Use of Granulation and E-Tongue for Taste-Masking of an Orally Disintegrating Tablet (ODT)

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Introduction

Taste-masking is an essential part of solid oral dosage form development to overcome unpleasant taste of the active ingredient or excipients used in the formulation. Poor palatability can have a negative impact on patient compliance[1], especially in the case of pediatric and geriatric patients, who may also have difficulty swallowing capsules or tablets. Taste-masking improves the acceptability of the medication and enhances therapeutic outcomes by ensuring a consistent dose intake by the patient. Coating of the active molecule is an effective way to achieve taste-masking, which can also enhance overall product stability by preventing degradation of the active ingredient due to exposure to external factors such as humidity, temperature, and light. In this study, an orally disintegrating tablet (ODT) was formulated using racecadotril, an active drug used in the treatment of diarrhoea. Oral disintegration is important for fast delivery of the active and taste-masking is necessary as there is immediate disintegration of the tablet in the mouth. The composition of the formulation was developed using HyperStart C2C™, Smart Formulation Hub and included StarTab®, Directly Compressible Starch, as a key excipient to improve mouth feel. Taste-masking was achieved through coating/granulation with Opadry® EC, Ethylcellulose Organic Coating System and the efficiency of taste-masking was assessed using an E-Tongue technique.[2]

Methods

Racecadotril was granulated in a VFC-LAB 1 Fluid Bed (Vector Corporation) using Opadry EC ethanol: water (90:10) solvent-based binder solution. Samples were taken at 8 and 12% weight gain for further evaluation. To avoid rupturing, the dry granules were not subjected to a milling step. The resulting granules were mixed with mannitol, StarTab, sweetener, flavouring and magnesium stearate and compressed using a Piccola BD-EU (Riva S.A.) tableting machine, fitted with 10 mm round tooling.

The composition of ODT is shown in Table 1. The inclusion or exclusion of a flavor enhancer, neohesperidin, was evaluated during the granulation process.

Table 1: Formulation of Orally Disintegrating Tablets (ODT)

Materials	Tablet (%)	Tablet (mg)
API granulated with Opadry EC	30.0	105.0
Mannitol	44.0	154.0
StarTab	22.0	77.0
Neohesperidin (flavor enhancer)	3.0	10.5
Magnesium stearate	1.0	3.5
Total	100	350

Results

Tablets were evaluated for weight, hardness, friability, and disintegration time. Taste-masking was evaluated using E-Tongue (Impedance Analyzer-Solartron 1260, at the University of Sao Paulo, Physic Institute of Sao Carlos. Either the ODT (350 mg) or the active drug (100 mg) was diluted in 10 mL of artificial saliva and a 20 µL sample is then placed at the tip of each electrode. Electrical impedance data of frequency range of 1 Hz - 1 MHz, applying 25 mV of voltage at 20°C is measured. Method flow is shown in Figure 1.

The ODTs exhibited acceptable mouth feel and good tablet characteristics, with average tablet hardness of 4-5 kp, friability of 0.3% and disintegration time of about 7 mins.

E-Tongue taste-masking evaluation was conducted on 7 samples, results are shown in Figure 2. These techniques are basically for pattern recognition of data. In the generated graphs, each impedance spectrum is represented by a point (symbol), and distant points mean that the spectra are quite different from each other. The electrical properties of the samples under analysis are quite distinct when the corresponding data are placed apart on a Principal Component Analysis (PCA) and hierarchical clustering analysis (HCA) plot.

It should be noted that in the analyses with electronic languages the hypothesis is adopted that a difference in electrical properties is correlated with difference in taste. Therefore, an electronic language is considered to mimic the biological flavor recognition system. The taste-masking results showed that samples 4 and 6 (granulation with 12% WG Opadry EC) are the most distinct in terms of electrical properties compared to API alone.

