Taste Masking Coating of Mini-Tablets with Cellulose Derivatives: Formulation and Analytical Challenges

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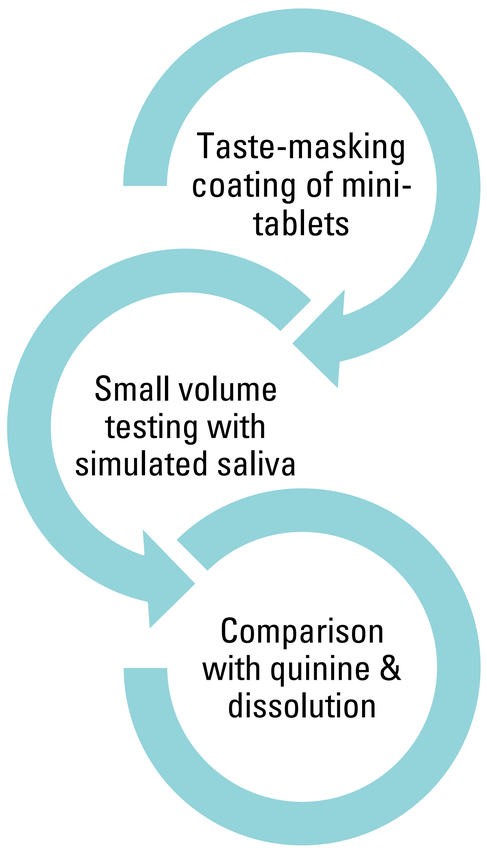
Introduction

An important step in patient compliance is palatability enhancement of drugs by improving or masking their taste. Within the methods available, covering the taste by applying a coating layer can be considered as easy to implement. However, one of the major challenges during the development of taste masking coatings is to have a fast feedback on the coating performance during the laboratory trials. We developed an easy taste-masking coating formulation and utilized a screening method to assess the masking property using low volume for dissolution testing with simulated saliva.[1-3]

Materials and Methods

Caffeine mini-tablets (round, 3 mm, 20 mg) were produced on a rotary press (Romaco Kilian Pressima). The taste-masking formulation is based on an enteric polymer (hypromellose acetate succinate: Shin-Etsu AQOAT® AS-HG) and a pore former (hypromellose: Tylopur® 606). Results were compared with a taste-masking coating premix commercially available. Mini-tablet coating was performed on a coating pan (Solidlab 1 Bosch) with the formulations given in the table. To mimic the oral cavity, the volume of dissolution media was adjusted to the amount of saliva available in the mouth (approx. 5 mL [1]) and quinine (bitter taste perception at 0.000008 M, 2.5 µg/mL) was selected as reference API concentration threshold value for successful taste masking. For low volume dissolution analysis, one coated caffeine mini-tablet was placed in the Ultra-Turrax tube drive vessel (5 mL simulated saliva pH=6.2, 400 rpm). A sample was drawn after 5 min (n=6) and analyzed in a Perkin Elmer Lambda 25 spectrometer (λ=275 nm). Regular dissolution test was carried out in an Erweka DT720 dissolution tester with UV analysis (USP, n=2x25 mini tablets, paddles, 50 rpm, 37 °C, 0.1M HCl, 900 mL, λ = 275 nm).

Study Outline

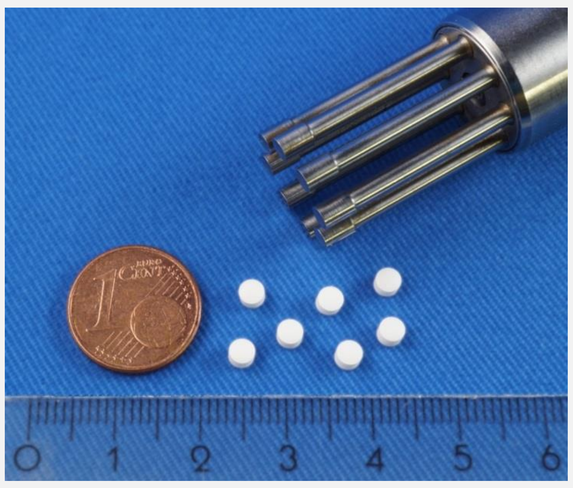


Mini-tablets Formulation / Attributes

Material	w/w [%]
Caffeine	20.0
L-HPC (NBD-021)	15.0
Lactose (Flowlac 90)	63.75
Silicon dioxide (Aerosil®)	0.25
Magnesium stearate*	1.0
Total	100.0

