Taste Masking of Drug Layered Pellets with Kollicoat® Smartseal 100P

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PURPOSE

Taste-masking has proven to be a useful technique to improve patient compliance of oral dosages having bitter actives, especially for pediatric and geriatric products [1]. Kollicoat® Smartseal 100P, a spray dried powder of methyl methacrylate-diethylaminoethyl methacrylate copolymer is an excellent coating polymer for taste masking as it is insoluble in saliva (pH 6.8-7.2) and dissolves quickly in the stomach (pH < 5.5) [2]. Highly soluble drugs when coated can generate high osmotic pressure, resulting in a high concentration gradient across the coating layer and accelerating the drug release. This causes challenges for taste masking of water-soluble actives [3]. In this study, the purpose is to evaluate the taste masking effect of Kollicoat® Smartseal 100P by using diphenhydramine HCl (DPH), a highly water-soluble drug with strong bitter taste as a model drug.

METHOD(S)

DPH and Kollicoat® IR (binder) were dissolved in water and layered onto microcrystalline cellulose (Glattair Cellets 200) pellets. Kollicoat® Smartseal 100P coating suspension was prepared by mixing the polymer powder with succinic acid, acetylbutyl citrate (ATBC), butylated hydroxytoluene (BHT) and talc in water. The formulation is shown in Table 1.

Table 1. Formulation of the coating dispersion

Ingredient	Content
Killicoat® Smartseal 100P	10.2%
Succinic acid (SA)	0.2%
Acetylbutyl citrate (ATBC)	1.6%
Butylated hydroxytoluene (BHT)	0.3%
Talc	8%
Water	79.7%
Total	100%

The coating processes of both drug layering and taste masking were conducted in a Hüttlin Solid Lab 1 fluid bed using a bottom-spray. The parameters for the drug layering and coating are shown in Table 2.

Table 2. Parameters of the drug layering and coating

Parameters	Values
Air flow (m^3/h)	15 - 20
Feed rate	8% - 10%
Inlet T (°C)	50 - 60
Outlet T (°C)	30 - 40
Bed T (°C)	35 - 45
Atomizing air pressure (bar)	0.25 – 0.35
Nozzle sweeping air (bar)	0.25 – 0.35

Pellet samples coated with Kollicoat® Smartseal 100P at weight gains of 10%, 20%, 30% and 40% (w/w) were collected. Samples were cured at 60 °C for two hours.

Scanning Electron Microscopic (SEM) images were captured using a Carl Zeiss EVO MA-15 Variable-Pressure Scanning Electron Microscope. Images were acquired in both secondary electron imaging (SEI) and backscattered electron imaging (BSE) modes. Energy dispersive X-ray spectroscopy (EDS) was performed using dual Bruker Xflash 6/30 X-ray Spectrometers. Dissolution studies were conducted using a USP apparatus 2 (paddle) in 900 mL pH 6.8 PBS (0.1M) or pH 1.0 HCl (0.1M) at 50 rpm and 37°C. The real-time drug release was recorded by a UV detector at 258 nm.

RESULT(S)

Figure 1 shows the SEM images of cured DPH-layered pellets coated with Kollicoat® Smartseal 100P at a coating level of 40%. Under the BSE imaging mode, the surface shows a structure with many inorganic talc particles, while under the SEI imaging mode, the surface appears smooth and dense. From the magnified images (Figure 1E and 1F), the dense structure is more evident.

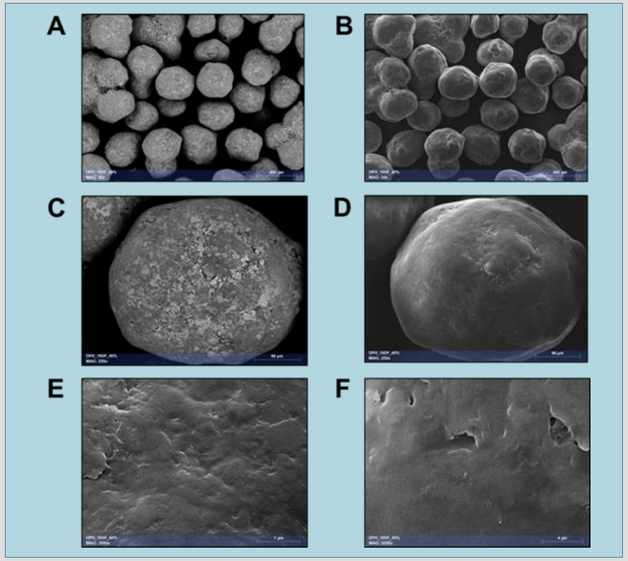

Figure 1. *SEM images of DPH-layered pellets coated with Kollicoat® Smartseal 100P at the coating level of 40% (cured) using BSE (A, C, E) and SEI (B, D, F) imaging modes.*

