Taste Masking of Bitter-tasting Drug Particles by Fluid Bed Coating with a Sustained Release Polymer, Kollicoat® SR 30 D

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Introduction

Orally disintegration tablets (ODT) and oral suspensions are becoming increasingly popular due to patient compliance. However, the bitter taste of certain active pharmaceutical ingredients (API) presents a challenge when formulating these APIs into ODT and suspensions. Taste masking the bitter API is then critical to the success of these formulations. Some common approaches for taste masking include the use of flavoring agents and sweeteners, ion-exchange resins and drug particles coating with a pH-dependent polymer.

Alternatively, drug particles coated with a sustained release polymer, Kollicoat® SR 30 D, has also shown taste-masking effect.[1] Kollicoat® SR 30D, a 30% aqueous dispersion of Polyvinyl Acetate, is a pH-independent insoluble polymer dispersion used for sustained release coating. The coating effectively blocks the release of API to achieve the taste masking effect. To negate the sustained release effect, a water soluble polymer can be combined with Kollicoat® SR 30D in the coating. In this study, the combination of Kollicoat® SR 30D and Kollicoat® IR is evaluated for the taste-masking effect on a model bitter-tasting active, Caffeine.

Objectives

- To develop a taste-masking coating for Caffeine granules using the combination of Kollicoat® SR 30D and Kollicoat® IR. The goal is to achieve effective taste masking, and in the meantime not to slow down the Caffeine release in dissolution
- To evaluate the effects of coating levels and the amount of Kollicoat® IR on Caffeine release
- To evaluate the stability of the coated Caffeine granules

Materials

- Caffeine Anhydrous granules, 0.2 – 0.5 mm particle size, BASF (Florham Park, NJ)
- Kollicoat® SR 30D, BASF (Florham Park, NJ)
- Kollicoat® IR, BASF (Florham Park, NJ)
- Other reagents, used as received.

Methods

Caffeine granules coating

Caffeine granules (particle size range 200 – 500 µm) were coated in a Bosch Unilab fluid bed processor. Table 1 shows the typical coating condition.

Fluidize Air volume	180 m3/h
Fluidize air temperature	50 - 55°C
Exhaust air temperature	37 - 39°C
Target product temperature	38°C
Spray rate	11 – 14%
Microclimate air	0.1 bar
Atomize air	1 bar

Table 1. Coating parameters for Caffeine granules

Taste testing panel

A taste testing panel was used to evaluate the effectiveness of the taste-masking coating. The panel was asked to hold a blinded sample of 50 mg in their mouth for 30 seconds before expectoration, and then record the "bitterness" level using a numerical scale. The oral cavity was then rinsed with water three times to avoid bias. The panelists were advised to wait 10 minutes before the next sample. The numerical scale was listed in Table 2. Score "1" stands for No bitterness, while score "5" represents the same bitterness as that of the pure Caffeine. The panel was also asked to record the timing of bitterness presenting, such as "after 10 seconds, the moderate bitterness (scale 3) was tasted".

No bitterness	Slightly bitter	Moderately bitter	Strongly bitter	Same as pure Caffeine
1	2	3	4	5

Table 2. Numerical scale in taste testing

Dissolution testing

The release profile of the coated Caffeine granules was determined by Type 2 USP dissolution method. 900 ml of 0.002% Dioctyl Sulfosuccinate Sodium solution at 37°C was used as the dissolution medium. The paddle speed was at100 rpm. Caffeine concentration was determined by HPLC at the wavelength of 275 nm.

Stability studies

Coated Caffeine granules with the equivalent potency of 65mg were packaged in 4ml glass vials for stability studies. The stability samples were stored in a humidity chamber at 40°C/75% relative humidity (RH). Samples were pulled at 1 month, 2 month and 3 month intervals and evaluated for any change in the dissolution profile.

Results and Discussion

Caffeine is moderately soluble in water at room temperature (2 g/100 mL). Kollicoat® SR 30D with no soluble pore former was initially used to slow down the drug release and achieve the taste masking effect. Table 3 shows the coating formulation, where Triethyl Citrate is used as a plasticizer at 10% polymer weight.

Ingredient	%
Kollicoat® SR 30D	63.3
Triethyl Citrate	1.9
Deionized water	34.8
Total	100.0

Table 3. Kollicoat® SR 30D coating formulation for taste masking

Figure 1 shows the dissolution of Kollicoat® SR 30D coated Caffeine granules. Without a soluble polymer imbedded in the coating, the dissolution slowed when compared with uncoated Caffeine granules. Higher coating levels further reduce the Caffeine release rate.

To match the uncoated Caffeine dissolution rate while maintaining the taste masking effect, a water soluble polymer, Kollicoat® IR was added to the Kollicoat® SR 30D coating formulation to accelerate the drug release. Table 4 shows the coating formulation with various Kollicoat® SR/Kollicoat® IR ratios based on their solid content. Figures 2, 3, and 4 show the drug release profiles of caffeine granules coated with Kollicoat® SR 30D and Kollicoat® IR in the ratio of 3:1, 2:1 and 1:1, respectively. Table 5 shows the taste masking effect of each formulation at various coating levels, as assessed by the taste panel. This result shows that the higher the ratio of Kollicoat® IR in the coating, the faster the release of Caffeine. As expected, formulation with high Kollicoat® IR needs higher coating level to mask the taste.

