

# Effect of Excipient and Binary Excipient Characteristics on Filling using Capsugel's



## Xcelodose® 120 S Precision Powder Micro-dosing System



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### Introduction

Segregation is the unwanted separation of differing components of the blend. This phenomenon is a result of particle size differences ultimately resulting in ending in different zones within the processing equipment (e.g., bin, hopper, etc.). Typical pharmaceutical blends separate from each other by three common mechanisms: Sifting/percolation results in segregation when there is range of particle sizes at a ratio of 2:1 while fluidization (air entrapment) segregation can take place when bed of aerated material settles, driving fines to the top of the bin. Similar to the fluidization mechanism, the dusting (particle entrapment) segregation occurs primarily with fine powders that vary in particle size or density. Xcelodose® marketed by Capsugel has a robust feature with capability to precisely dispense dose weights from 0.1 mg to 100 mg. This work is an evaluation of the ability of commercially available excipients & binary excipient blends on filling using Xcelodose® 120 S Powder Dosing System.

### Objectives

To manufacture low/middle/high strength gelatin capsules. To collect capsules at the beginning, middle, and end of the encapsulation process. To evaluate the impact of filling different physical characteristic materials and their potential segregation by performing particle size analysis of the capsule filled material.

### Methods

#### Choice of Excipients

The encapsulation process included filling size 00 gelatin white CS opaque capsules with commercially available Avicel® grades such as PH-102, PH-105, & PH-200 that differ in density and particle size distribution. Both the individual excipients and 1:1 binary mixtures of the three Avicel® grades were also considered for evaluation.

#### Choice of Dispense Head

An ideal dispense head size was chosen from a quick method evaluation study. This evaluation was performed for chosen individual excipient studies of Avicel® PH-102, PH-105, PH-200, and 1:1 binary blends of PH-102 with PH-105, PH-102 with PH-200, and PH-105 with PH-200 (mixed in Turbula® blender for five minutes).

#### Encapsulation Process

Approximately five grams was added into respective above chosen dispense heads and filling process was conducted without refilling the dispensing head to collect separately beginning, middle, and end process samples. The dispense head for each excipient/binary blend was varied while other tapping parameters such as tapping frequency was held constant throughout the study. At each beginning, middle, and end steps of the process, the material was filled from the dispense head into approximately 600, 60, and 30 capsules for 2.5, 25, and 50 mg strengths, respectively.

#### Segregation Evaluation

The capsule contents particle size distribution of beginning, middle, and end process samples were analyzed on the Beckman Coulter LS 13 320 Laser Diffraction Analyzer using dry module.

### Results

The fill weight RSD of less than 2.5 % throughout the encapsulation process indicates that there was very consistent capsule filling. The lower mean variation numbers noticed in the Avicel® PH-200 grade is due to the higher granular size of the excipient probably leading to passage of larger material first from the dispense head. The particle size distribution curve of the filled material versus the unfilled demonstrates no significant shift in the mean,  $d_{50}$ , and  $d_{90}$  values (data available upon request) demonstrating that there was no noticeable segregation (Figures 1 through 6).

