Pharmaceutical Technology (I)
(Analytical) Assessment of taste masking properties

Pharmaceutical Bio-Engineering
Lecture and Practical Course
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taste masking! … ?

from: Katharina Woertz et al., International Journal of Pharmaceutics 2010, 400, 114-123

Rational development of taste masked oral liquids guided by an electronic tongue

from: Zelalem Ayeneh et al., Recent Patents on Drug Delivery & Formulation 2009, 3, 26-39

evaluation of taste masking

„gold standard“

1. human taste panel
   • 1.1 threshold determination
   • 1.2 training of the panelists
   • 1.3 evaluation of the taste of a drug formulation
   • 1.4 critical aspects

analytical evaluation methods

2. UV probe
   • 2.1 Measurement principle
   • 2.2 calibration procedure
   • 2.3 How to carry out an experiment
   • 2.4 evaluation of the results
   • 2.5 critical aspects

3. electronic tongues
   • 3.1 Measurement principle
   • 3.2 calibration procedure
   • 3.3 How to carry out an experiment
   • 3.4 evaluation of the results
   • 3.5 critical aspects

“gold standard“ analytical evaluation methods
1. human taste panel

based on Albertini et al., EJPS 21 (2004) 295-303

1.1 threshold determination

• preparation of different API solutions
• pre-testing
• first evaluation
• second testing
• threshold determination

1.2 training of the panelists

1.3 evaluation of the taste of the drug formulation
1.1 threshold determination

evaluation of the bitterness recognition threshold of pure drug:

1. preparation

solution A: 0.00 % (w/v)
solution B: 0.01 % (w/v)
solution C: 0.02 % (w/v)
solution D: 0.04 % (w/v)
solution E: 0.08 % (w/v)
solution F: 0.17 % (w/v)
solution G: 0.34 % (w/v)

2a. pre-testing

5 ml for 5 s
1.1 threshold determination

2b. first evaluation

a) I do not feel any difference between solutions D and A.

b) I feel something but I can not identify the taste.

c) I feel a bitter taste.

3. second evaluation

solution E: 0.08 % (w/v)

4. threshold determination

• mean Perception threshold (LOD) = 0.08 %

• mean bitterness recognition threshold (LOQ) = 0.11 %

solution C: 0.02 % (w/v)
1.2 training of the panelists

in order to have an homogeneity sensation of the bitterness intensity between the volunteers:

different concentrations of the drug, dissolved in water

particular bitterness scores (0-100)
1.3 Evaluation of the taste of a drug formulation

Drug formulation is dissolved in water

- Resulting concentration of the drug > recognition threshold
- Dissolution time: 3 min (?)
- Assign a bitter score

Drug formulation is directly placed on panelist’s tongue

- Resulting concentration of the drug > recognition threshold
- Time point of evaluation?
- Assign a bitter score
1.4 critical aspects

- Regulatory: ethical concerns?
- Varying implementation: comparability of the results?
- Panelists: what about children and animals?
- Formulation pre-treatment?
- Time point of assessment?
2. UV fibre optical probe


dissolution apparatus 2 (Ph. Eur.)
2.1 measurement principle

- spectroscopic, based on the Lambert-Beer-Law

\[ A = \varepsilon \cdot c \cdot d \]

- requirements?

- transmission dip probe

- in-line measurement
2.2 calibration procedure

- sodium phenylbutyrate ($\lambda=268$ nm)

- range of validity of the Lambert-Beer-law?
2.3 how to carry out an experiment

- sample weight and volume of the dissolution medium and sample weight according to calibration
- dissolution temperature according to temperature in the mouth
- recording the dissolution procedure
2.4 evaluation of the results

![Graph showing drug release over dissolution time for different drug formulations.]

- **Drug formulation 1**
- **Drug formulation 2**
- **Drug formulation 3**
- **Drug formulation 4**

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2.5 critical aspects

- evaluation: taste-masking criteria?
- method: limited application possibilities
- analytical setup vs. „true setup“
- aromatic compound?
- floating drug formulation?
3. electronic tongues

TS-5000Z
Insent Inc.
Atsugi-Shi, Japan

αAstree
Alpha MOS
Toulouse, France
3.1 measurement principle

- potentiometric, based on the Nernst law:

\[ U = U^o + \frac{R \cdot T}{z \cdot F} \cdot \ln c \]
3.1 measurement principle

modified after: Kobayashi et al, Sensors (10), 2010
3.2 calibration procedure
### 3.3 how to carry out an experiment

Does a given suspending vehicle show taste-masking properties?

<table>
<thead>
<tr>
<th>sample</th>
<th>API (mg)</th>
<th>in water (100,0 ml)</th>
<th>in suspending vehicle (100,0 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pure API (225 mg)</td>
<td>225</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>capsule content (à 225 mg pure API)</td>
<td>225</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>granules (t-m) (à 225 mg pure API)</td>
<td>225</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>'good taste'-model</td>
<td>-</td>
<td>-</td>
<td>✓</td>
</tr>
</tbody>
</table>
3.4 evaluation of the results

**univariate**: to evaluate each sensor response separately
3.4 evaluation of the results

**multivariate**: considering the combined information of all sensors
3.5 critical aspects

- Evaluation: taste-masking criteria?
- Drug formulation: solid vs. liquid?
- Analytical setup vs. "true setup"; physico-chemical properties of the analyte
- Formulation pretreatment?
- Dissolution and sampling?
3.5 critical aspect - sampling

- **in-line** dissolution profile of enalapril minitablets
3.5 critical aspect - sampling

- **off-line** dissolution profile of enalapril minitablets
- Sample volume: 100 ml

![Graph showing dissolution profile](https://via.placeholder.com/150)

results based on a students work (I. Speer, N. Hoffeins, WPP SS 2012)
conclusion

• Each method shows advantages besides disadvantages.

• Analytical assessment gains in importance – but still needs improvement

• On the basis of human data, protocols should be standardized.
Thank you for your kind attention!

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