

Investigation of Taste Masking Performance of an Aqueous Ethylcellulose Dispersion (Surelease®) on Acetaminophen Granules

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Purpose

There is a significant interest in the development of taste masked formulations, especially ones that consist of pediatric approved ingredients. The purpose of this work is to evaluate the use of Surelease, a barrier membrane coating formulation with pediatric precedence of use, on taste masking of acetaminophen (APAP) immediate release granules.

Methods

Materials

APAP granules (Compap PVP3, Mallinckrodt, USA), Surelease®, aqueous ethylcellulose dispersion, E-7-19040 and hypromellose-based Opadry®, complete film coating system, Colorcon, Inc., USA) were used.

Dispersion

Coating formulations consisting of Surelease and a hypromellose-based Opadry pore former at ratios of 85:15 and 80:20 were prepared by dispersing the Opadry in deionized water and then adding to Surelease to obtain a total solid content of 12% w/w.

Fluidized Bed Processing

Trials were performed in a fluidized bed (GCPC-3 Glatt Air Techniques, USA) configured for top spray coating. Fine particles were removed from the APAP granules by elutriation while fluidizing the powders at 20 CFM for 5 minutes. This was performed to minimize the potential for inclusion of fines into the taste masking coating. APAP granules were coated up to 30% weight gain with the Surelease:Opadry coating formulations. Coating conditions are shown in Table 1. A portion of coated APAP granules were heated at 60°C in an oven (OV-510A-2, Blue M Electric Company, IL, USA) for 1 hour.

Table 1. Process Parameters for Fluidized Bed Coating

Parameter	Values
Batch Size (kg)	2.0
Fluidizing Airflow (CFM / m ³ /hour)	40-45 / 68-77
Inlet Air Temperature (°C)	64-67
Product Temperature (°C)	42-45
Spray Rate (g/minute)	15
Atomizing Pressure (Pounds/inch ² / MPa)	30 / 0.21

Size Characterization

The size and shape of the coated and uncoated granules were characterized using a Malvern Mastersizer 2000 (Malvern Instruments, USA) and Camsizer, (Horiba, USA). Micrographs of the coated and uncoated granules were taken with a Leica EC3 camera on a Leica S8 APO stereo microscope. Agglomeration was determined by sieve analysis through a 500 micron (35 mesh) screen, as % retain on the screen.

Dissolution Characterization

Dissolution testing of uncoated, coated, and post coating heat-treated APAP granules was conducted following USP guidelines. Testing was conducted in 900 mL of a pH 5.8 phosphate buffer solution with USP Apparatus II at 75 RPM and samples were taken at 1.5, 5, 10, 15, 25, 30 and 45 minutes using a Varian VK7000 dissolution tester (Varian, USA).

Results

Coated Granule Size and Shape

As received APAP granules had a median granule size (d50) of 179 μm and were generally spherical in shape. The elutriation process removed the fine particles as shown in Figures 1a and 1b and led to a 7.5% reduction of material and an increase in the (d50) to 196 μm . Particle size analysis indicates that fines with a size less than 65 μm were removed following elutriation as shown in Figure 2.

Figure 1. Optical Micrographs of APAP granules (a) as received, (b) following elutriation, (c) coated with Surelease:Opadry (85:15) at 15% weight gain