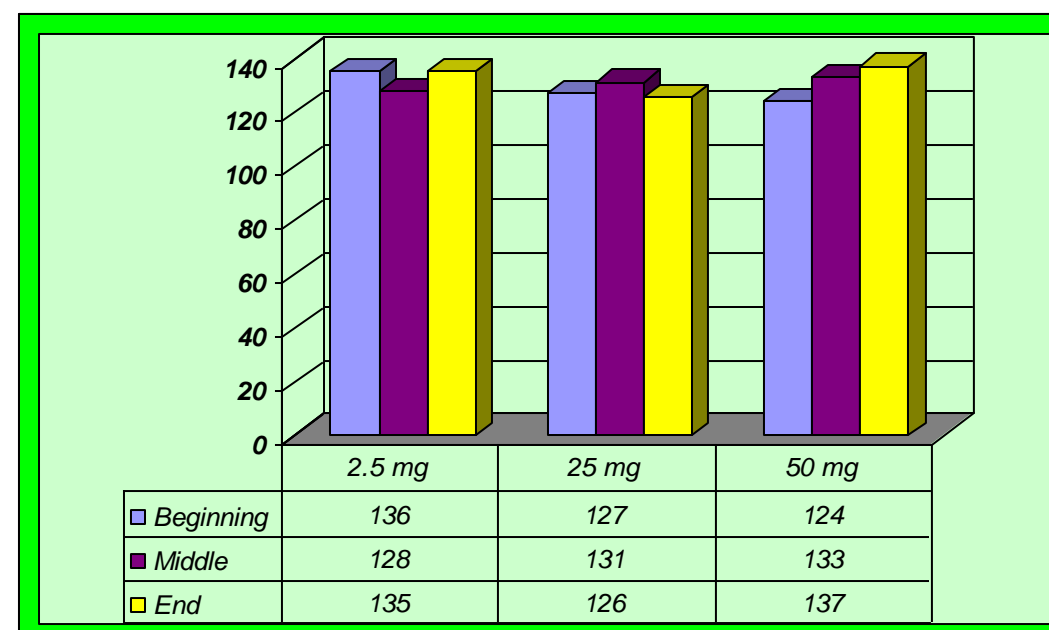


Figure 1: Mean Particle Size of Avicel® PH-102 (mean of unfilled Avicel® PH-102 – 127 um)

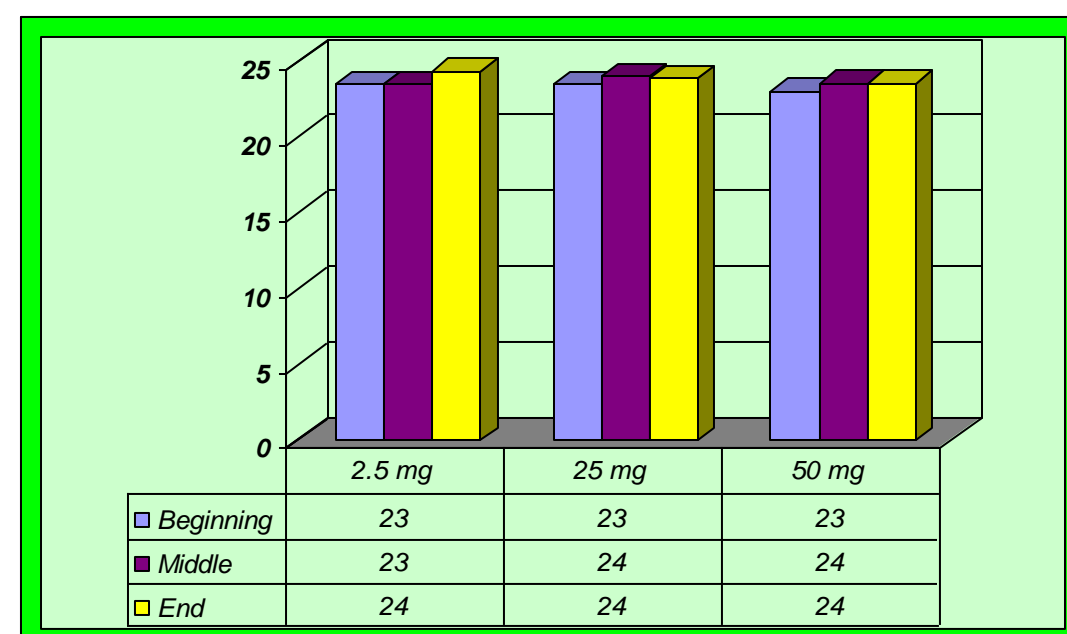


Figure 2: Mean Particle Size of Avicel® PH-105 (mean of unfilled Avicel® PH-105 – 23 um)

