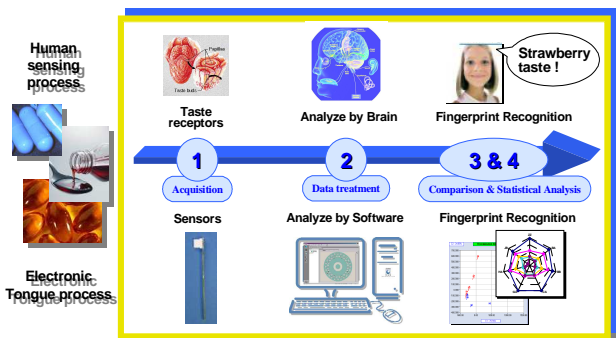


Results obtained at Alpha MOS Laboratory,
Toulouse, France

Objective

Many pharmaceutical active principles are known to have a strong bitter taste; that is why various excipients such as sweeteners and flavors are used in oral formulations in order to mask the bitterness. The objective of this study was to investigate the optimal formulation of excipients in order to achieve the best masking of active principle bitterness.

Taste Assessment of Pharmaceutical Products with ASTREE E-TONGUE



Working Principle of Electronic Tongue compared to Human Taste



Electronic Tongue Analyzer

- 1 16 or 48 position Autosampler (80 or 15 mL beakers)
- 2 Array of 7 electrochemical sensors (cross-selective & partially specific) + 1 reference electrode → potentiometric measurement
- 3 Electronic unit for acquisition & autosampler control

Method

In order to approach the optimal masking efficiency in an oral form under development, various active formulations and their corresponding placebos (same formulations without active principle) were analyzed for taste measurement and comparison. Pure water and water containing active principle were also analyzed for comparison purposes.

An experimental design was carried out in order to determine the optimal values of variable parameters and optimize API bitterness masking.

The variable parameters selected in the Central Composite Model of Experiments were:

- ▶ the concentration of sweetener (6 values between 0.2-4 mg/mL).
- ▶ the concentration of flavor (6 values in the range 0.2-2 mg/mL).
- ▶ the concentration of buffer (6 values in the range 18-50 mM).

The response observed was the distance (active formulation-placebo).

Sixteen formulations and sixteen placebos were thus prepared by blending various excipients (preservatives, sweeteners, flavors, texture agents, etc).

Experimental Conditions & Samples

Sample set

Sample designation	Description
1_A to 16_A	16 active formulations with different amounts of sweetener, flavor & buffer.
1_P to 16_P	16 corresponding placebo formulations.
Water	Pure water
Water A	Pure water + active principle

E-Tongue Analytical Conditions

Sample volume:	25 mL
Sample temperature:	ambient
Time per analysis:	180 s
Acquisition time:	120s

Taste Masking Efficiency Evaluation

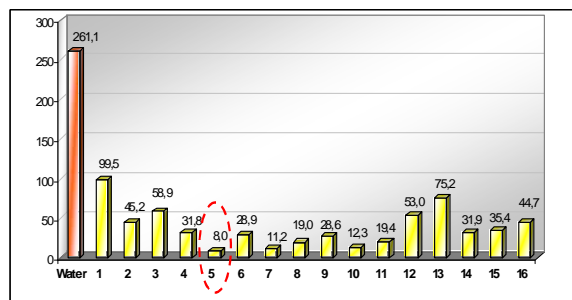


Fig.1: Distance between each formulation and its corresponding placebo

The ASTREE measurement showed a high repeatability (for all sensors measurement, the Residual Standard Deviation observed was below 1.5%).

The efficiency of the bitterness masking was evaluated by calculating the taste distance between each formulation and the corresponding placebo. The shortest the distance, the better the masking.

Based on the ASTREE Electronic Tongue measurements, the formulation that achieves the best masking of the API bitterness is formulation 5 as the distance formulation-placebo is the lowest (= 8.0).

Conclusion

An important number of candidate formulations could be investigated and their taste assessed thanks to the instrumental measurement from the ASTREE Electronic Tongue.

This demonstrates that the taste of oral forms can be significantly improved using an experimental plan to optimize ingredients quantities and an E-Tongue for rapid and testing without human safety concerns.