SCIENTIFIC RESEARCH BRIEF
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Dissolution Development of Parvulet® Technology Oral Tablets

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INTRODUCTION

Parvulet® Technology is a patented oral dosage form capable of being dispensed to patients in tablet or powder formats, and converted into a semi-solid at the time of dosage through activation with water. The final dosage is easily administered, as a soft food like texture, ideal for pediatric and geriatric populations (including those with dysphagia). The Parvulet® technology can be combined with our taste-masking and controlled release technologies, providing greater flexibility in advancing patient centric solutions. (see Figure 1 below).

Figure 1. Example of Parvulet® Tablet Swelling

OBJECTIVES

With the development of a dissolution method for Parvulet®, it is necessary to study the possible dissolution artifacts associated with the dosage form. In this study, several of these potential artifacts were evaluated. Specifically, the impact on the dissolution profile of pre-swelling the tablet before adding to the dissolution vessels and the impact of delayed administration into the vessel after pre-swelling was investigated. Other possible artifacts including coning and other unusual behaviors in the vessel, sample loss on transfer, and the effect of no swelling or incomplete pre-swelling on the dissolution profiles were evaluated. The goal of the experimentation was to explore the dissolution behavior and the effect of possible dissolution artifacts on the expected immediate-release profile.

METHODS

Parvulet® Tablets containing 160 mg of Acetaminophen were used as the model for the study. The Acetaminophen Tablets USP monograph for dissolution was used in the experimentation (USP 2, 50 RPM, 900mL of pH 5.8 phosphate

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buffer). The samples were analyzed by HPLC-UV with the following method: Phenomenex Kinetex 2.6 µm C18 100Å 75x4.6mm column at 40°C, Water: Methanol (90:10) at 1.0 mL/min, 245 nm.

A series of dissolution experiments were conducted:

- Dissolution on tablet as is (no pre swelling prior to adding to the dissolution vessel).
- Pre-swell the tablets on a spoon and immediately transfer to vessels by briefly swirling in the media.
- Pre-swell and wait 1 minutes before addition to dissolution vessel using procedure as above.
- Pre-swell and wait 3 minutes before addition to dissolution vessel using procedure as above.
- Pre-swell and wait 5 minutes before addition to dissolution vessel using procedure as above.

Each dissolution was observed and the observations were collated for comparison. The dissolution profiles were generated using the procedure noted above.

RESULTS

The Dissolution profiles generated from the experiments listed previously are summarized in **Figure 2** below.

Figure 3 (next page) shows the dissolution progression for an un-swelled tablet versus a tablet that was pre-swelled and held for 5 minutes before addition to the dissolution vessel. After 1 minute both samples have significant dispersion of the sample throughout the vessel. By 10 minutes it is difficult to visually determine one sample from the other. The samples that were pre-swelled had larger masses of suspended particles than the un-swelled sample. No significant coning was witnessed in any of the samples tested. While no loss of sample was seen during testing the potential for it was present. Sample loss could have occurred if the sample was not completely removed from the spoon used for pre-swelling, the sample addition to the vessel caused sample material to stick to the paddle shaft or to the vessel above the surface of the media.

