A New Taste Masking Excipient for Organic Solvent- or Water-based Film-Coating

Felicitas Guth[1], Silke Gebert[1], Monika Meller[2], Claudia Di Nunno[2], Verena Geiselhart[3],Thorsten Cech[3], and Joao Assis[4]

[1] Research and Development Pharma Solutions, BASF SE, Ludwigshafen, Germany
[2] Technical Product Pharma Solutions, BASF SE, Ludwigshafen, Germany
[3] Application Lab Pharma Ingredients & Services Europe, Pharma Solutions, BASF SE, Ludwigshafen, Germany
[4] Global Technical Marketing Pharma Solutions, BASF Corporation, Tarrytown, USA

Introduction

Taste masking

With the increasing popularity of orally dispersible tablets and the need to develop pediatric medicines, taste masking has gained significant importance in formulation development and life-cycle management.

Coating bitter drug granules, pellets, or small particles with a taste-masking film is essential for patient compliance and convenience when developing an ODT formulation.

Kollicoat® Smartseal 30 D and 100 P

Kollicoat® Smartseal (diethylaminoethyl-methacrylate and methyl- methacrylate copolymer) is an innovative film-forming polymer designed to cover unpleasant drug taste.

Due to its insolubility at neutral pH but immediate solubility at pH <5.5, efficient taste masking is combined with instant drug release in the stomach.

The polymer is available as aqueous dispersion (Kollicoat® Smartseal 30 D) and powder (Kollicoat® Smartseal 100 P). The solvent for Kollicoat® Smartseal 30 D is water and Kollicoat® Smartseal 100 P can be redispersed in water or dissolved in organic solvents [1, 2].

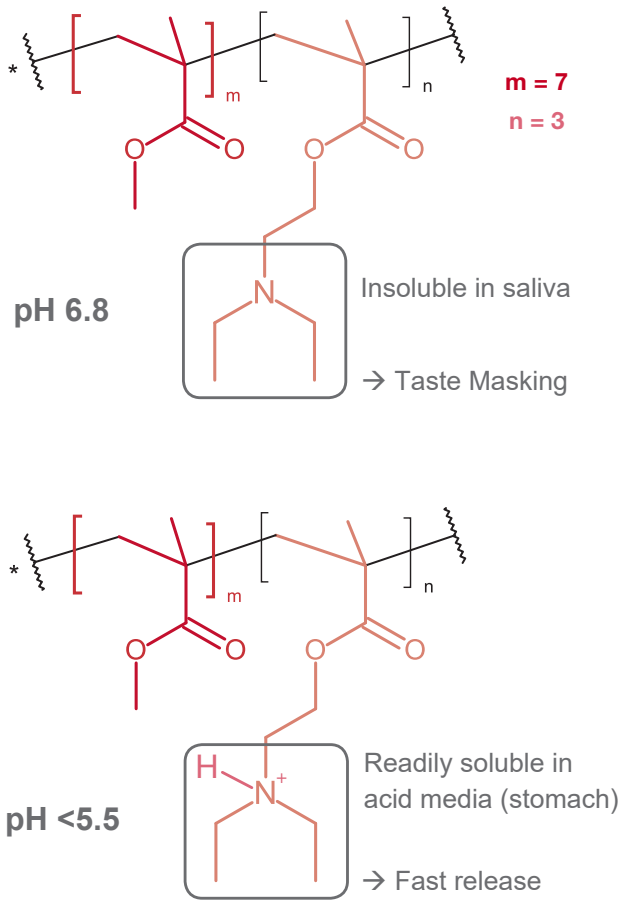


Figure 1: Structural formula of Kollicoat® Smartseal.

Methods

Reconstitution and formulation of an aqueous dispersion from Kollicoat® Smartseal 100 P

Partial neutralization of the amino functional groups with an acid is necessary to redisperse the powder.

Divalent carboxylic acids, such as succinic acid, are the most suitable ones for the amino neutralization [3]. In the case of succinic acid, 2% weight based on the amount of polymer (2 g of succinic acid per 100 g of polymer) has shown optimal results.

