Investigating the influence of the core formulation on the gastric resistant functionality of a solid oral dosage form coated with a Kollicoat® MAE 30 DP based coat

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INTRODUCTION

Developing a gastric resistant coating formulation can be quite demanding. There are a lot of interactions between polymer and active ingredient or non-functional excipients which have to be heeded [1, 2].

Even if all incompatibilities could be eliminated, the disintegration characteristics of the core might interfere with the coating functionality. This work was set to investigate the influence of the core formulation on the functionality of the applied coat based on poly(methacrylic acid-co-ethyl acrylate) (MAE).

MATERIALS AND METHODS

Materials

As gastric resistant film forming polymer, Kollicoat® MAE 30 DP (BASF) in combination with the plasticiser triethyl citrate (TEC) (Jungbunzlauer) was chosen.

As subcoat, a Kollicoat® IR (BASF) based instant release coat was applied.

The following components were used for the core formulations: Aspirin™ (Selectchemie); Caffeine gran. 0.2–0.5 (Siegfried), Ludipress® LCE, Kollidon® CL (all BASF); Avicel® PH-102, Ac-Di-Sol® (both FMC BioPolymers); Primojel® (DMV-Fonterra Excipients); Aerosil® 200 (Evonik); stearic acid (Merck) and magnesium stearate (Baerlocher).

Formulations

Two core formulations with two different actives were tested in this investigation: caffeine (Table 1) and Aspirin™ (Table 2).

Table 1.
Composition of the caffeine cores.

Excipient	Content [%] # 1	# 2	# 3	# 4
Caffeine	15.5	15.5	15.5	15.5
Avicel® PH102	79.0	79.0	-	-
Ludipress® LCE	-	-	79.0	79.0
Ac-Di-Sol®	5.0	-	5.0	-
Kollidon® CL	-	5.0	-	5.0
Mg-stearate	0.5	0.5	0.5	0.5

Table 2.
Composition of the aspirin cores.

Excipient	Content [%]
Aspirin™	65.0
Avicel® PH102	26.0
Primojel®	5.0
Aerosil® 200	1.0
Stearic acid	3.0

As functional coating formulation MAE containing 15% of TEC was applied. In the case of the Aspirin™ formulation, a sub-coat based on Kollicoat® IR was applied with a weight gain of 3.5%.

Coating process

As coating equipment, the XL Lab 01 (Manesty) was used. The coater was assembled with the mid-sized drum (diameter 480 mm). As nozzle, the OptiCoat gun with a orifice of 0.8 mm was used.

Round-shaped tablets with a diameter of 8.0 mm (caffeine) and 11.0 mm (Aspirin™) were coated according to schema (Table 3).

Table 3.
Set-up coating trials.

	Sub-coat	Top-coat
Batch size	4.0 kg	4.0 kg
Drum speed	12 rpm	12 rpm
Inlet air temperature	65°C	55°C
Inlet air quantity	450 m³/h	450 m³/h
Spray rate	13 g/min	13 g/min
Atomising pressure	1.8 bar	1.8 bar
Pattern air pressure	1.8 bar	1.8 bar

MAE was applied with different coating levels.

Dissolution testing

The dissolution test (n=3) was conducted for the first 2 hours at pH 1.1 (HCl, 0.08 mol/L; volume 880 mL) and 37°C (±1 K). A paddle speed of 50 rpm was set. By adding 20 mL of a concentrated sodium phosphate buffer system, the pH value was adjusted to 6.8 for an additional 60 minutes time. The drug release was determined photometrically via online measuring.

RESULTS AND DISCUSSION

A tablet could deliver instant release functionality, even though it is coated with a functional polymer such as MAE (Figure 1). Reason for that is the core formulation. Formulations containing high amounts of microcrystalline cellulose (MCC) or high quantities of disintegrant attract so much water in such a short time that the functional coat cracks. Typically, this leads to an instant drug release. By choosing the excipients properly, trouble during the dissolution testing can be prevented.

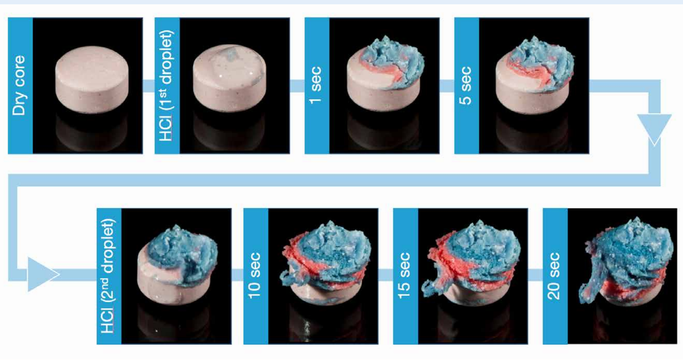

Figure 1.
Disintegration of a tablet coated with MAE, after exposure to a droplet of acid.

The described effect very much depended on the core formulation, though. MCC for instance was attracting much more water than the lactose based Ludipress® LCE. But the disintegrant used in the formulation also played a decisive role (Figure 2-Figure 5).

Figure 2.
Core of formulation #1 exposed to a droplet of acid.