	Kollicoat® SR/IR Solid Ratio 3:1	2:1	1:1
Kollicoat® SR 30DP		63.3	
(30% dispersion)	50.0	46.7	33.3
Kollicoat® IR	5.0	7.0	10.0
Triethyl Citrate	1.5	1.4	1.0
DI Water	43.5	44.9	55.7
Total	100.0	100.0	100.0

Table 4. Taste-masking coating formulations with various Kollicoat® SR/Kollicoat® IR ratio

% coating	Kollicoat® SR/IR Ratio 3:1	2:1	1:1
10%	NA	2	3
15%	1	2	3
20%	1	1	3
25%	1	1	2

Table 5. Panel evaluation of taste masked Caffeine granules

Stability testing

The coated caffeine granules were stable when stored at 40°C/75%RH after 3 month. Figure 5 shows selected dissolution profiles of Caffeine granules coated with Kollicoat SR/IR at 1:1 ratio. The dissolution profiles of the stability samples matched that of the initial. The taste profile remained the same.

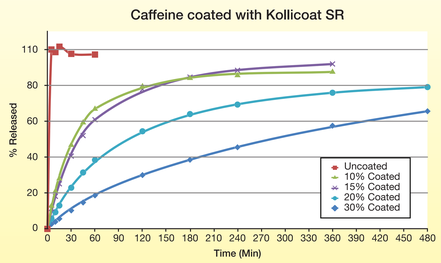

Figure 1. Dissolution profiles of Caffeine granules coated with Kollicoat® SR 30D

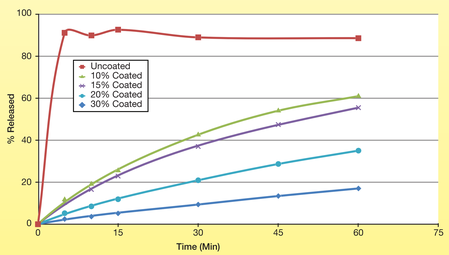

Figure 1a. First 60 minutes dissolution of Caffeine granules coated with Kollicoat® SR 30D

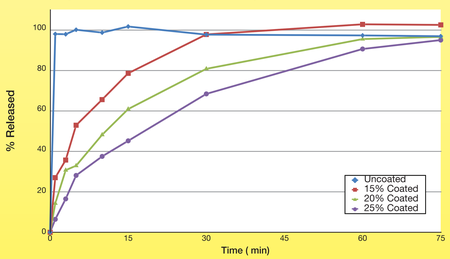

Figure 2. Dissolution of Caffeine granules coated with Kollicoat SR/IR® 3:1

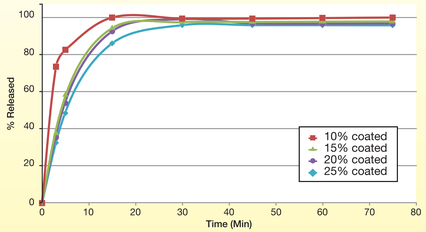

Figure 3. Dissolution of Caffeine granules coated with Kollicoat® SR/IR 2:1

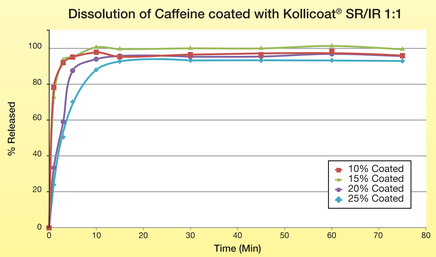

Figure 4. Dissolution of Caffeine granules coated with Kollicoat® SR/IR 1:1

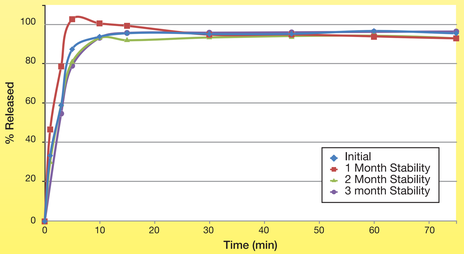

Figure 5a. Stability of Caffeine granules coated with Kollicoat® SR/IR 1:1 stored at 40°C/75%RH (20% Coated)

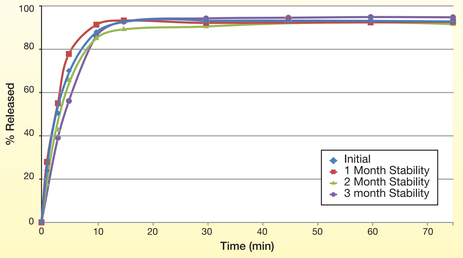

Figure 5b. Stability of Caffeine granules coated with Kollicoat® SR/IR 1:1 stored at 40°C/75%RH (25% Coated)

Conclusions

- Taste masking of Caffeine granules is achieved by coating with a combination of Kollicoat® SR 30D and Kollicoat® IR.
- Caffeine granules coated with pure Kollicoat® SR 30D showed significant slowdown in drug release.
- Optimizing the ratio of Kollicoat® SR 30D and Kollicoat® IR and the levels of the coating can achieve maximizing the taste masking effect while still maintain the same fast dissolution as the uncoated Caffeine.
- When stored at 40°C/75%RH for 3 months, the coated Caffeine granules maintained a stable dissolution profile.

References

1 Karl Kolter, An advantageous combination for taste masking: Kollicoat SR 30 D with soluble and swellable pore formers, 2000 AAPS Annual Meeting and Exposition

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