Attributes	
Av. Weight [mg]	19.9
Hardness [N]	42
Friability [%]	0.01
Disintegration in water 37ºC [min.]	3

* Magnesium stearate added before tableting



3 mm mini tablets and multi-tip tool

Coating Formulations / Parameters

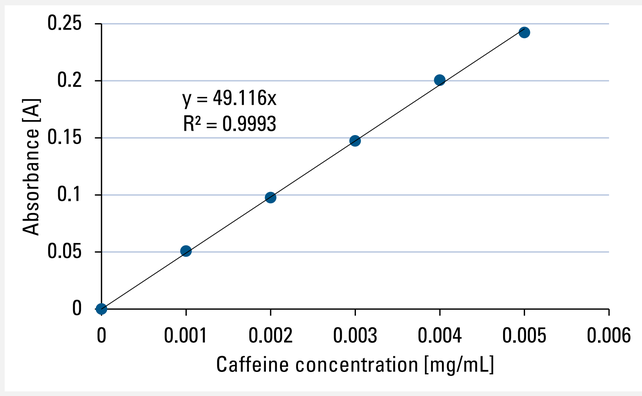
Material	Content [%]			
	F1	F2	F3	F4
HPMCAS AS-HG (Shin-Etsu AQOAT®)	6.3	3.5	0.7	-
Hypromellose (Tylopur® 606)	0.7	3.5	6.3	-
Ammonia (as NH_3)	0.08	0.045	0.009	-
Eudragit® EPO ReadyMix	-	-	-	15.0
Purified Water (H_2O)	92.92	-	92.92	85.0
Total	100.0	100.0	100.0	100.0

- F1-F3: Shin-Etsu AQOAT® AS-HG was dispersed in H_2O followed by NH_3 (removed during drying). Finally Tylopur® 606 was added.
- F4: Eudragit® EPO ReadyMix was dispersed into H_2O.

Coating Parameters	F1/F2/F3	F4
Machine	Solid lab 1 (Bosch)	
Nozzle	0.5 mm Schlick ABC	
Inlet temperature [°C]	54	52
Inlet air flow [m³/h*kg]	40	40
Spraying rate [g/min]	5.0	4.0
Core temperature [°C]	32	33
Weight gain [%]	Up to 20	

Low-Volume Dissolution: Analysis

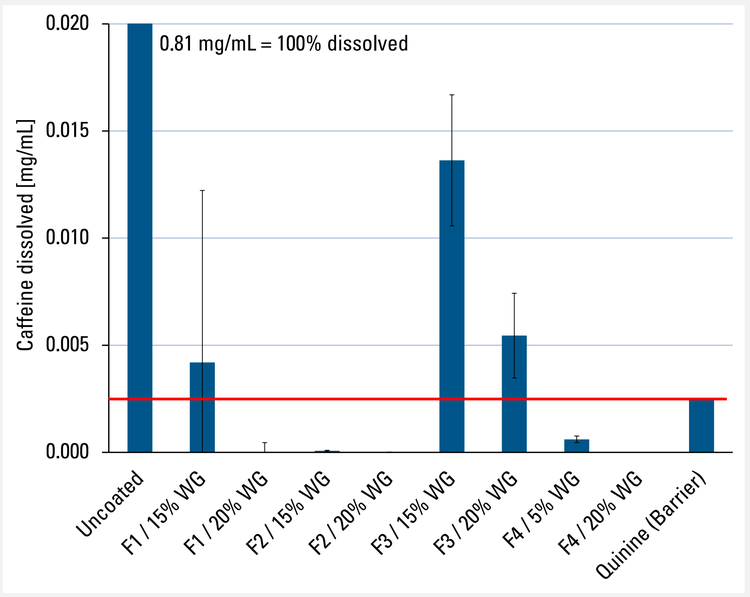
- Caffeine concentration below 2.5 µg/mL (0.0025 mg/mL) in the low volume dissolution test is considered as a successful taste-masking. Suitability of UV analysis was assessed via a calibration curve.



