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Understanding the Integrity of Coating for Taste-Masked Granules Before and After Tablet Compression

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SUMMARY

Raman microscopy was used to visualize the integrity of a barrier membrane coating at the various stage of chewable tablets development. The effect of substrate morphology and particle characteristics was found to be important in maintaining the integrity of the coating throughout the process of chewable tablets manufacture. Furthermore, the observations from the Raman image analysis provide an understanding of the factors affecting drug release.

INTRODUCTION

The effective taste masking of particles for incorporation into chewable dosage forms is influenced by the consistency and integrity of the applied barrier membrane coating. During the tablet compression process, the coating around the drug particles may fracture, leading to an adverse taste profile in the final dosage form. In addition to the barrier coating composition and application levels, the substrate morphology, strength and particle size also influence the final integrity of the coated particles (Pearnchob and Bodmeier, 2003; Terebesi and Bodmeier, 2010). In this study, Raman microscopy was used to generate images and visualize the integrity of barrier membrane coatings on two different grades of acetaminophen (APAP) granules with differing morphologies. Raman imaging was used to evaluate granule characteristics from each stage of the manufacturing process, from coating to blending to compression. Further, the observations from the Raman image analysis were correlated with in vitro drug release.

MATERIALS AND METHODS

Two grades of APAP, Compap (amorphous, spray dried, d(50): 181µm) and special granular (crystalline granules, d(50): 332µm) (Covidien, USA) were coated using Surelease® aqueous ethylcellulose dispersion combined with a hypromellose-based Opadry® (Colorcon Inc., West Point, USA) as a pore former, at a ratio of 85:15 w/w. The coating was applied to the granules using a top spray fluid bed coater (Glatt GPCG-2) up to 30% weight gain (WG). The coated APAP granules of both morphologies were each blended with Parteck® ODT (Merck KGaA, DE), sweetener, disintegrant, glidant and lubricant and compressed to form the chewable APAP tablets.

The coated APAP granules, tableting blend and compressed APAP chewable tablets were observed

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under a Raman microscope (Horiba LabRamHR) to examine the integrity of the barrier membrane coating around the particles. Further, in vitro dissolution studies for the coated granules, tableting blend and compressed chewable tablets were carried out using USP Apparatus II (paddles) at 75 rpm in 900 ml of pH5.8 phosphate buffer. Drug release was determined spectrophotometrically at a wavelength of 243 nm.

RESULTS AND DISCUSSION

Raman images of the coated granules confirmed the presence of the coating surrounding the particle surfaces for both grades of APAP (Fig 1). However, non-uniformity of the coating around the edges of the irregular shaped Compap granules was also observed. Raman imaging comparing coated granules in the tableting blend and after compression into chewable tablets indicated some breakage/ elimination of the coating from the particle surface after compression. However, this breakage was much more pronounced with the irregular shaped Compap granules compared to the more regular shaped crystalline granule surface.

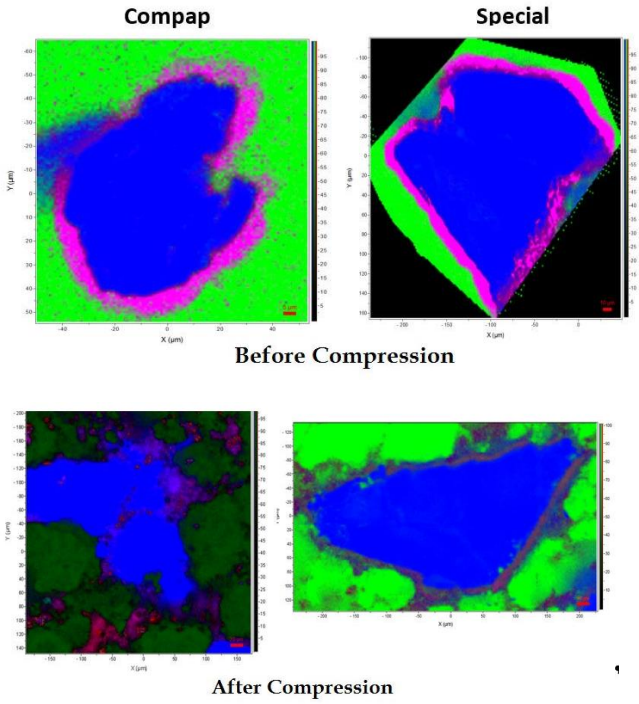

Fig. 1. *Raman Imaging of Coated APAP Granules before compression (top) and after compression (bottom).*

Dissolution tests showed that the initial release of the drug from the compressed tablet was low for both formulations, indicating that the applied coating functioned as desired for taste masking (Fig 2). However, earlier onset of drug release from the irregular Compap granules tableting blend and chewable tablets indicated differences in coating effectiveness, resulting from the substrate morphology. The difference in drug released at 5 mins between coated Compap granules and compressed granules was 41% compared to 5% difference between the coated crystalline granules before and after compression.

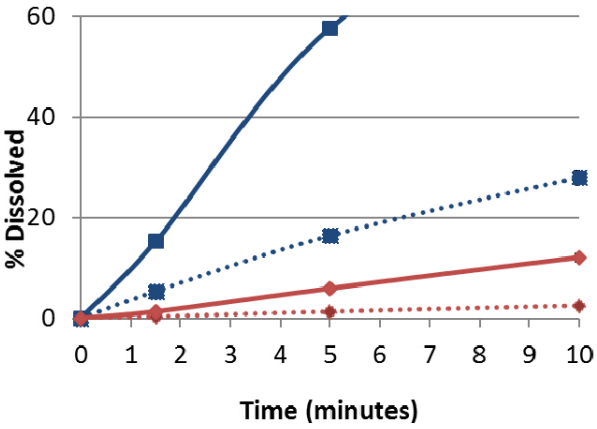

Fig. 2. *Compap (blue) and Special (red) coated granules drug release before (……) and after compression (___).*

CONCLUSIONS

In this study, drug particles were successfully coated with Surelease to provide the reduced initial drug release desirable for taste masking applications. The effect of substrate morphology and particle characteristics were found to be important in maintaining the integrity of the coating throughout the process of manufacturing chewable tablets. Raman microscopy was found to be a useful technique to visualize the integrity of barrier membrane at the various stage of chewable tablets development and to provide understanding of factors affecting drug release.

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