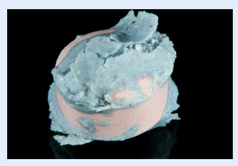

Figure 3.
Core of formulation #2 exposed to a droplet of acid.

Figure 4.
Core of formulation #3 exposed to a droplet of acid.

Figure 5.
Core of formulation #4 exposed to a droplet of acid.

Similar results could be found in the dissolution testing. No functionality could be achieved for the MCC based core, even at high coating levels (Figure 6). Much better was the performance of the lactose based core (Figure 7).

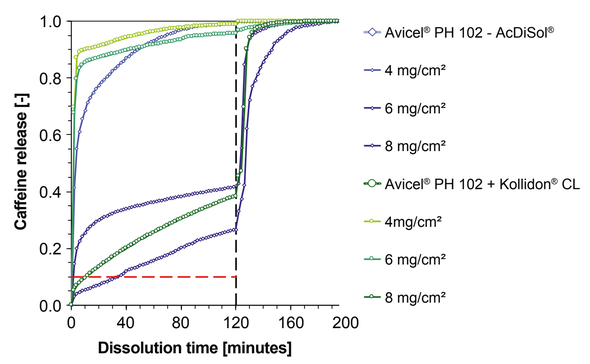

Figure 6.
Dissolution profiles of formulation #1 and #2.

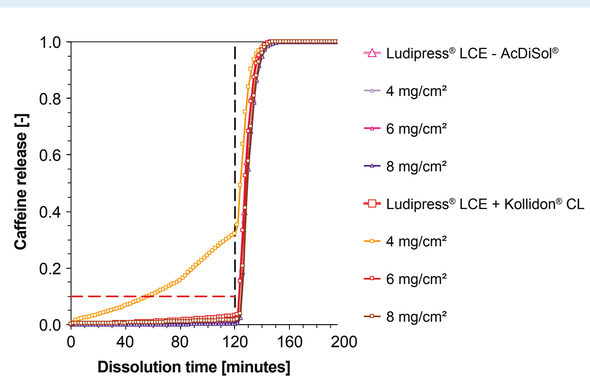

Figure 7.
Dissolution profiles of formulation #3 and #4.

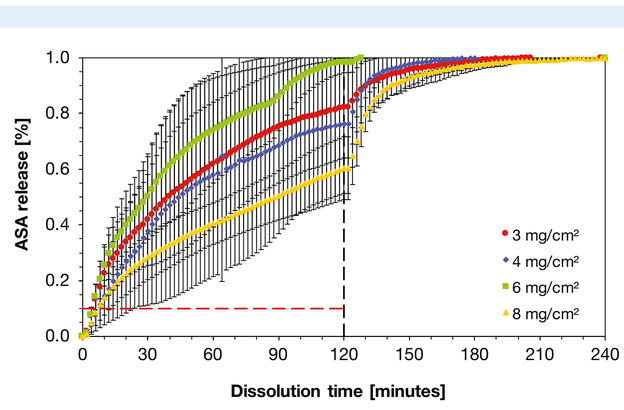

Figure 8.
Dissolution profiles of the Aspirin™ formulation without sub-coat.

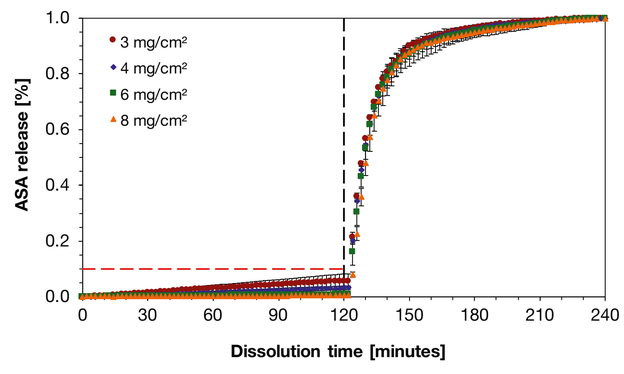

Figure 9.
Dissolution profiles of the Aspirin™ formulation with sub-coat.

Unfortunately, it is sometimes impossible to reformulate the core to meet all required features. The MCC-based Aspirin™ formulation for instance presented an instant drug release as well (Figure 8). Yet, without reformulation, the desired release profile could be achieved via the application of an instant release sub-coat (Figure 9). This second coating layer reduced the permeation speed of water into the core, which allowed the MAE layer to take-up water as well. This water was acting as an additional plasticiser resulting in a more elastic film. Eventually, swelling of the core was still observed, yet the gained elasticity prevented cracks in the functional coat.

CONCLUSION

The core formulation markedly influences the functionality of a gastric resistant coat. A high water up-take of the core leads to an increase in volume which in turn cause cracks in the functional coat, followed by an instant drug release. A high risk comes with fillers such as MCC which attract huge amounts of water. Advantageous are lactose based core formulations.

The application of an instant release sub-coat was also found to be an appropriate method to prevent an early drug release. This delays the water permeation allowing MAE to take-up water which acts as an additional plasticiser.

REFERENCES

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[2] K. Mäder, K. Bräunig, K. Kolter, K. Meyer; Development and stability of enteric omeprazole formulations based on Kollicoat® MAE polymers; 32nd CRS; June 18 – 22, 2005; Miami (FL), U.S.A.

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