film tackiness. Taste-masked MUPS ODT using preliminary granules of 30% KG-1000 and 70% Erythritol showed sufficient tablet hardness and friability and fast disintegration. Besides, taste masking profiles was maintained after tabletting because highly flexible film absorbed damage during compaction.

## REFERENCES


### RESULTS AND DISCUSSION

Obtained tablets met required criteria of ODT (Tablet hardness: ≥ 40N, Friability: ≤ 1%, disintegration time: ≤ 60s). Tablet weight RSD and API content RSD showed required level (≥1% and ≤2%).