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Comparative Study of Theoretical Versus Actual Weight Gain for a Surelease® Barrier Membrane on Coated Pellets

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INTRODUCTION

Multiparticulate systems for drug delivery have become increasingly popular due to their use in multi-drug formulations to achieve superior clinical effects and flexible release profiles. The quantity of polymer deposition or thickness of the functional film on the multi-particulates, is the critical factor affecting the integrity of the systems as well as drug release rates. There has been major interest in the industry to correlate the theoretical and actual polymer deposition of these systems during formulation, scale up and manufacturing. The aim of this study was to analytically quantify ethylcellulose deposited on drug loaded nu-pariels, coated with Surelease to various theoretical weight gains. Chlorpheniramine Maleate release profiles from the Surelease coated pellets were evaluated.

MATERIALS AND METHODS

Drug Loading

Four batches of SureSpheres™, drug layering substrate, 14-18 mesh, 18-20 mesh, 20-25 mesh and 30-35 mesh were drug loaded [Chlorpheniramine Maleate (37.5 mg/gm)] in the rotor unit of the Glatt GPCG-3 using PVP K30 as the binding agent.

Surelease Coating

Drug loaded beads were then coated with Surelease (diluted to 15% solids w/w) in the Wurster unit of the GPCG-3 (Table 1). Samples were pulled every 4 percent weight gain from 1-20% weight gain of Surelease.

Ethylcellulose Content Evaluation

Approximately 500 mg of coated beads were ground and the ethylcellulose was extracted into tetrahydrofuran after 30 minutes of shaking. The extracted samples were analyzed for ethylcellulose content by GPC/HPLC with a Waters refractive index detector using a Shodex KF-801 GPC column. Results were calculated using the area under the peak and reported as percent ethylcellulose content.

Drug Release Method

Chlorpheniramine Maleate release from 1 gram of coated pellets in 1000 mL of deionized water was measured using a USP Apparatus I (baskets) method at 100 rpm (37.0 ± 0.5°C). Drug release was detected using a UV spectrophotometer at 267nm.

RESULTS & DISCUSSION

The system suitability and calibration curve (R^2=0.9999) for ethylcellulose content evaluation were determined. Figure 1 shows the refractive index detector output for selected standards and Surelease coated bead samples. Figure 2 shows the actual ethylcellulose content of the pellets coated with Surelease against theoretical weight gain for various size fractions of pellets. There was a strong correlation between the actual and theoretical ethylcellulose content (correlation coefficients: R^2 as shown in Table 2) irrespective of pellet size fractions used here.

Table 1. Coating process parameters

Average Parameter Values				
Nu-Pariel Sizes	**14-18 mesh**	**18-20 mesh**	**20-25 mesh**	**30-35 mesh**
Inlet Air Temp (°C)	56.6	59.9	59.6	60.5
Product Temp (°C)	43.1	42.6	42.3	42.6
Exhaust Air Temp (°C)	41.5	40.4	40.8	40.4
Fluid Del. Rate (gm/min)	24.5	24.3	25.0	24.0
Atomizing Air Press (Bar)	2.0	2.0	2.0	2.0
Exhaust Flap Setting (%)	60.0	60.0	60.0	60.0
Air Volume (m^3/hr)	106.9	78.1	73.7	73.9
Air Velocity (m/s)	8.3	7.6	7.5	7.2