Calibration curve for caffeine in in simulated saliva

IKA Ultra-Turrax tube drive

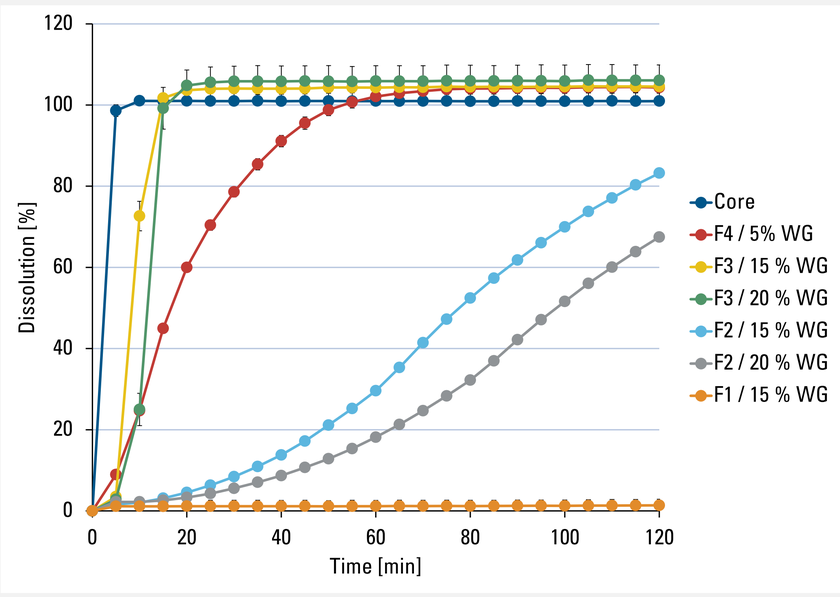
Dissolution Results



Caffeine concentration after 5 minutes low-volume dissolution test (n=6).

Low volume dissolution in simulated saliva:
- Formulations F1 and F2 minimum 15% coating weight gain (WG) needed for taste masking
- F3 slightly above defined threshold
- Taste masking achieved with 5 % coating weight gain for formulation F4

Standard dissolution in 0.1 M HCl
- F1: no dissolution observed
- F2: delayed release of API at pH=1.2
- F3: short lag time of around 5 min. then immediate dissolution
- F4: fast dissolution of the API



Dissolution profile in pH=1.2, 0.1M HCl, n=2x25 mini-tablets

Summary

- Mini-tablet coating was performed without any agglomeration issue.
- Taste masking performance of coatings could be easily assessed by UV analysis and low volume dissolution (5 mL) in simulated saliva (quinine threshold).
- Immediate release of API in gastric fluid was achieved with F3 and F4. Delayed release with F2. Enteric properties with F1.
- Shin-Etsu AQOAT® (HPMCAS AS-HG) is suitable for delayed release taste masked dosage forms with adjustable dissolution profile.

References

1. Gustafson, T., Taste masking assessment, AAPS **2017.**
2. Sona, P.S and C. Muthulingam, Formulation and Evaluation of Taste Masked Orally Disintegrating Tablets of Diclofenac Sodium, *Int J Pharmtech Res.*, **2011**, 3, 819-826.
3. Shin-Etsu technical information, **2016**, A-045/H-013, A-048/H014.