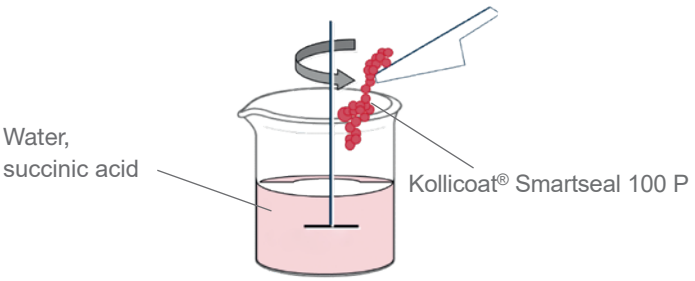


Figure 2: Preparation of Kollicoat® Smartseal 100 P in water with succinic acid.

Dissolve succinic acid in water.

Slowly add Kollicoat® Smartseal 100 P.

Gently stir for 10–15 minutes until the powder is dispersed.

Add the plasticizer, talc (optional), and antioxidant [3].

Final solids concentration: 20 %

Preparation of an organic coating suspension from Kollicoat® Smartseal 100 P

For organic solvent-based coating, the polymer can directly be dissolved in acetone. Acetone solutions can then be diluted with isopropanol up to a maximum ratio of 1:2 acetone to isopropanol.

Due to the viscosity of the organic polymer solution the recommended solids content of the final coating formulation is lower.

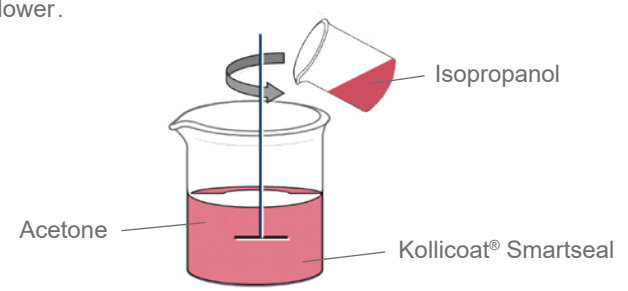


Figure 3: Preparation of an organic solution of Kollicoat® Smartseal 100 P.

Dissolve Kollicoat® Smartseal 100 P in acetone.

If needed, add isopropanol until the maximum ratio is reached.

Add the plasticizer and antioxidant to the solution.

If necessary, add (micro) talc or blend it after coating.

Final solids concentration: 10%

Experiments

Substrate: Caffeine granules (particle size 0.5–1 mm)

Equipment: Glatt, GPC G3; bottom spray (Wurster at 25 mm); nozzle diameter; 1.0 mm; batch size: 1.3 kg

Organic solvent-based coating: Inlet air temperature: 25–43° C; inlet air volume speed: 78–110 m³/h; spray rate: 16–20 g/min; product temperature: 25–35°C

Aqueous coating: Inlet air temperature 55°C; Inlet air volume speed: 88–100 m³/h; product temperature 31–35°C; spray rate: 16–19 g/min; final drying until 45°C product temperature

Dissolution: USP Type II; paddle speed: 50 rpm; 37°C in 900 mL phosphate buffer pH 5.5 & pH 6.8, as well as 0.08 N HCl pH 1.1

Talc was used to reduce tackiness: 6% talc were added to aqueous formulations; 1% micro talc was applied in a post-coating blending step after organic solvent-based coating.

Aqueous coating

Table 1a: Kollicoat® Smartseal 100 P formulation for aqueous coating.

Ingredient	Content
Kollicoat® Smartseal 100 P	12.4%
Succinic acid (2% related to polymer)	0.25%
Butylhydroxytoluene (BHT) (2.5% related to polymer)	0.30%
Acetyl tributyl citrate (ATBC) (10% related to polymer)	1.24%
Talc	6%
Water	79.8%
Total:	**100%**
Solids concentration	20%
Weight gain	15%, 20%, 25% & 30%
Curing	4 h @ 60°C

Organic solvent-based coating

Table 1b: Kollicoat® Smartseal 100 P formulation for organic solvent-based coating.