Figure 1: Ethlycellulose Chromatograms for Standard and Surelease Coated Pellets

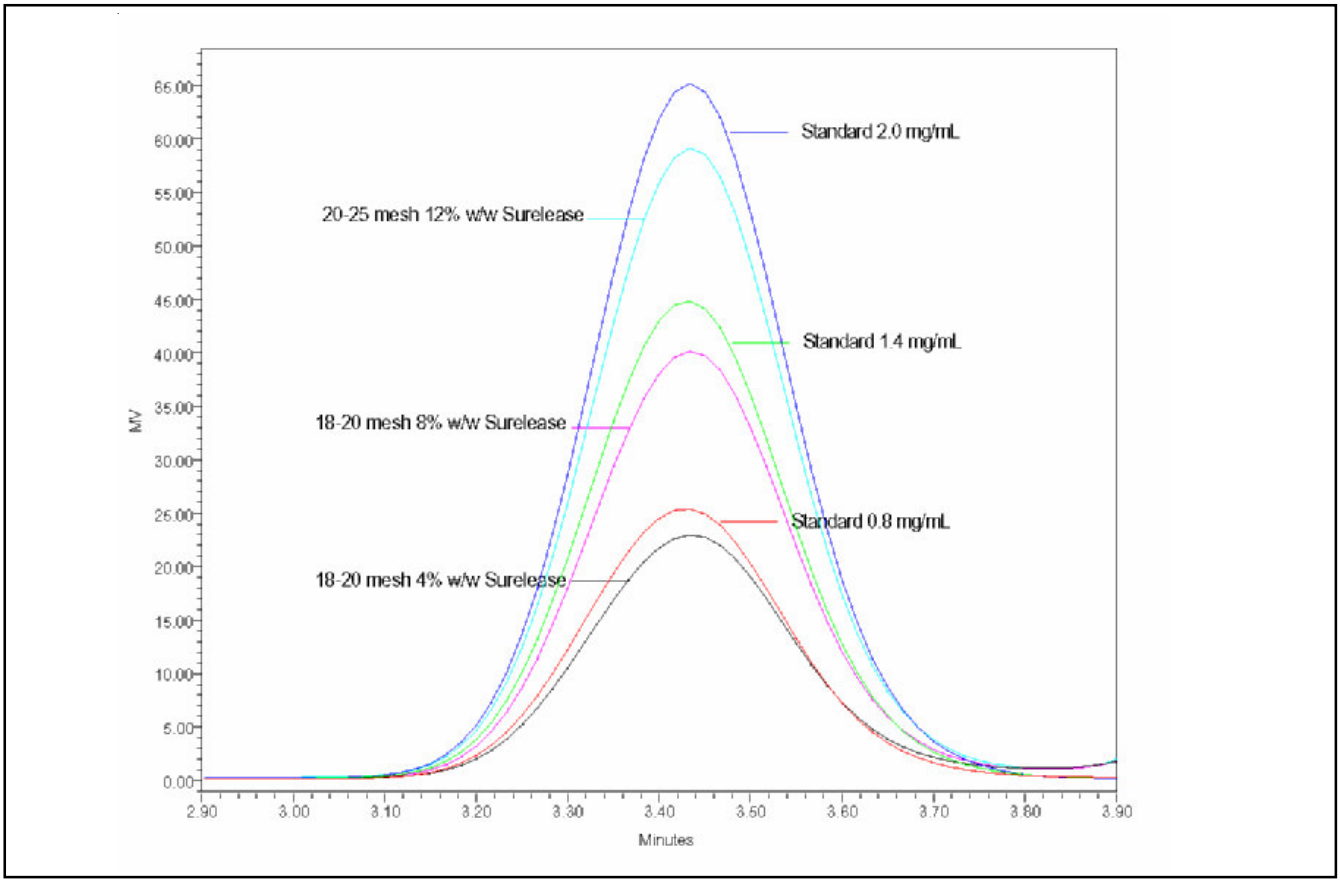


Figure 2. Theoretical Weight Gain vs. Actual Ethlycellulose Content on Surelease Coated Pellets