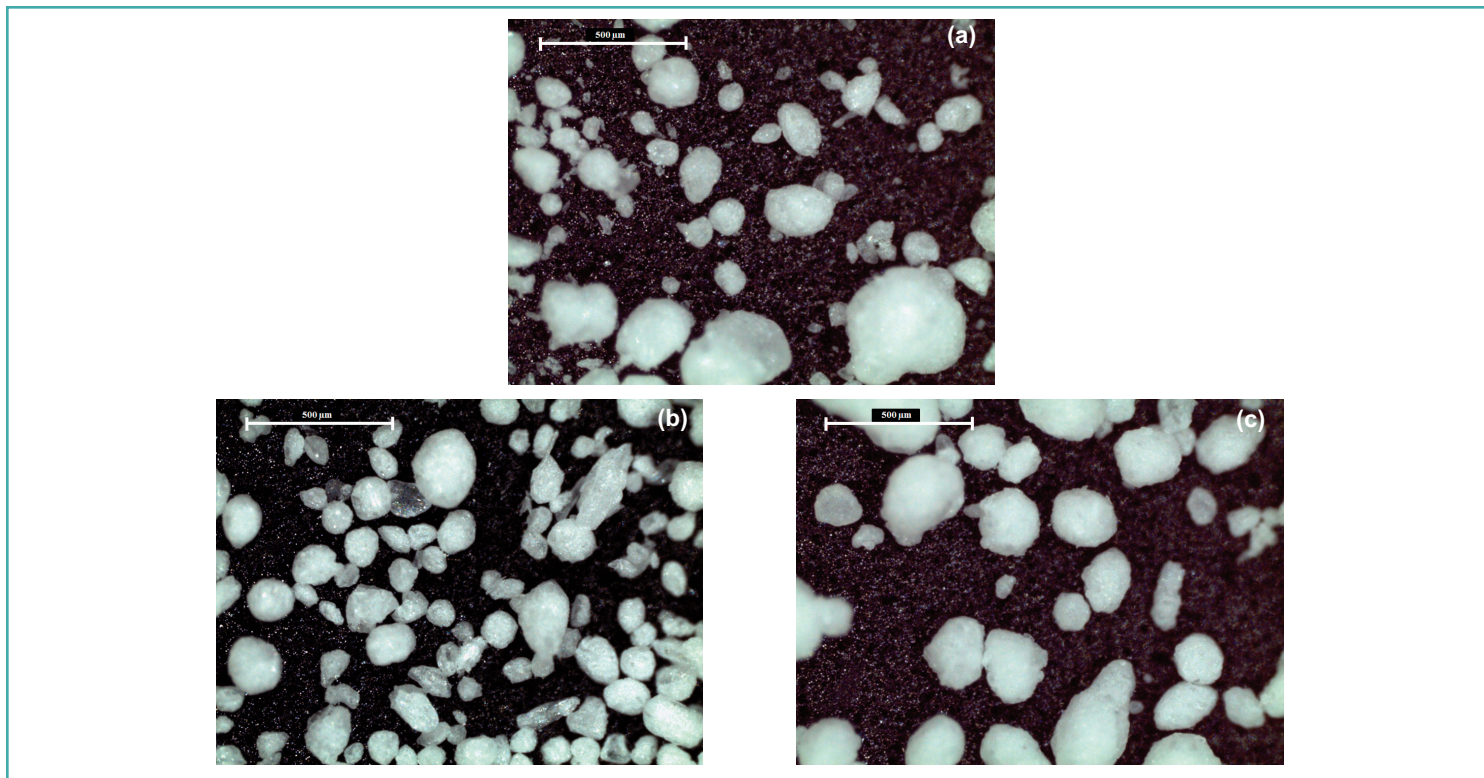
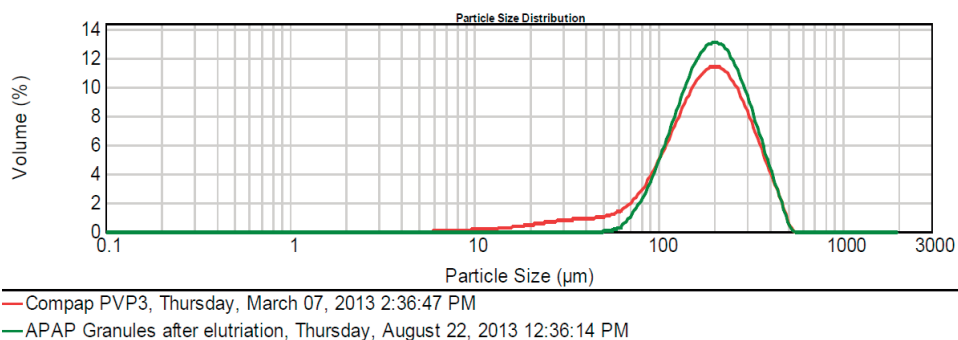