The pellets with a 40% coating weight gain were embedded in carbon and the cross-sectional structure was investigated. Figure 2 shows that the coating (drug layer and taste masking layer) has a thickness ranging from 20 to 35 µm with an average thickness of ~25 µm (Figure 2A and 2B). The X-ray element dot maps in Figure 2C-2G show that the oxygen and carbon rich areas are in the MCC core (Figure 2C and 2D) and the magnesium, silicon, and chlorine are mainly located in the shell. The element mapping overlay in Figure 2H further confirms the core-shell structure.

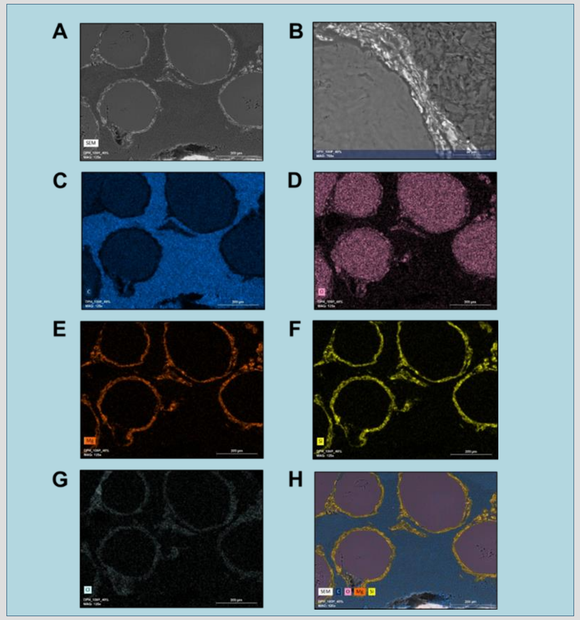

Figure 2. *DPH-layered pellets coated with Kollicoat® Smartseal 100P at the coating level of 40%. VP-BSE images of microtomed cross-sections of pellets embedded in carbon element (A and B) and X-ray dot maps of element carbon (C), oxygen (D), magnesium (E), silicon (F), chlorine (G) and overlay (H).*

The drug dissolution of the coated samples is shown in Figure 3. It is seen that higher coating levels of Kollicoat® Smartseal 100P result in longer delayed drug dissolution time in PBS (pH 6.8). 10% drug release was observed in the first ~ 3 min from the sample with a 40 % coating weight gain. Due to the presence of tertiary amino groups, Kollicoat® Smartseal 100P dissolves in acidic conditions, leading to instant release in HCl solution (pH 1.0). Curing of the coated pellets can increase the film density, resulting in delayed drug dissolution, thus enhancing the taste-masking effect and duration (Figure 3) [2].

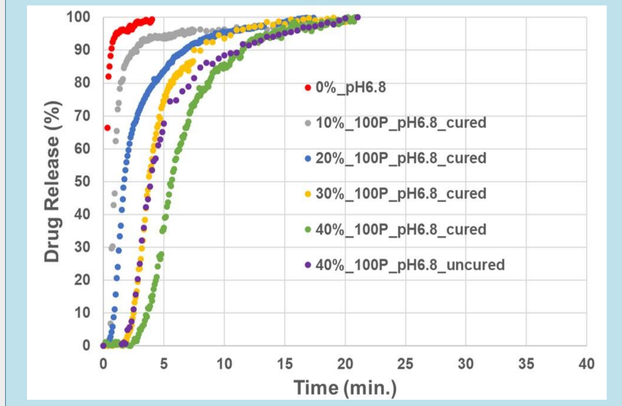

Figure 3. *Dissolution of DPH-layered pellets coated with Kollicoat® Smartseal 100P of various coating levels and formulations.*

CONCLUSION(S)

- DPH layered pellets were coated with Kollicoat® Smartseal 100P and the bitterness of DPH was successfully masked for at least ~3 min
- Taste masking effect can be adjusted by controlling the coating level
- The taste masked pellets can be further used to prepare orally disintegrating tablets, sachets or oral suspensions.

REFERENCE

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2. S Chalamur, K Kathala, Y Tu, N Langley, J Zhang, Y Lan; Dry powder coating of a novel polymer for taste masking, AAPS 2019, San Antonio TX, USA.
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