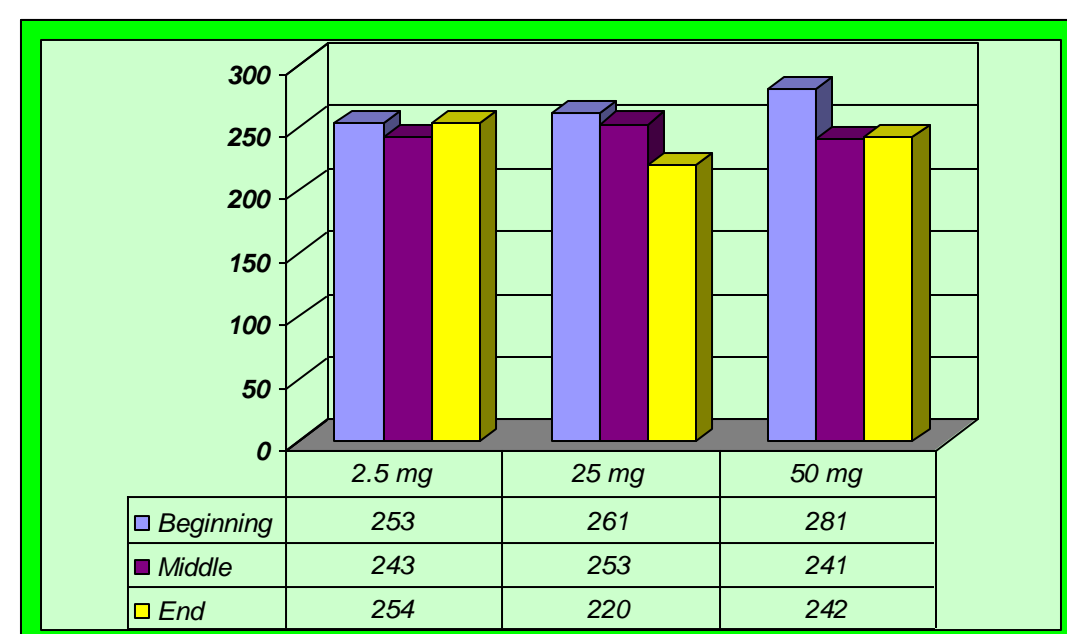


Figure 3: Mean Particle Size of Avicel® PH-200 (mean of unfilled Avicel® PH-200 – 254 um)

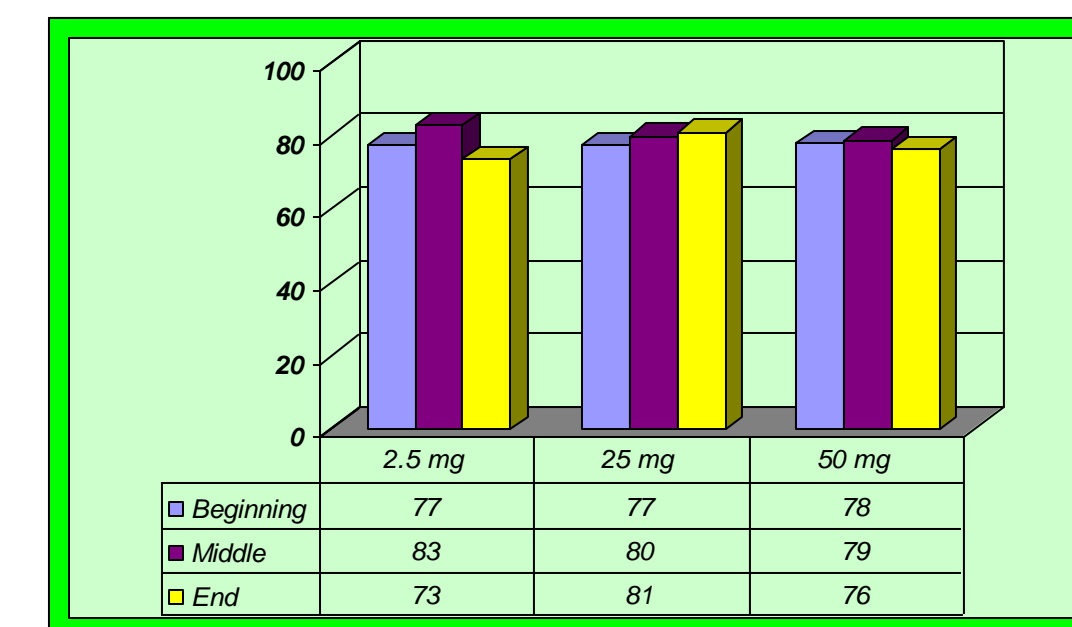


Figure 4: Mean Particle Size of Binary Blend of Avicel® PH-102 & PH-105 (mean of unfilled Avicel® PH-102 & PH-105 blend – 74 um)