Figure 2. Particle size of APAP granules before and after elutriation

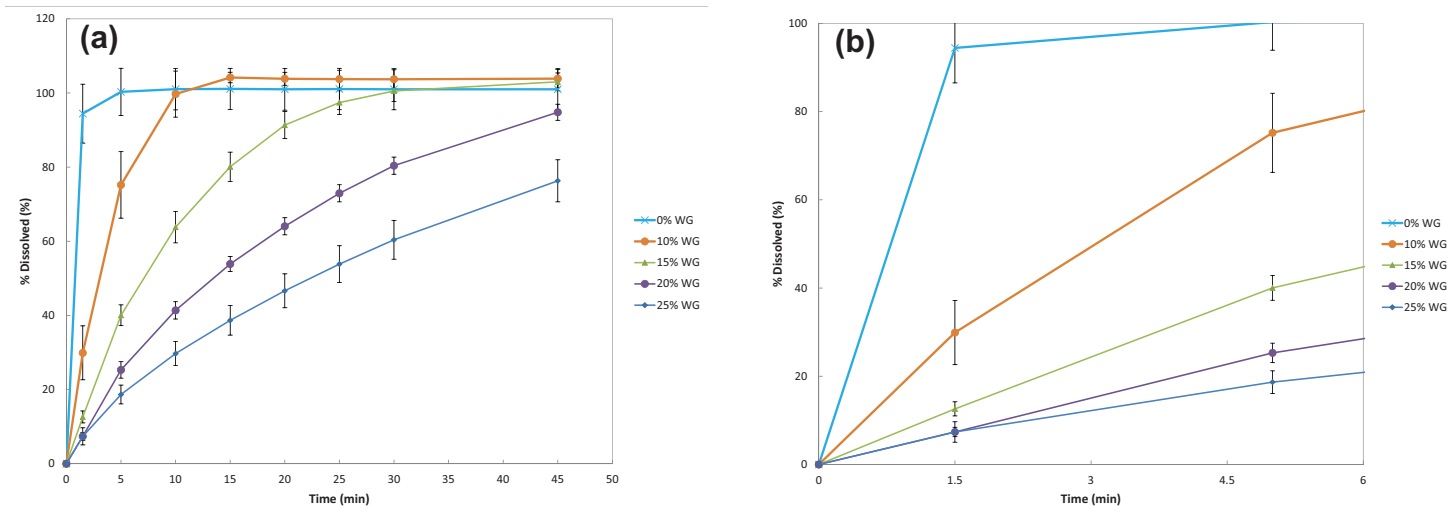


The coated APAP granules (Figure 1c) maintained their sphericity following coating and had a median particle size (d50) of 274 μm . Minimal agglomeration was observed following coating, with less than 1.25% retained on a 500 micron (35 mesh) screen.