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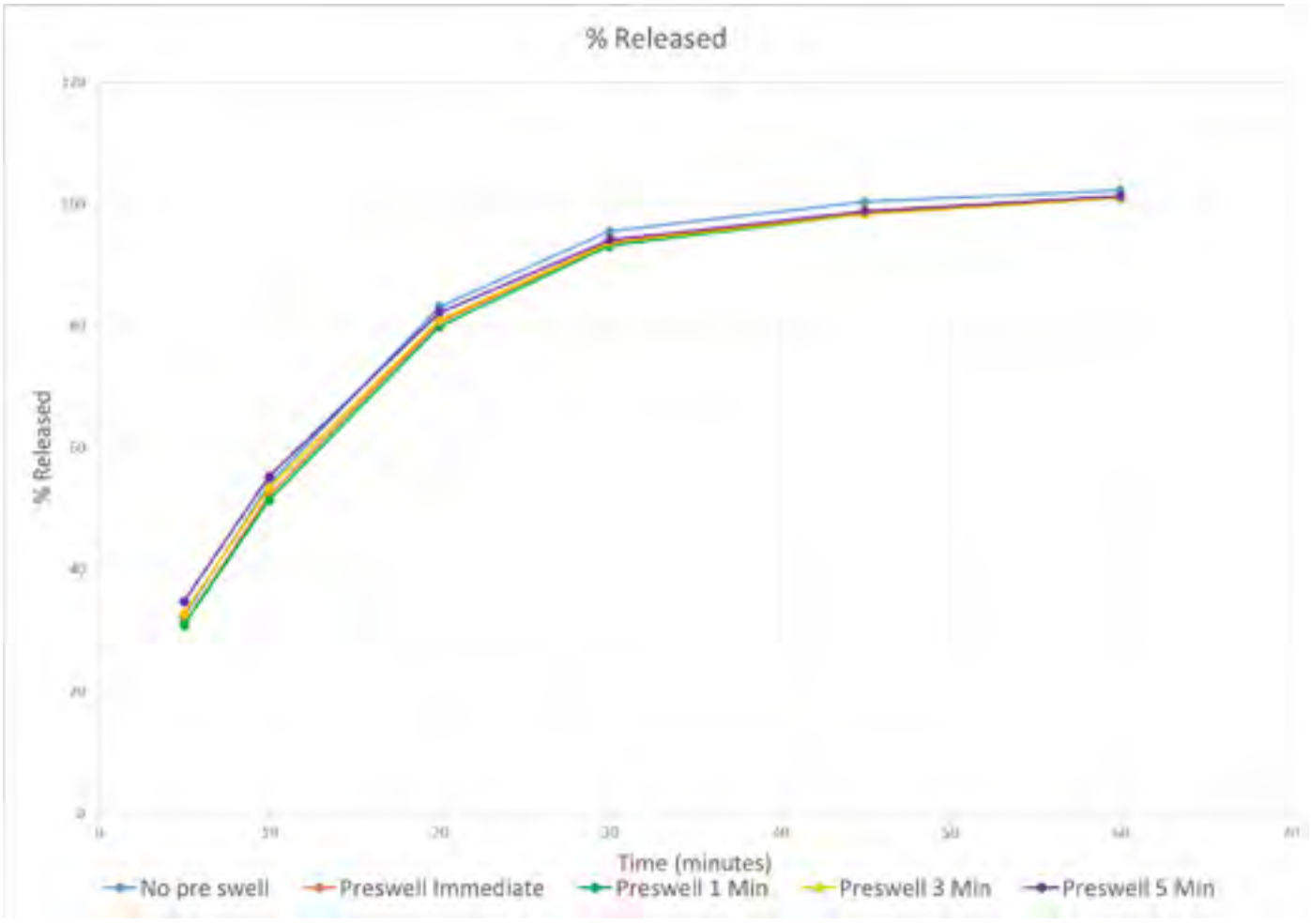

Figure 2. Dissolution Profiles investigating the Impact of Pre-swelling of Parvulet® Tablet.