Ingredient	Content
Kollicoat® Smartseal 100 P	8.89%
Butylhydroxytoluene (BHT) (2.5% related to polymer)	0.22%
Acetyl tributyl citrate (ATBC) (10% related to polymer)	0.89%
Isopropanol	45%
Acetone	45%
Total:	**100%**
Solids concentration	10%
Weight gain	15%, 20%, 25% & 30%
Post-coating blending	1% micro talc

Results

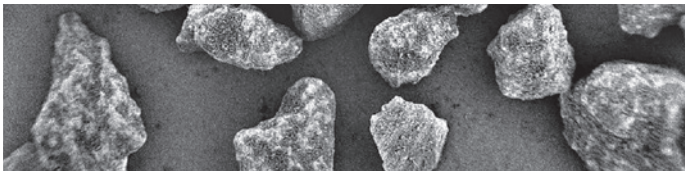
Drug release resistance in phosphate buffer (pH 6.8) was used to measure the taste-masking functionality. Coating levels between 20% and 25% weight gain showed a good level of drug release resistance (low drug release) that should correlate with an acceptable taste-masking effect for caffeine granules (Figures 5 and 6).

The impact of curing (4 h, 60°C) was evaluated for water-based formulations: Release profiles in phosphate buffer for cured and uncured coated particles were comparable (Figure 5). Curing might be needed to ensure complete coalescence of the polymer particles from aqueous dispersions but is generally not required when Kollicoat® Smartseal 100 P is applied as an organic solution because the polymer is solubilized.

Organic solvent-based film coatings provided stronger resistance at the same weight gain percentage compared to water-based formulations of Kollicoat® Smartseal 100 P (Figures 5 & 6). As talc was used for aqueous formulations, the net polymer content at a certain weight gain was lower. In addition, partial neutralization renders the polymer slightly more soluble.

Even at coating levels of 25% and 30% weight gain, the active ingredient dissolved quickly and completely in the acidic environment as well as intermediate pH 5.5 (Figure 7).

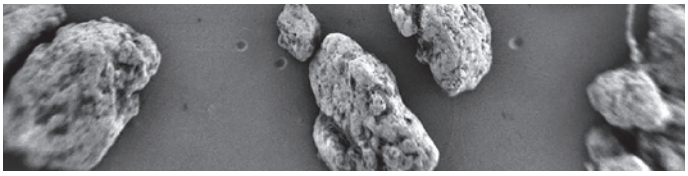
Substrate: Caffeine granules (uncoated)



4a

1 mm

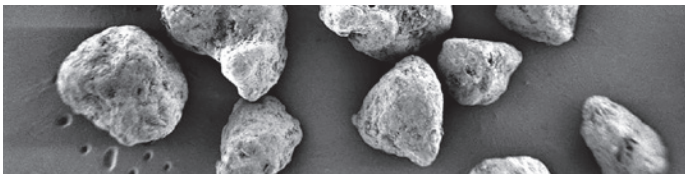
Coated granules organic (25% weight gain)



4b

1 mm

Coated granules aqueous (25% weight gain)



4c

1 mm

Figure 4: SEM pictures of uncoated caffeine granules (4a), coated with 25% weight gain by organic solvent-based (4b), and coated with 25% weight gain by the aqueous coating with succinic acid (4c).

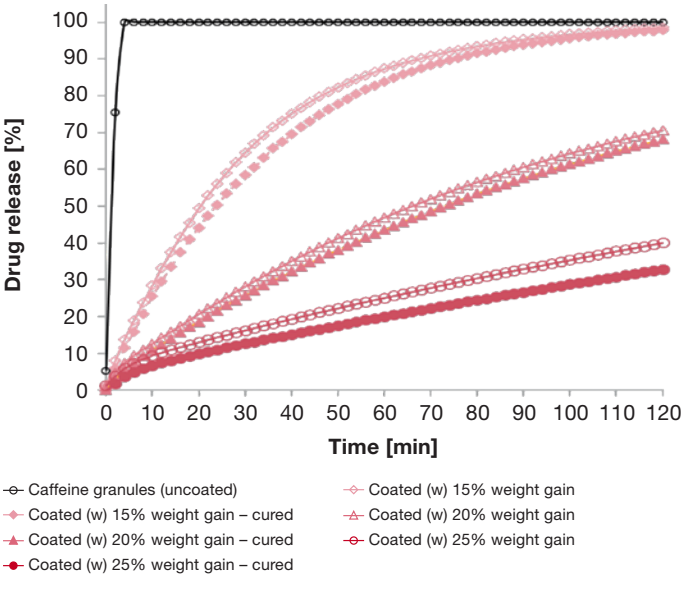


Figure 5: Aqueous coating (w): Dissolution at pH 6.8 with increasing weight gain and in dependency of curing.

