Kollicoat® MAE: comparing the three different grades regarding preparation and functionality features in enteric release film-coating applications

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INTRODUCTION

Various active pharmaceutical ingredients (APIs) are either aggressive to the stomach's mucosa or vulnerable to the acidic nature of the gastric juice. Solid oral dosage forms carrying one of these APIs thence require gastric resistant functionality to prevent drug liberation and acid up-take in the stomach. In order to introduce this release pattern to a formulation, poly(methacrylic acid-co-ethyl acrylate) based film-coating formulations are most frequently applied [1].

Poly(methacrylic acid-co-ethyl acrylate) [MAE] is available in three different grades: as aqueous dispersion, and as spray dried non-neutralised material, and partially (6 mol%) neutralised powder. The latter grades allow coating formulations based on organic solvents. However, both powders are typically redispersed in water for processing, due to higher solid matter contents possible with aqueous based formulations.

The aim of this study was to compare the three different polymer grades in regard to their individual handling during preparation of their aqueous film-coating dispersion, and their respective application and functionality features.

MATERIALS AND METHODS

Proton-pump inhibitors are known to require enteric release coatings, due to their sensitivity to acid. Therefore, pantoprazole (prone to degradation when exposed to acid) was selected as model active pharmaceutical ingredient. Round shaped tablets (Ø=9.0 mm), containing 40 mg API (Formulation Table 1) were produced, using a rotary press (XL 100, Korsch).

In order to prevent interactions in-between API and the carboxylic acid groups of the functional polymer (MAE), an instant release sub-coat based on poly(vinyl alcohol)-poly(ethylene glycol) graft copolymer (Kollicoat® IR, BASF) was sprayed onto the tablets. Subsequently, the enteric release top-coat was applied based on one of the three products investigated in this study: methacrylic acid – ethyl acrylate copolymer (1:1) dispersion 30 per cent (Kollicoat® MAE 30 DP, BASF), methacrylic acid – ethyl acrylate copolymer (1:1) type A (Kollicoat® MAE 100-55, BASF), and methacrylic acid – ethyl acrylate copolymer (1:1) type B (Kollicoat® MAE 100 P, BASF).

All formulations were prepared as aqueous dispersions, holding a solid matter content of 20% and being plasticised with triethyl citrate (TEC), added in a concentration of 10% (based on the polymer) [2].

All coating trials were conducted in a side vented pan coater (XL Lab 01, BOSCH Manesty) equipped with one OptiCoat nozzle (further details Table 2).

Table 1.
Ingredients and content of tablet formulation.

Ingredient	Functionality	Brand name (source)	Content
Pantoprazole sodium hydrate	API	(Glenham Life Science)	12.12%
Co-processed lactose	Filler	Ludipress® LCE (BASF)	76.88%
Copovidone	Dry binder	Kollidon® VA 64 Fine (BASF)	5.00%
Crospovidone	Disintegrant	Kollidon® CL (BASF)	5.00%
Magnesium stearate	Lubricant	MG Siel 1 (Bärlocher)	1.00%

Table 2.
Process settings for application of sub- and top-coat.

Parameter	Settings sub-coat	Settings top-coat
Nozzle orifice	1.2 mm	0.8 mm
Drum diameter	610 mm	406 mm
Drum speed	7 rpm	12 rpm
Batch size	20.0 kg	2.5 kg
Inlet air quantity	400 m³/h	300 m³/h
Process air temperature	55°C	55°C
Spray rate	27 g/min	10 g/min
AA/PA pressure	1.2 bar/1.2 bar	1.0 bar/1.0 bar
Product temperature	39°C	42°C

RESULTS AND DISCUSSION

Dispersing water insoluble particles in a liquid leads to structure viscose flow characteristics. Consequently, one needs to appreciate a reading error when applying standard rotational rheological measurements to determine dynamic viscosity. Nevertheless, the method was suitable to investigate the differences in the preparation characteristics of the three Kollicoat® MAE products.

