# Investigation of Enteric Coating of Mini-Tabs Using a Perforated Pan or a Fluid-Bed Machine

## ABSTRACT SUMMARY

This study investigated the enteric coating efficiency of mini-tabs using a perforated pan or a fluid-bed coating machine. For both types of equipment, good enteric coating efficiency was obtained and the results were comparable. The main benefit of using the perforated pan was a shorter process time.

## INTRODUCTION

Multi-particulate (MP) modified release drug delivery systems have several performance advantages vs. single unit dosage forms. After ingestion, MP units are released from the capsule in the stomach, predictably transit to the small intestine [(1)] and spread along the gastro-intestinal tract resulting in a consistent drug release with reduced risk of local irritation. MP formulations generally have a more reliable *in-vivo* dissolution performance when compared to a single unit dosage form, resulting in more uniform bioavailability and clinical effect.[(2)]

Mini-tabs combine the advantages of MP dosage forms with the established manufacturing techniques in tableting and have fewer constraints compared to extrusion/spheronization.[(3)] Direct compression of mini-tabs is an attractive alternative to pellets since the use of liquids is avoided. Like other MP technologies, mini-tabs can either be filled into hard capsules or compacted into larger tablets which, after disintegration, release the sub-units as MP's.[(4)] Additional benefits of mini-tabs include excellent size uniformity, regular shape and smooth surface, offering a substrate which is easy to coat with polymeric membranes for modified release purposes.

Coating of MP's is normally carried out in a fluid-bed coating machine. In this study the feasibility of using a perforated coating pan was evaluated and compared to a fluid-bed machine. Differences between the two processes, in terms of coated tablet appearance, physical properties and enteric protection were studied.

## EXPERIMENTAL METHODS

Placebo mini-tabs contained lactose monohydrate (Friesland Foods Domo, Netherlands), powdered cellulose (Elcema F150, JRS Pharma GmbH, Germany), pre-gelatinized starch (Starch 1500®, Colorcon, Inc., USA), fumed silica (Aerosil 200, Evonik Degussa, Germany) and magnesium stearate (Akcros, Netherlands). They were manufactured by direct compression (35 rpm, 1.1 kN compression force) on a modified instrumented 10-station rotary press (Piccola, Riva, Argentina) fitted with 2 mm standard concave tooling.

Mini-tabs were initially seal-coated with an 8% w/w aqueous dispersion of Opadry® Clear 03K19229 (Colorcon, Inc.) to 5% weight gain (WG). They were then coated with a 20% w/w aqueous dispersion of a fully formulated enteric acrylic system, Acryl-EZE Clear 93F19255 (Colorcon, Inc.) to 10 - 60% WG. The coating trials were conducted in a Glatt GPCG 1.1 fluid-bed machine or in a Manesty XL lab 12" perforated pan with a 500 µm nylon mesh insert (Manesty, UK) using coating process parameters listed in Tables 1 and 2, respectively.

***Table 1: Process Parameters for Fluid-Bed Coating***

| Process parameters | Seal-coat | Enteric coat |
|---|---|---|
| Tablet charge (kg) | 0.5 | 0.5 |
| Fluidizing air volume ($m^3/h$) | 98 – 105 | 98 – 110 |
| Inlet air temperature ($^oC$) | 64 – 67 | 51 – 53 |
| Exhaust air temperature ($^oC$) | 45 – 48 | 32 – 36 |
| Atomizing air pressure (bar) | 1.5 | 1.5 |
| Spray rate (g/min) | 5 -6 | 7 - 10 |
| Process time (min) | 53 | 136 |
| Total weight gain (%) | 5 | 60 |

***Table 2: Process Parameters for Perforated Pan Coating***

| Process parameters | Seal-coat | Enteric coat |
|---|---|---|
| Tablet charge (kg) | 0.4 | 0.4 |
| Air volume ($m^3/h$) | 250 | 250 |
| Inlet air temperature (°C) | 65 | 40 – 45 |
| Exhaust air temperature (°C) | 48 – 58 | 33 – 45 |
| Product temperature (°C) | 47 – 57 | 29 – 33 |
| Atomizing air pressure (bar) | 1.0 | 1.0 |
| Spray rate (g/min) | 6 – 11 | 10 – 11 |
| Process time (min) | 30 | 114 |
| Total weight gain (%) | 5 | 60 |

Breaking force and friability values for uncoated and coated mini-tabs were determined using Schleuniger-4M (Pharmatron AG, Switzerland) hardness and Copley TA (UK) friability testers, respectively.