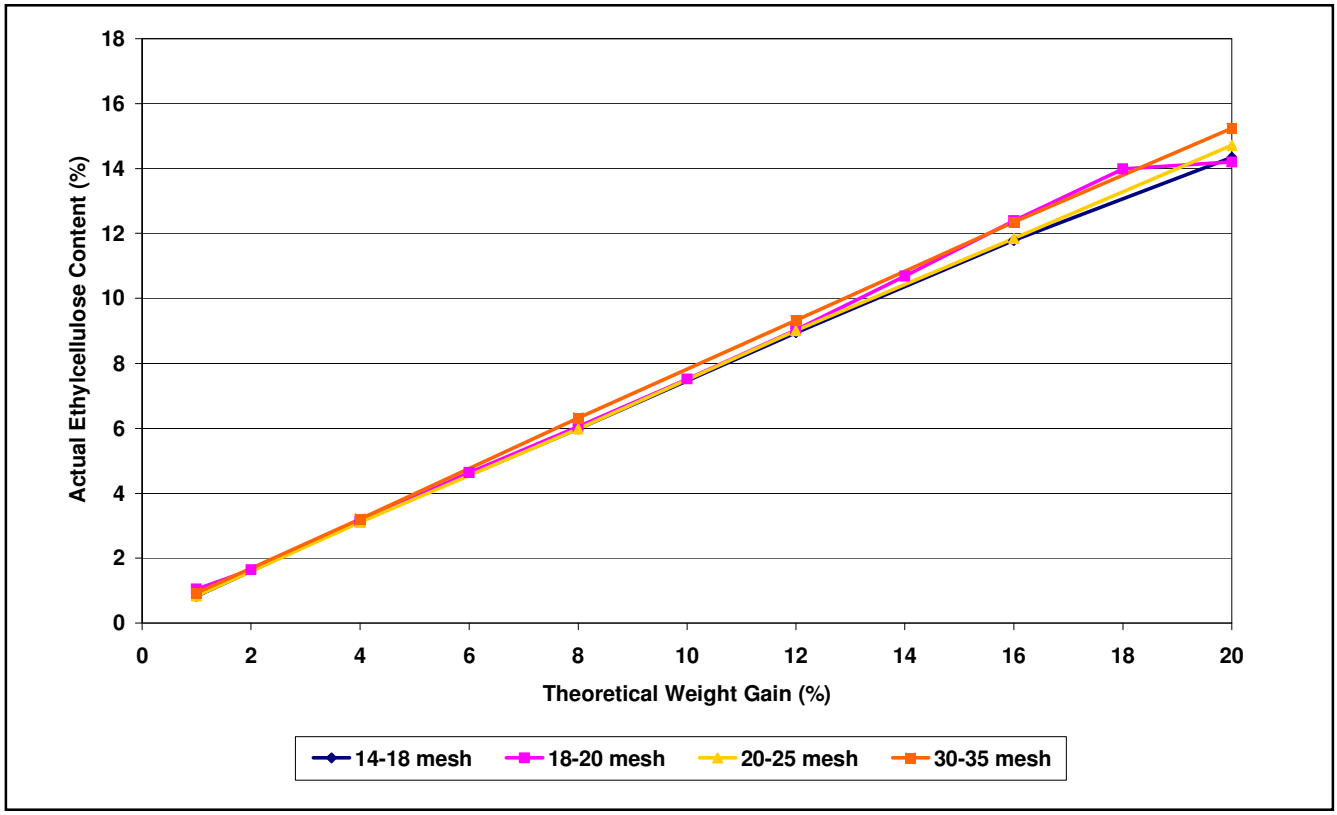


Table 2. Correlation coefficient (R^2) values for curves in Figure 2.

R^2 Values				
Bead Size	14-18 mesh	18-20 mesh	20-25 mesh	30-35 mesh
R^2 Values	0.9994	0.9956	0.9999	0.9999

Decreasing particle size of a unit weight of beads will lead to a significant increase in the surface area available for polymer deposition. Therefore, the polymer coating weight gain required for a known quantity of smaller beads to achieve similar release profiles to those for larger beads will be much higher. Drug release from Surelease coated pellets is governed by Ficks first law of diffusion:

$$\frac{dQ}{dt} = \frac{ADk\Delta C}{l}$$

Where, A is the surface area of the pellets, D is the diffusion coefficient, k is the partition coefficient, ΔC is the concentration gradient, and l is the film thickness.

Hence larger particles that had a thicker film exhibited slower release of the drug (Figure 3).

In an attempt to match the release profiles for samples of varying weight gain and size fraction, the f2 similarity factor was utilized to mathematically compare the dissolution profiles.

The profiles compared in Figure 3 have f2 values between 75 and 94 indicating the similarity of the profiles.