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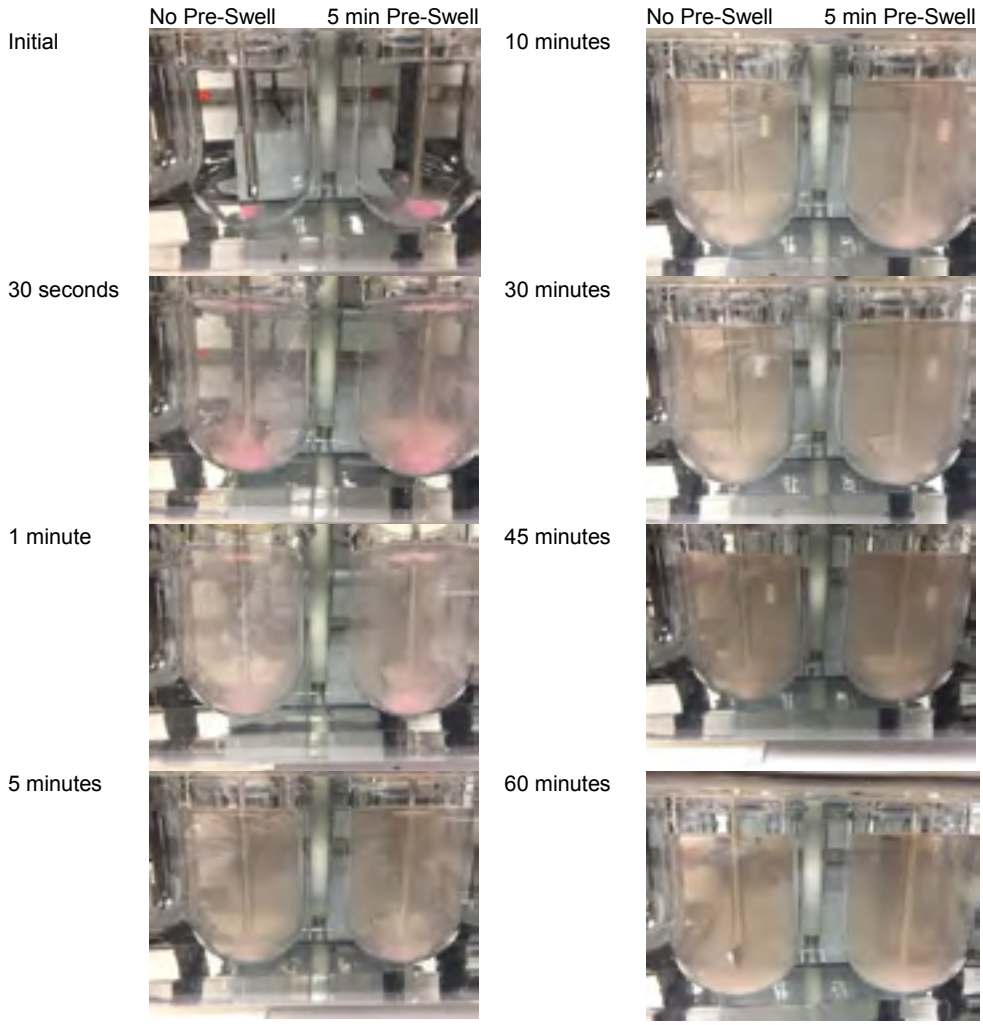

Figure 3. Side by side comparison of not pre-swelled tablet and pre-swelled tablet with 5 minute wait.

SUMMARY

There was no significant change in the dissolution release rate between tablets that were pre-swelled and tablets that were not pre-swelled. It is therefore not necessary to pre-swell the tablets before addition to the dissolution vessels. Since there is no effect on the dissolution profile between an un-swelled tablet and those that were pre-swelled and held for up to 5 minutes it can be concluded that there would be no change to the dissolution profile of an incompletely swelled tablet.

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Jennifer is a Research and Development Analytical Scientist. She has over 20 years of pharmaceutical experience at Adare Pharma Solutions. Jennifer specializes in method development and validation, as well as microscopic analysis of intermediates and finished dosage forms. She holds both a Bachelor's degree and Master's degree in Chemistry from Wright State University.

Adare Pharma Solutions is a global technology-driven CDMO providing end-to-end integrated services, from product development through commercial manufacturing and packaging, with small molecule expertise focusing on oral dosage forms. Adare's specialized technology platforms provide taste masking, controlled release, solubility enhancement, and patient-centric dosing solutions. With a proven history in drug delivery, Adare has developed and manufactures more than 65 products sold by customers worldwide.