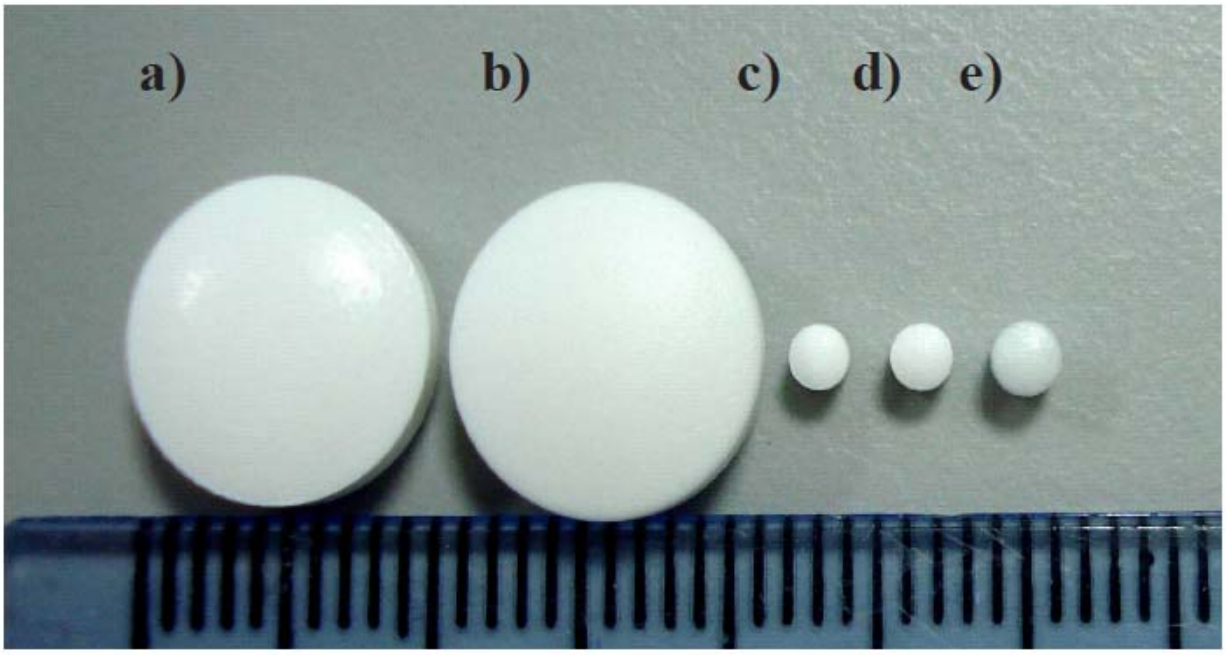
Enteric protection of the Acryl-EZE® coated mini-tabs was evaluated by acid uptake testing. Enteric coated mini-tabs (n = 6) were weighed individually and placed in a Copley ZT54 disintegration tester with a round 500 µm mesh (Erweka GmbH, Germany) fitted to the base of the testing tube. After 2 hours in either 0.1N HCl or pH 4.5 acetate buffer at 37 ± 1ºC, the mini-tabs were removed from the vessel, excess surface moisture was eliminated with a paper towel and the tablets were re-weighed. The difference in the weights was reported as percent acid uptake.

## RESULTS AND DISCUSSION

Mini-tabs were manufactured at 1.10 ± 0.06 kN upper compression force without any damage to the tooling. Low ejection force values (less than 50 N) were obtained. Uncoated mini-tabs had the following properties: 7.8 ± 0.1 mg weight, 1.963 ± 0.016 mm thickness, 1.6 ± 0.1 kp breaking force, 0.69% friability and 2.3 ± 0.5 minutes disintegration time. Uncoated and coated mini-tabs had no visually evident defects (Figure 1). No obvious differences were visible between tablets coated in the fluid-bed versus the perforated pan coating machines.

***Figure 1: Appearance of Mini-Tabs Compared to 10 mm Diameter Tablets***

*a) 10 mm, Uncoated; b) 10 mm, 10% Enteric WG; c) 2 mm, Uncoated; d) 2 mm, Seal-Coated; e) 2 mm, Seal- and Enteric coated (40% WG)*




As expected, tablet mechanical strength improved significantly after applying the seal-coat. Breaking force values increased from 1.6 kp for uncoated mini-tabs to 4 kp and 3.2 kp when coated in the fluid-bed or perforated pan coating machines, respectively. Friability decreased from 0.69% for uncoated to less than 0.01% for seal-coated mini-tabs.

Enteric protection evaluation for delayed release dosage forms is typically conducted in pH 1.2 acid media. While this is suitable for the majority of enteric coated products, it has been found that in some cases the stomach environment has elevated pH making the standard test parameters unsuitable. One such case involves patients taking proton pump inhibitors (PPI) where gastric media pH is typically above 4.[5] Therefore, in this study enteric protection of the Acryl-EZE coated mini-tabs was evaluated in both 0.1N HCl (pH 1.2) and acetate buffer (pH 4.5). The acid uptake results were similar for mini-tabs coated in the fluid-bed or perforated pan machines (Figures 2 & 3).