CONCLUSIONS

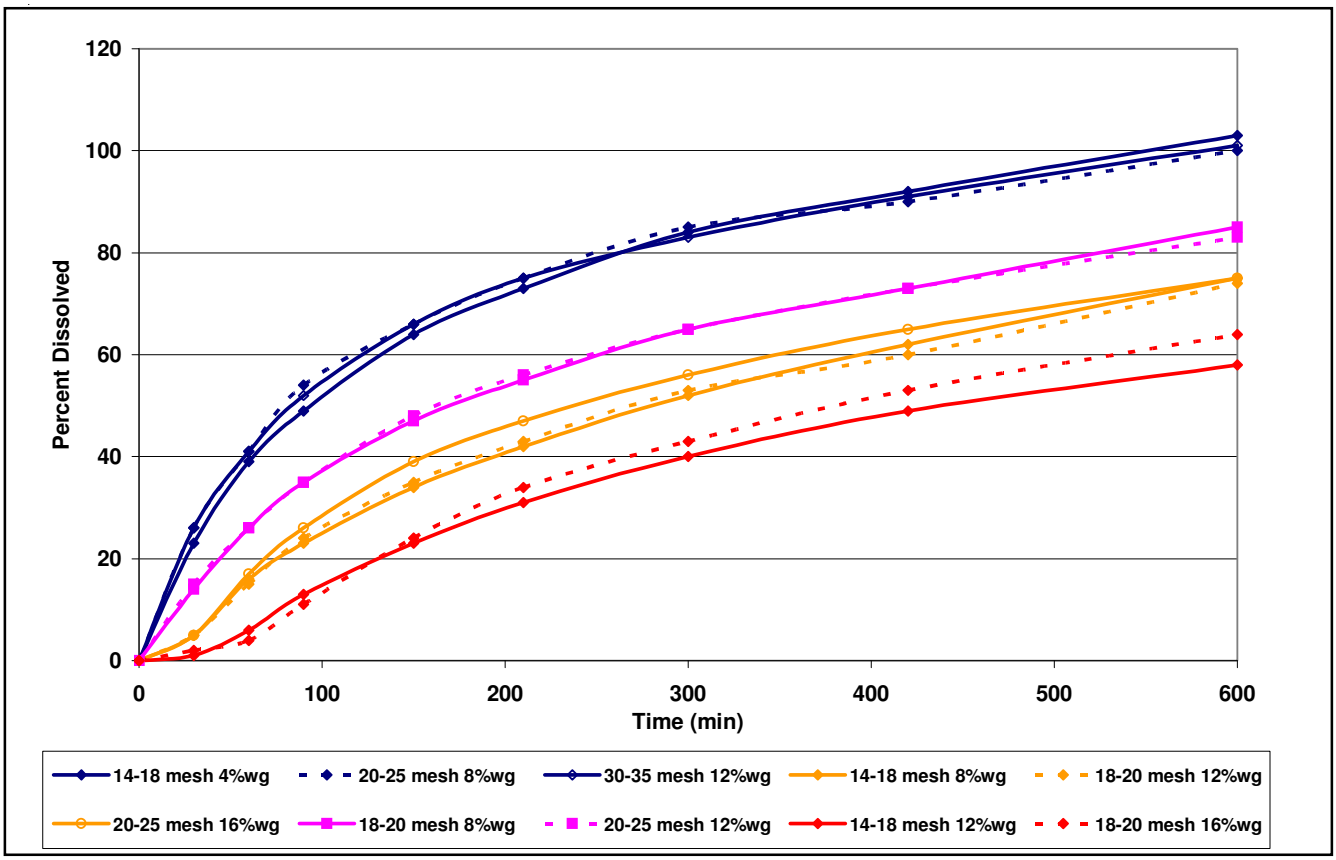
Ethylcellulose assay coupled with dissolution testing are complementary techniques allowing prediction of release rates when working with various size particles and coating weight gain. Analytical quantification of ethylcellulose on the coated pellets showed a strong correlation between the theoretical weight gain and the actual level of ethylcellulose on the pellets.

Assay of pellets for ethylcellulose may provide a valuable tool to determine weight gain during product development, scale-up, and commercialization in order to validate the coating process.

REFERENCE

1. Jeffery W. Moore, Henry Flanner, “Mathematical Comparison of Dissolution Profiles”, Pharmaceutical Technology, pg. 64 June 1996.

Figure 3. Chlorpheniramine Maleate Release Profiles from Pellets Coated with Surelease.



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