The aqueous dispersion could directly be diluted and mixed with the plasticiser TEC. The spray dried product needed to be partly neutralised (4 to 6 mol% of the carboxylic acid groups) to allow its readily re-dispersion in aqueous media. Sodium hydroxide or ammonia could be used for this purpose. The partially neutralised powder allowed its re-dispersion without further additives. However, due to its partially neutralised, dynamic viscosity increased, before it levelled off in the same range as the other two products (Figure 1).

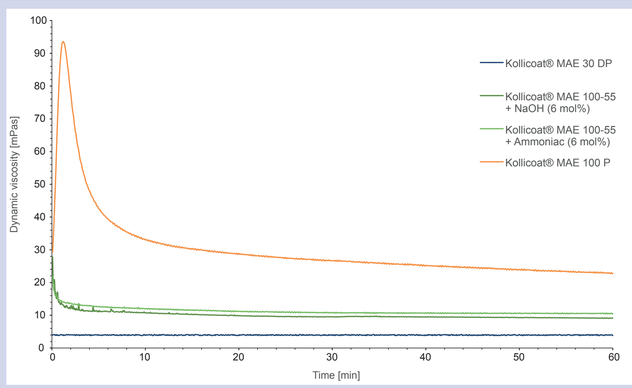

Figure 1. Dynamic viscosity as function of time.

The resulting mobility (or zeta-potential) of all three dispersions was very identical. This suggested that all products offered quite similar stability in regard to shear stress, additives or changes in the pH-value (Figure 2).

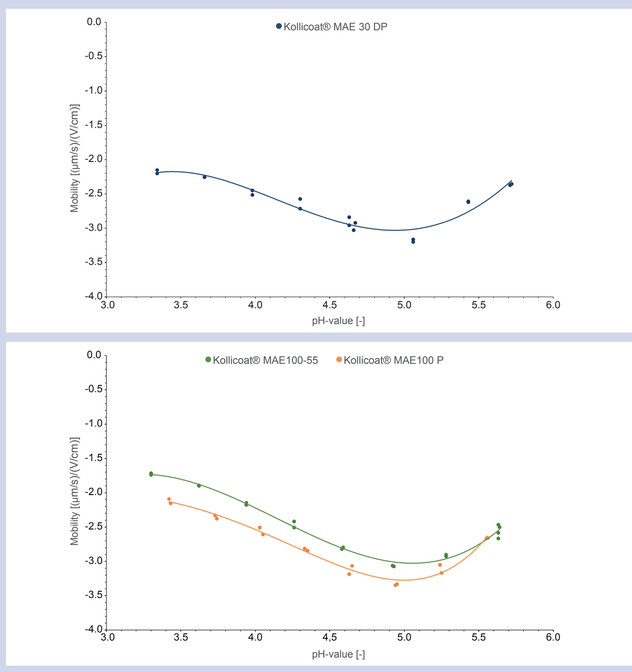

Figure 2. Mobility (zeta-potential) as function of pH-value.

The overall preparation time was roughly the same for all formulations. Even though, the powders needed to be re-dispersed, the limiting factor was the generally recommended 2 hours' incorporation time of the plasticiser.

All three formulations showed the same processing characteristics. A coating level of about 3 mg/cm² resulted in a sealed core, not allowing any API liberation in 2 hours' dissolution testing in artificial gastric juice. However, partial neutralisation of the carboxylic acid groups improved the solubility of the polymer, allowing a quicker dissolution at pH 6.8 (Figure 3).

In order to meet the additional requirement of preventing acid up-take during the residence time in artificial gastric juice, higher coating levels were required. The formulation based on the dispersion merely needed 5 mg/cm² whereas the higher permeability of the partly neutralised products led to a required coating level of 8 mg/cm² for these formulations (Figure 4).