Granule Dissolution Profiles

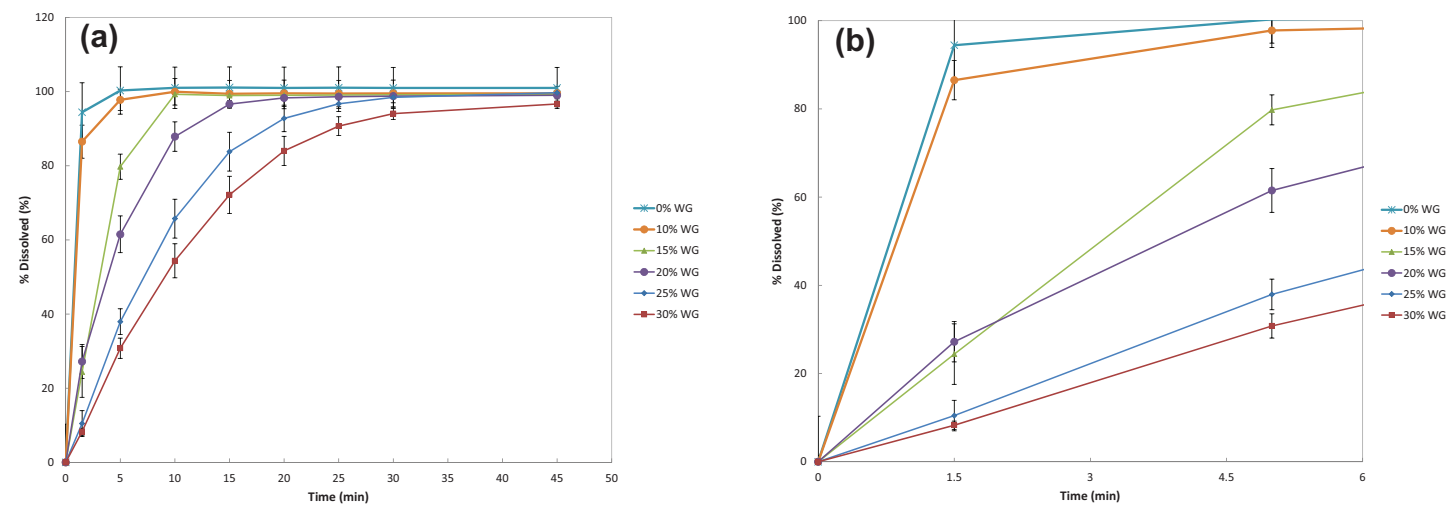
Taste masking applications often require both immediate release functionality and minimal drug release in the mouth. The dissolution profiles for the coated and uncoated APAP granules are shown in Figure 3 for the 85:15 ratio. As the coating weight gain increased from 0 to 25% w/w, the release profile substantially slowed. The uncoated APAP powders provide 94% drug release in 1.5 minutes, while a 25% weight gain of the barrier taste masking coating gave less than 8% drug release at the same time point. At a 15% weight gain a desirable compromise of reduced initial drug release and immediate release functionality is obtained.

Figure 3. Dissolution profile on APAP granules coated with Surelease:Opadry 85:15 coated APAP at 0–25% weight gains (a) full profile: 0–45 minutes, (b) initial release profile: 0–6 minutes.



When the pore former ratio was 80:20, the release rate was significantly faster at each weight gain than the 85:15 ratio as can be seen by comparing Figure 3 and Figure 4. The results show that by tuning the weight gain of the coating and ratio of Surelease to pore former it may be possible to tailor the film coating of drug granules to achieve suitable taste masking applications for different drugs.

Figure 4. Dissolution profile of APAP granules coated with Surelease:Opadry 80:20 coated APAP at 0–30% weight gains (a) full profile: 0–45 minutes, (b) initial release profile: 0–6 minutes.



The influence of post coating heat treatment of the coated granules at 60°C for 1 hour in an oven on the APAP release profiles for 85:15 at a 15% weight gain and 80:20 at a 25% weight gain are shown in Figures 5 and 6. In both cases, slower release rates were observed for the heat treated samples, but the influence of heat treatment was reduced for the 80:20 ratio.

Figure 5. Comparison of APAP granule dissolution profiles for 85:15 at 15% weight gain with and without heat treatment (a) full profile: 0–45 minutes, (b) initial release profile: 0–6 minutes.

