Understanding acceptance and swallowability of bitter tasting tablets in children

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Introduction

There is growing evidence that children will accept and swallow small tablets. Previous research has shown that 91% of children between 6-11 years old could swallow a small (7 mm) round tasteless tablet (with training and money as an incentive) [1]. However, it is recognised that many pharmaceutical ingredients taste bitter which presents a key barrier to palatability and hence acceptability. This study explored acceptability of small bitter tasting tablets in children (with no training or incentive).

This work:
Small (7.5mm) round tablets were coated with taste-masking or non-functional coatings to assess the impact of bitterness on acceptability. Two factors of acceptability: swallowability and palatability (appreciation of taste).

Methodology

A single centre crossover study design was used to investigate the acceptability of tablets in children aged 4-12 years (Table 1). Ethical approval was obtained from the Ethical Review Committee, University of Birmingham (ERN 18-17825).

Children received two tablets for swallowing and two further tablets for palatability assessment. The swallowing task was performed without any constraint; children were permitted to spit out the tablet, if it was too difficult to swallow.

Table 1 Formulations of film coatings included in the study (coating level: 4% weight gain).

<table>
<thead>
<tr>
<th>Code</th>
<th>Coating type</th>
<th>Coating formulation</th>
<th>Taste-masking functionality</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>Basic</td>
<td>HPMC, Glycerol</td>
<td>No (reference)</td>
</tr>
<tr>
<td>F2</td>
<td>Emulsion based</td>
<td>HPMC, Hydrogenated cottonseed oil, Caprylic / Capric mono-diglycerides, Talcum, Titanium dioxide</td>
<td>Yes</td>
</tr>
<tr>
<td>F3</td>
<td>Increased viscosity</td>
<td>HPMC, Glycerol Xanthan gum, Talcum, Titanium dioxide</td>
<td>Yes</td>
</tr>
<tr>
<td>F4</td>
<td>Reverse enteric</td>
<td>Basic Butylated Methacrylate Copolymer, Titanium dioxide</td>
<td>Yes</td>
</tr>
<tr>
<td>F5</td>
<td>Insoluble / soluble polymer</td>
<td>Ethyl cellulose dispersion : HPMC (80:20), Glycerol, Talcum, Titanium dioxide</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Table 2 RROs results.

<table>
<thead>
<tr>
<th>Code</th>
<th>Swallowed/ Spit out</th>
<th>Sum of negative facial expressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>67 / 37 / 0</td>
<td>60</td>
</tr>
<tr>
<td>F2</td>
<td>51 / 44 / 5</td>
<td>46</td>
</tr>
<tr>
<td>F3</td>
<td>67 / 33 / 0</td>
<td>32</td>
</tr>
<tr>
<td>F4</td>
<td>48.5 / 48.5 / 5 / 7</td>
<td>70</td>
</tr>
<tr>
<td>F5</td>
<td>57 / 40 / 3</td>
<td>57</td>
</tr>
</tbody>
</table>

Findings

Success of swallowing vs. demographics
Of the 101 participating children 63% were able to swallow at least one 7.5 mm tablet.

Age range
- 4 - 6 years: 27.7%
- 7 - 9 years: 39.6%
- 10 - 12 years: 32.7%

Ethnicity
- White: 57.4%
- Asian: 17.8%
- Mixed: 16.8%
- Other: 1.0%
- Not disclosed: 6.9%

Boys were more likely to swallow the tablet (p<0.005), while ethnicity did not correlate with swallowing success (p=0.170).

The number of children able to swallow the tablet was lower than previous reports [1, 2], perhaps due to the lack of incentive and freedom to spit out or refuse the sample.

Success of swallowing vs. coating type
The success of swallowing did not correlate with the type of coating applied (p=0.644), suggesting that taste-masking did not influence the success of swallowing the tablet.

Palatability vs. coating type
The formulation of the coating had a major impact on the palatability of tablet, i.e. liking score (p < 0.005).

Only two coatings (F2, F3) decreased the perceived bitterness. Coated tablets which were perceived as less bitter were more liked (Figure 2). These results were corroborated by the sum of the negative facial expressions (Table 2).

Acceptability measures

RROs
- Record of negative facial expressions
- Success of taking the sample
- the child swallowed - spat out
- refused to take a tablet

PROs
- Ease-of-swallowing
- Bitterness
- Liking

44.5% Not disclosed
55.5%

4.6 - 7.9
84.4% swallowed a tablet

4 - 6 year olds
10 - 12 year olds

In their own words

"Light?"
"Easy peasy lemon squeezy!"
"That one was really hard to swallow."
"Didn't feel anything. Very slippery. Very young children can take it."
"I wouldn't take it everyday."

Conclusions

The study measured acceptability of coated tablets with an incorporated bitter tasting agent. As children are more sensitive to bitterness than adults, it was expected that bitterness would reduce acceptability.

• The presence of a bitter taste reduced the palatability, but it did not affect swallowability
• Formulations with good taste-masking properties, improved the PROs of ease-of-swallowing.

Compared to previous studies overall swallowability rates were lower. Similar to previous studies swallowability increases with the age of the child. Addition of a bitter agent to the tablets was useful to better understand acceptability of tablets in children.

References