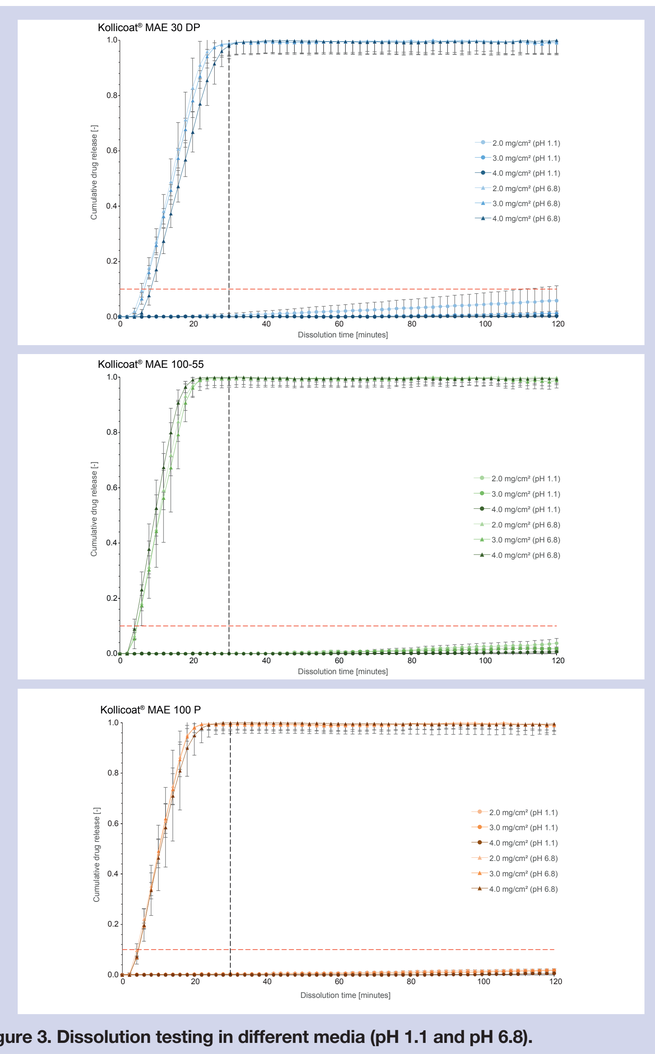

Figure 3. Dissolution testing in different media (pH 1.1 and pH 6.8).

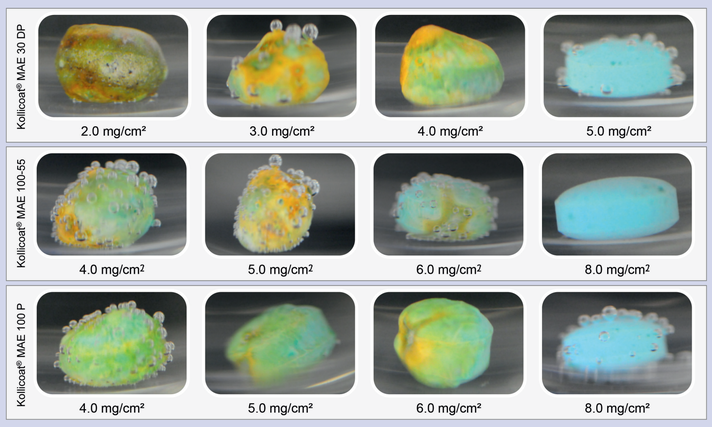

Figure 4. Tablets after 2 hours' dissolution testing (pH 1.1) – blue colour: sub-coat, yellow colour: degradated API.

CONCLUSION

The different physico-chemical properties of the three poly (methacrylic acid-co-ethyl acrylate) grades impacted the preparation procedure of the dispersions. However, all three aqueous dispersions were alike in their processing characteristics. A coating level of 3 mg/cm² was required to prevent drug liberation during dissolution testing in artificial gastric juice. A higher coating level was needed to additionally prevent acid up-take during that time, though.

The required partial neutralisation (for re-dispersion in aqueous media) of the powder grades improved the solubility of the polymer. As a result, drug release was faster at pH 6.8 and acid permeation was increased. In order to prevent acid up-take, a coating level of 8 mg/cm² instead of 5 mg/cm² was required.

REFERENCES

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