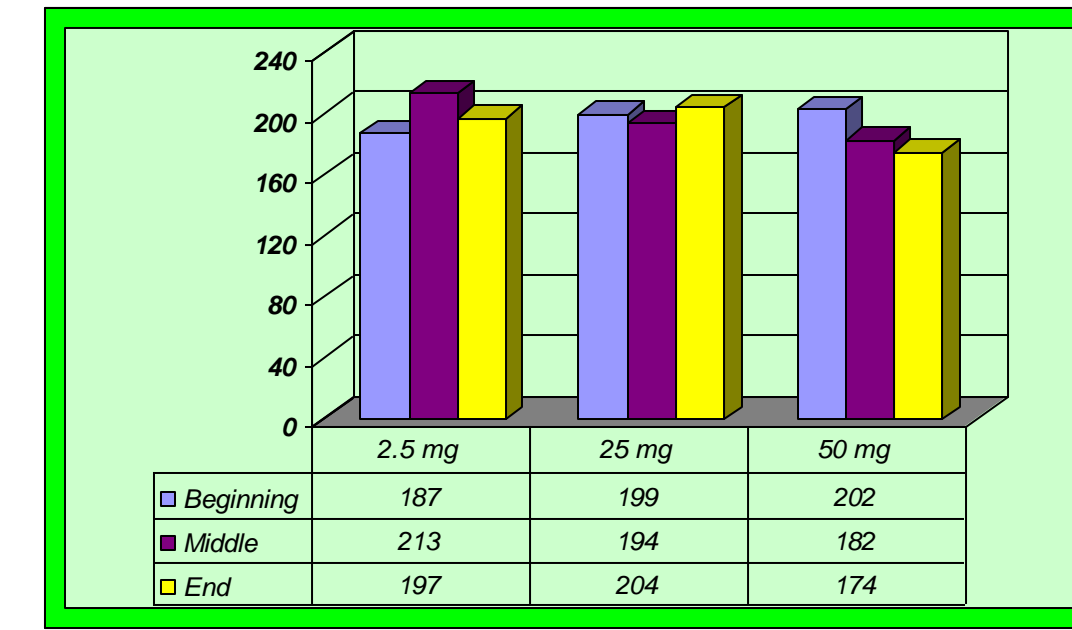


Figure 5: Mean Particle Size of Binary Blend of Avicel® PH-102 & PH-200 (mean of unfilled Avicel® PH-102 & PH-200 blend – 217 um)

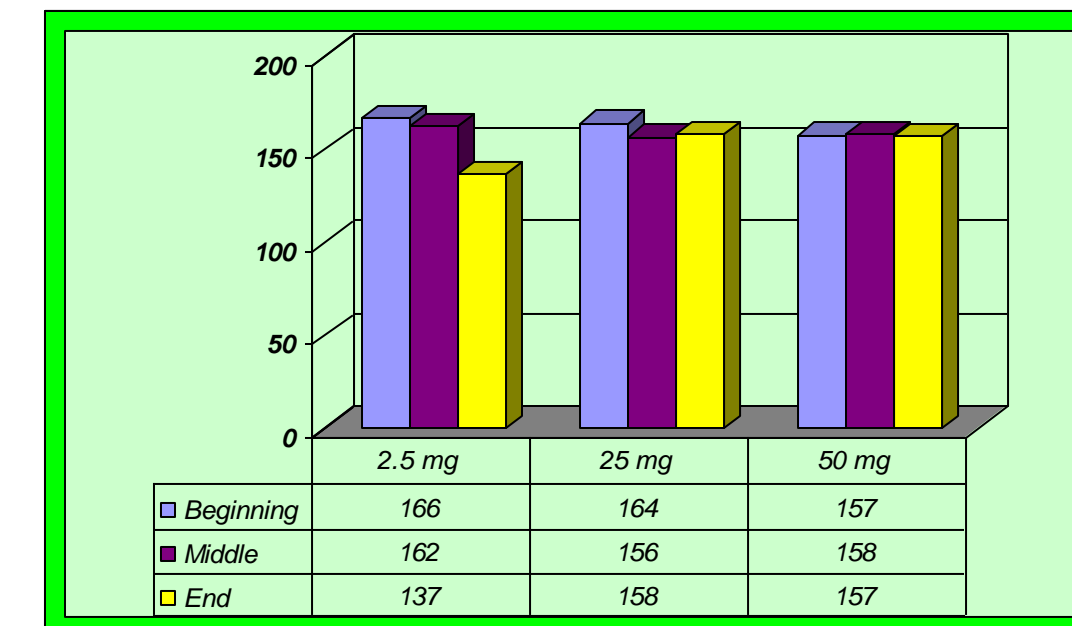


Figure 6: Mean Particle Size of Binary Blend of Avicel® PH-105 & PH-200 (mean of unfilled Avicel® PH-105 & PH-200 blend – 157 um)

### Conclusions

The difference in density and particle size distribution does not appear to influence the fill or segregation of powder by particle size in Capsugel's Xcelodose® Precision Powder Micro-dosing System.

### References

1. FMC BioPolymer. "Avicel® for Solid Dose Forms," Retrieved October 26, 2010, from <http://www.fmcbiopolymer.com>
2. Marcel Dekker Inc. (2001). Drugs & the Pharmaceutical Sciences. Volume 118.