Enteric coating WG is generally dependent on the substrate size, shape and the surface area. Figures 2 and 3 indicate that approximately 30 to 40% enteric coating WG was sufficient to provide acid resistance for the mini-tabs studied.

***Figure 2. Acid Uptake for Acryl-EZE Coating Mini-Tabs in 0.1N HCl and Acetate Buffer (n=6)***

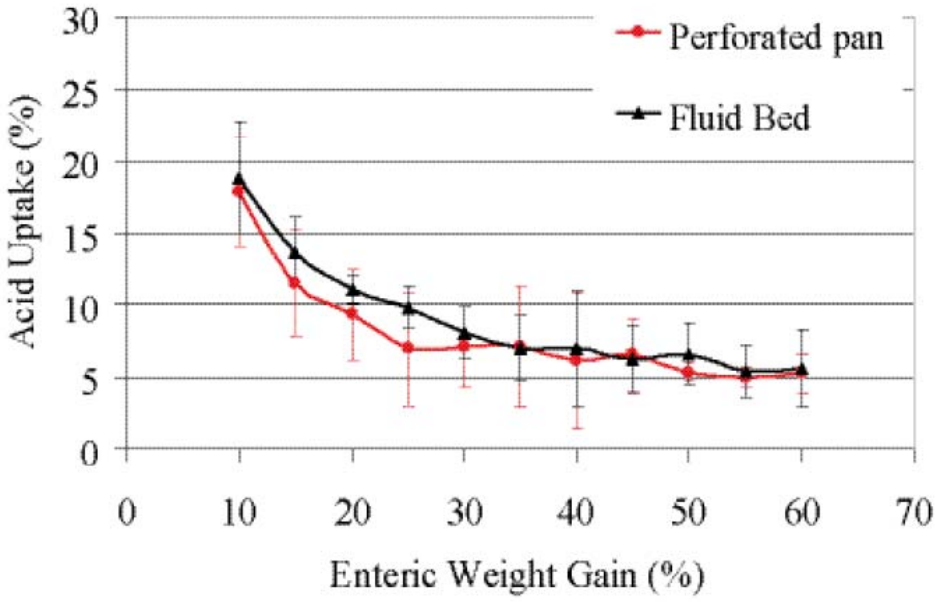
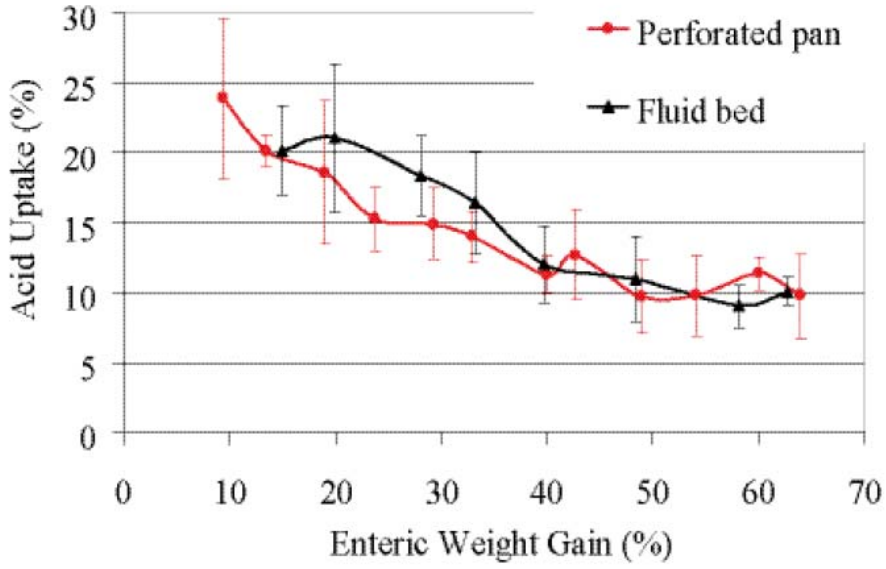



***Figure 3: Acid Uptake for Enteric Coated Mini-Tabs in Acetate Buffer pH 4.5***




Further investigation is underway to study the enteric coating efficiency of mini-tabs containing a PPI, Lansoprazole as a model drug.

## CONCLUSIONS

No significant differences in the appearance, physical and enteric properties of mini-tabs were observed when coated in a perforated pan or fluid-bed coating machines. The overall coating process time in the perforated pan machine was shorter than that in a fluid-bed coating machine.

It was found that 5% WG of the seal-coat was essential for improving mechanical properties of mini-tabs prior to the application of the enteric coat. It was further determined that a minimum 30% enteric coating WG was required to provide acid resistance.

Reprint of poster presented at the Annual Controlled Release Society Meeting 2008.
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PR_Vuong_AAPS2008_mini_tabs_perf_fluid_ver2_12_2013