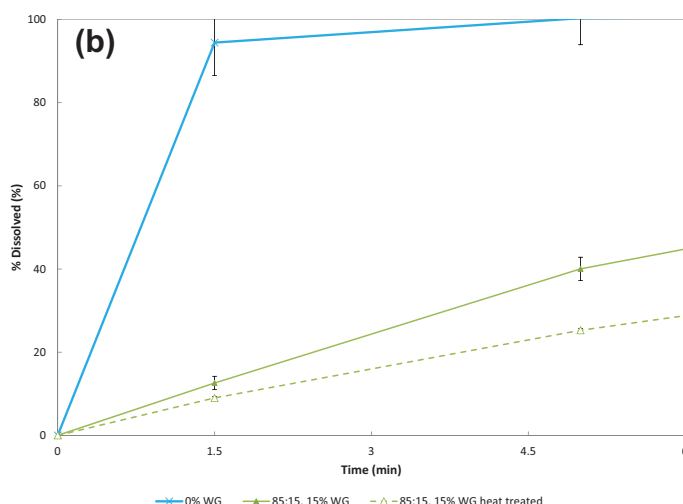
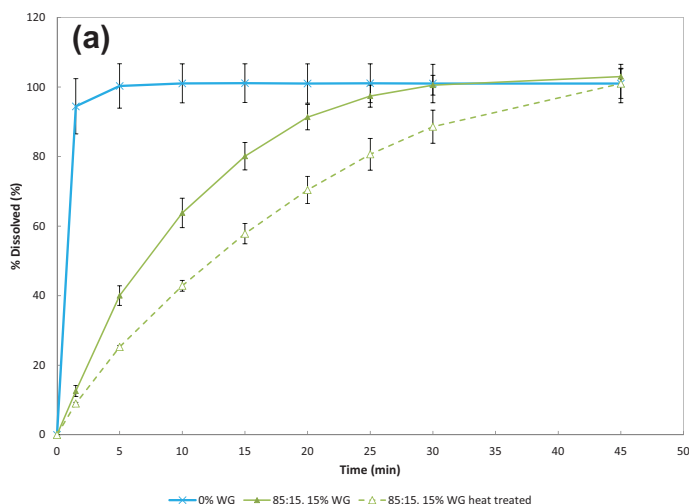
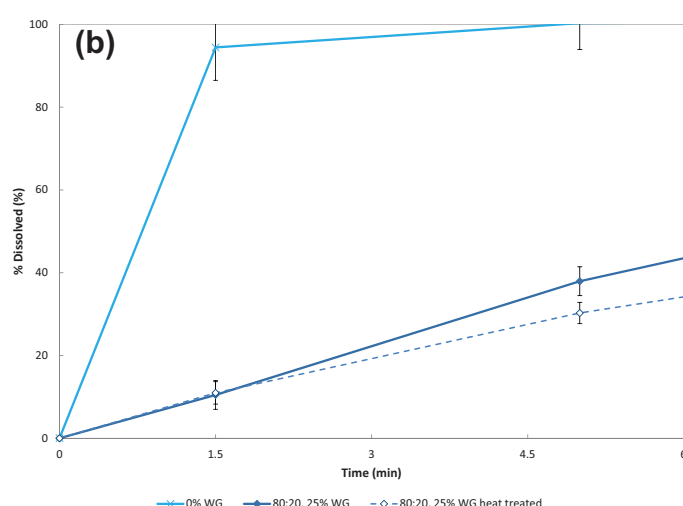
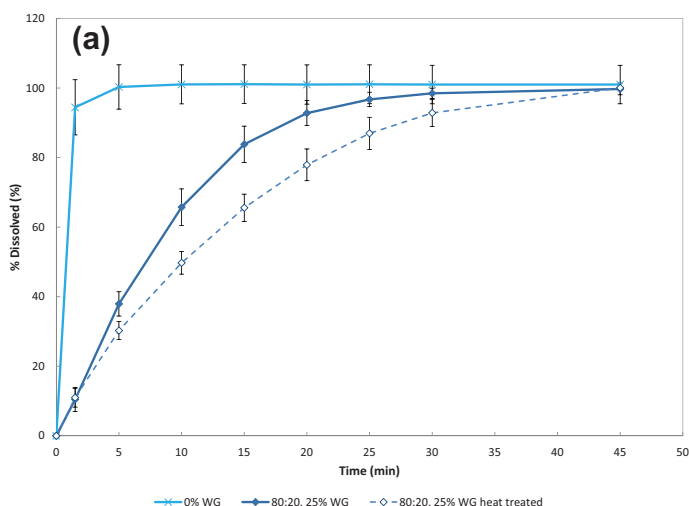


Figure 6. Comparison of APAP granule dissolution profiles for 80:20 at 25% weight gain with and without heat treatment (a) full profile: 0–45 minutes, (b) initial release profile: 0–6 minutes.



Conclusions

The dissolution profiles of APAP granules were successfully modified using a Surelease:Opadry barrier membrane coating that can provide slow initial drug release to mask objectionable tastes, yet retain immediate release functionality, which are suitable for taste masking of drug granule applications. The combination of Surelease and Opadry is easy to apply and by modifying the pore former ratio and coating weight gain it was possible to obtain a range of release profiles within 45 minutes. The materials used in this study all have precedence of use in pediatric applications.

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