Novel approach to disintegration testing of orodispersible films: *In vitro* oral cavity simulator

**Mariagiovanna Scarpa**¹; Andrew Redfearn²; Ben Hanson²; Mine Orlu¹

¹UCL School of Pharmacy, University College London, Department of Pharmaceutics, 29-39 Brunswick Square, London WC1N 1AX – UK, m.scarpa@ucl.ac.uk; m.orlu@ucl.ac.uk
²UCL Department of Mechanical Engineering, University College London Roberts Engineering Building, Torrington Place, London WC1E 7JE – UK, a.redfearn.12@ucl.ac.uk; b.hanson@ucl.ac.uk

**Background**
- Previous studies have confirmed that orodispersible films (ODFs) (Fig. 1) are acceptable dosage forms for preschool children, and infants (Orlu et al., 2017).
- ODF disintegration is a key characterisation parameter, not only for quality control purposes (Gittings et al., 2015), but also as an indicator of the end-user acceptability (Scarpa et al., 2018).
- There are currently no standard *in vitro* methods for the disintegration assessment of ODFs.

**Rationale**
- There is the need for *in vitro* predictive decision support tools to be implemented in the pharmaceutical industry, in order to guide the product design.

**Method**

1. **ODF sample composition**

<table>
<thead>
<tr>
<th>ID</th>
<th>Polymer</th>
<th>Molecular weight (kDa)</th>
<th>Concentration (w/v)</th>
<th>Size (cm²)</th>
<th>Dye</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>Poly(vinyl) alcohol</td>
<td>30</td>
<td>5%</td>
<td>6</td>
<td>Red (0.4% w/v)</td>
</tr>
<tr>
<td>P2</td>
<td>Poly(vinyl) alcohol</td>
<td>205</td>
<td>5%</td>
<td>6</td>
<td>Red (0.4% w/v)</td>
</tr>
<tr>
<td>C1</td>
<td>Carboxymethyl cellulose</td>
<td>355</td>
<td>1%</td>
<td>6</td>
<td>Red (0.2% w/v)</td>
</tr>
<tr>
<td>C2</td>
<td>Carboxymethyl cellulose</td>
<td>725</td>
<td>1%</td>
<td>6</td>
<td>Red (0.2% w/v)</td>
</tr>
<tr>
<td>Listerine® Multiple</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Green</td>
</tr>
</tbody>
</table>

2. **Oral cavity simulator**

- The original design of the Oral Cavity Simulator (OCS) involves a silicone body mimicking the human tongue, moving vertically, and applying a controlled compression onto a clear flat acrylic plate mimicking the human palate (Fig. 2).
- Four dried ODFs were prepared by solvent casting (Tab. 1), and positioned on the tongue. Listerine®-breath strips were also tested as benchmark.
- A compression and retraction phase of 0.7s was followed by a pause of 2s.
- Simulated salivary fluid (SSF) was sprayed inside the oral cavity every two compression cycles, in order to achieve a 1.5 mL/min flow rate (Smitka et al., 2015).
- A camera (Sony RX100 M4) was positioned above the acrylic plate, and a video of the dissolving ODF was taken (Fig. 2).

3. **Video analysis**

- A video data processing program was developed using Matlab (MathWorks, Natick, MA, USA).
- From the video file, a frame was extracted at the beginning of the compression sequence during the ‘open’ position.
- The background and ODF areas were selected manually by a ‘crop’ function from the first extracted image (Fig. 3 a, and b).
- A manual thresholding function allowed to accurately define the film area (Fig. 3 d)
- One frame was subsequently extracted at each compression sequence during the ‘open’ position.
- For each extracted frame, the Red, Green, and Blu signal intensities were recorded from each pixel of the background and film areas.

4. **Signal intensity calibration**

**Results**

- The average ODF % volume reduction at 180 s was >90% for sample P1 and Listerine®, and 85%, 48%, and 37% for samples C1, P2, and C2 respectively (Fig. 5 a).
- The lower molecular weight ODF of each polymeric species disintegrated faster than their high molecular weight counterparts.
- The ODF volume reduced linearly in samples P1 and Listerine®, and in a non-linear fashion in the preschool samples.
- A difference in ODF breakdown behaviour was observed between PVOH-based and CMC-based films (Fig. 5 b).
- Proportionality between *in vitro* and previously reported in vivo measured perceived disintegration time (Fig. 6 a and b) was maintained.

**Discussion**

- The presence of non-linear regions in the disintegration profile, and the increase of disintegration time of high-molecular weight ODF might depend on:
  1. Hydration and disentanglement of long polymeric chains in liquid media
  2. Higher availability of substitution groups responsible for hydrogen bonding (Linsenstorfer et al., 1997)
  3. Adhesion mechanisms between polymeric chains and acrylic material (Tophiät et al., 2016)
- The difference in breakdown behaviour of ODF might be explained by the availability of different substitution groups (Linsenstorfer et al., 1997)

**Conclusions**

- A mechanical oral cavity simulator designed to mimic the adult oral cavity was adapted for the *in vitro* measurement of the disintegration behaviour of ODFs.
- The OCS could detect differences in disintegration behaviour of ODFs prepared with different film-forming polymers.
- Results maintained proportionality with previously reported in vivo data on perceived disintegration time in the adult population, potentially informing on the end-user acceptability.
- As the anatomical, and physiological features of the infant’s oral cavity can be mimicked in the OCS, the model holds potential to predict in *vivo* disintegration behaviour of paediatric oodispersible dosage forms.

**References**