Figure 1: Schematic Flow of E-Tongue Method

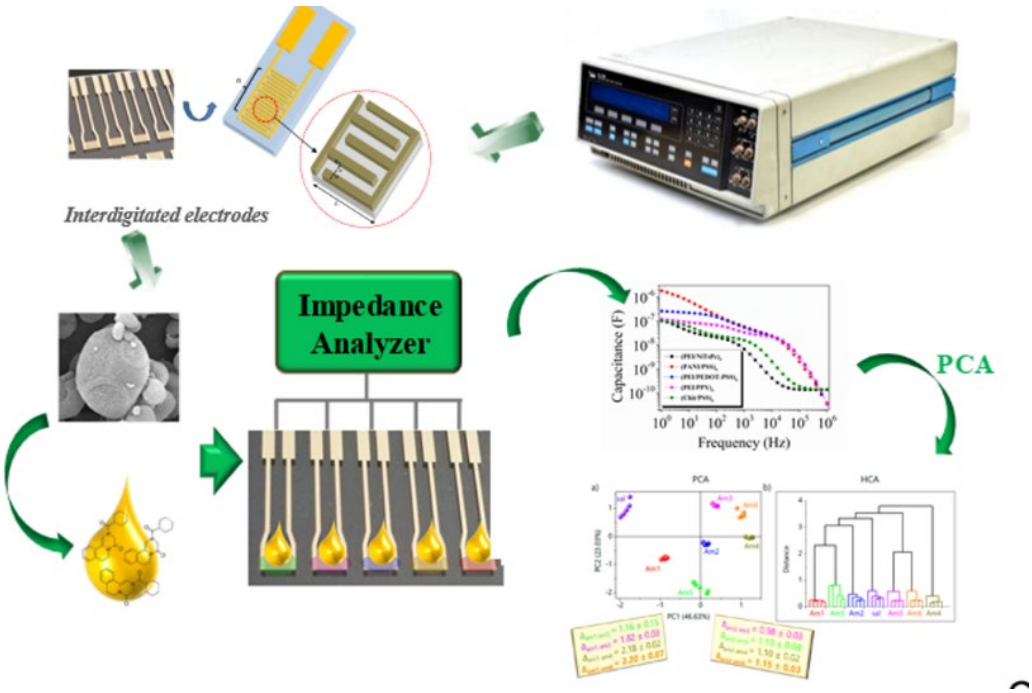
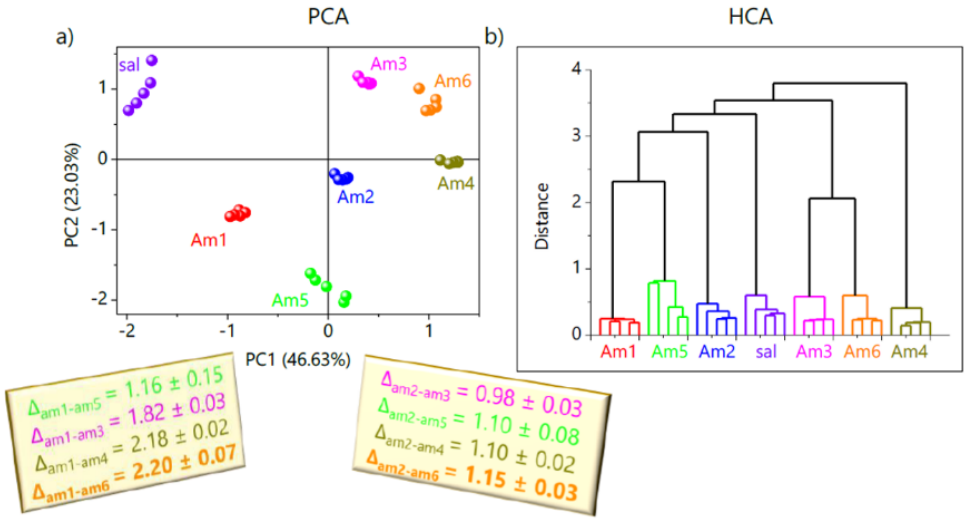


Figure 2. Results Obtained Using E-Tongue



Sample Reference

PCA = principal component analysis
HCA = analysis of hierarchical components
Am1 = API only
Am2 = Placebo
Am3 = Formula with 8% Opadry EC
Am4 = Formula with 12% Opadry EC
Am5 = Direct compression formula (Not granulation, no use of Opadry EC)
Am6 = Formula with 12% Opadry EC (with Neohesperidin)
Am7 = Artificial saliva

Conclusions

Excellent orally disintegrating tablets (ODT) were developed based on the recommended HyperStart C2C formulation, saving time on initial formula design. Use of the starch-based excipient such as StarTab may improve the mouth feel and reduce disintegration times. This work showed that use of Opadry EC in granulation at 12% WG achieved excellent taste-masking and would deliver a positive experience for patients to improve compliance. The use of neohesperidin may improve mouth feel and assist with taste-masking.

References

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