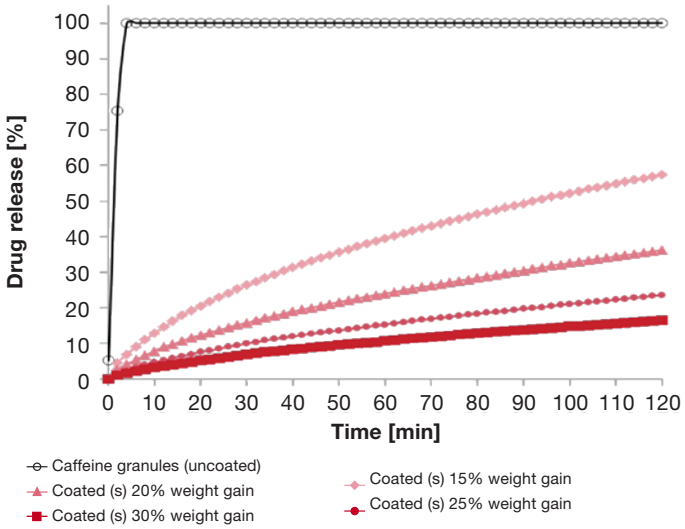


Figure 6: Organic solvent-based coating (s): Dissolution at pH 6.8 with increas-ing weight gain.

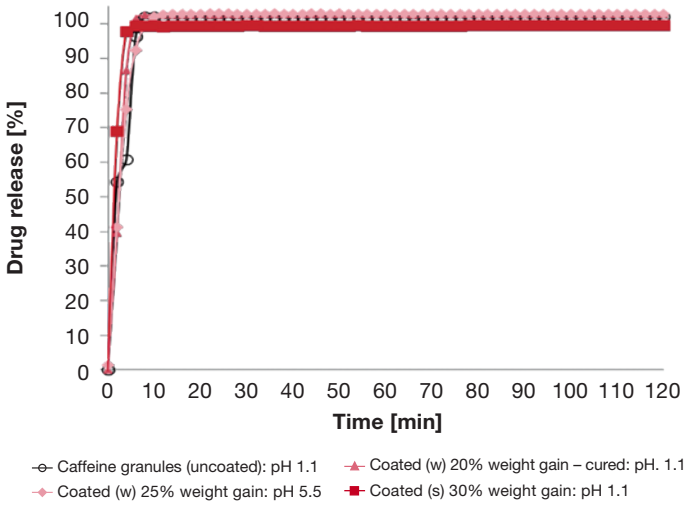


Figure 7: Organic solvent-based (s) and aqueous coating (w): Quick and complete drug release at pH 1.1 and pH 5.5.

Conclusions

Kollicoat® Smartseal 100 P is a powder grade complementing Kollicoat® Smartseal 30 D.

Kollicoat® Smartseal 100 P provides effective taste masking and it is suitable for aqueous and organic solvent-based coating.

Organic solvent-based coating with Kollicoat® Smartseal 100 P is particularly advantageous when taste masking needs to be achieved with lower coating levels.

References

[1] Kolter, K. et al.: Effective taste masking based on the new coating dispersion Kollicoat® Smartseal 30 D. 38th Annual Meeting and Exposition of the Controlled Release Society, National Harbor, USA, 2011.

[2] Guth, F. et al.: A new excipient for taste masking at low coating levels. AAPS, Annual Meeting and Exposition, Washington, USA, 2018.

[3] Kollicoat® Smartseal 30 D. Technical Information. BASF SE, 2019.

Kollicoat® Smartseal 30 D

Kollicoat® Smartseal 100 P

BASF's functional polymer for taste masking is available as an aqueous dispersion and free flowing powder.

- ✓ Unparalleled taste masking
- ✓ Fast release of active ingredients
- ✓ Effective sealing against moisture
- ✓ Easy and economical film coating
- ✓ Optimal coating polymer for ODT formulations, pellets and particles

Meet your Virtual Pharma Assistants!

ZoomLab™, **RegXcellence®**, and **MyProductWorld**,
your interactive guides for optimizing drug formulations, navigating quality and regulatory compliance, and
browsing ingredients.

Learn more and sign up at **https://virtualpharmaassistants.basf.com**

Inspiring Medicines for Better Lives

For more information visit us on
www.pharma.basf.com

For sample requests
pharma.basf.com/request-a-sample

BASF
We create chemistry