

## Evaluation of a Continuous Coating Process for the Application of a Regulatory Compliant Nutritional Enteric Coating on Soft Gelatin Capsules

### INTRODUCTION

Continuous film coating processes are recognized for their high production rates, but have not gained wide acceptance for pharmaceutical products due to potential product losses during start-up and shut-down. Improvements in continuous coater design now allow for processing in both batch and continuous modes. Automatic sequencing of spray guns and additional control mechanisms have been developed to ensure uniform and consistent coating for all substrates from start to finish, minimizing the potential for product loss.

The purpose of the study was to evaluate a continuous coating process for the application of a delayed release (DR) coating system onto soft gelatin capsules. The effect of coating application levels and process throughput rates were evaluated for their effects on enteric performance.

### METHODS

Soft gelatin capsules (Nutra Manufacturing, Greenville, SC) filled with mineral oil (1700mg) were used as the substrate for DR coating. The Colorcon coating system used was Nutrateric<sup>®</sup>, nutritional enteric coating system, which is based on Surelease<sup>®</sup>, aqueous ethylcellulose dispersion (E-7-19040), and an enteric coating additive, NS Enteric<sup>®</sup>, nutritional enteric component (29Z19241). Both of these formulation components have regulatory approval for use in nutritional supplement applications. The ratio of Surelease to NS Enteric was 85:15 prepared at a 10% final dispersion solids concentration. The NS Enteric powder was hydrated in water for >60 minutes. Surelease was then added to the tank and the dispersion was gently mixed for an additional 30 minutes prior to spraying.

Three trials were conducted in a 24 in. diameter by 13.3 ft. long continuous coater, equipped with a modular spray bar (Thomas Engineering), comprising 24 independently controlled spray guns (ABC type, Schlick), Figures 1 and 2.

**Figure 1. Pan Exterior View**



**Figure 2. Pan Interior View**



The continuous coating pan was equipped with a pneumatically controlled plate at the discharge end of the unit to prevent the substrate from exiting the pan in the initial stages of loading and coating. The pan was loaded with softgels via a weigh belt feeder from the in-feed side of the pan to a total fill of 95 kg. The softgels were tumbled gently during the fill process and then heated to 30° - 33°C. Once the pan was filled, the spray commenced only through the spray gun closest to the discharge end of the pan.

### **Process start-up**

As the softgels closest to the discharge of the pan obtained necessary coating levels (calculated as a fraction of the total amount of coating to be applied across the horizontal pan load), the next spray gun in line began spraying.

This sequencing of the spray guns continued until the softgels at the discharge end of the pan were fully coated and softgels in the remaining section of the pan obtained the equivalent level of coating that would be seen in that location during the continuous mode of processing. This start-up mode was controlled via computerized automatic recipe control. At the conclusion of the start-up mode, the pneumatically controlled plate at the discharge end of the coater was opened allowing the fully coated softgels to enter the discharge zone of the coater. At the same time, the automatic weigh belt feeder began introducing uncoated softgels into the in-feed side of the coater.

### **Process shut-down**

The start-up process was reversed with closure of the discharge end of the pan and reverse sequencing of the spray guns. The aim of this process was to ensure that all of the softgels were consistently coated to the same level throughout the start-up, continuous process and shut-down modes.

The throughput rate of the coater was determined by the speed (kg/hr) of the weigh belt feeder introducing softgels into the coater. Spray rates were adjusted to ensure the target weight gain of coating applied vs. softgel feed rate. The individual trial parameters are listed in Table 1.

**Table 1. Coating Trial Parameters**

	<b>Trial 1</b>	<b>Trial 2</b>	<b>Trial 3</b>
Target weight gain (%)	4	3.5	4
Target throughput rate (kg/hr)	130	200	200
Solids concentration (%) <sup>1</sup>	10	10	10
Spray rate (g/min)	865	1165	1335
Process air flow (cfm) <sup>2</sup>	6800	6800	6800
Inlet temperature (°C)	47	55	57
Exhaust temperature (°C)	35	38	38
Bed temperature (°C)	33	33	33
Product temperature at discharge (°C)	30	33	32
Pan speed (rpm)	10	10	12
1. Nutrateric can be prepared as high as 12% solids concentration depending on pumping systems. At 12%, throughput would be increased by 20%. 2. Typical air flow setting would be 10,000 cfm but was not met due to development laboratory air handler limitations. At 10,000 cfm, typical throughput rate for this product would be >300kg / hour.			

Samples were taken every 5 minutes for the duration of each trial and were tested for acid resistance in simulated gastric fluid (SGF) and disintegration performance in simulated intestinal fluid (SIF). At the completion of trial 3, samples were taken from 4 locations within the pan and as the last of the softgels exited the pan upon discharge.

### **Acid resistance**

Testing of the coated softgels utilized the six-tablet basket-rack disintegration apparatus as described in USP test method 701. Select samples were then transferred to SIF solution for disintegration testing.

### **Results**

The coating trials were free of problems and no issues were encountered with respect to achieving the desired target process conditions. The coated softgels were uniform in appearance with no signs of damage or deformation as a result of the coating process.

### **Acid resistance**

All samples from all three trials were intact with no ruptures after a 60 minute test in SGF. The disintegration times of all samples tested in SIF were within 60 minutes indicating that all samples from the three trials met the disintegration test requirements (Figure 3).

**Figure 3. Disintegration Test Results**

Trial 1		
Sample time	Disintegration time in SGF (n=6)	Disintegration time in SIF (n=6)
0	> 60 min	27.5 min
5	> 60 min	not tested
10	> 60 min	
15	> 60 min	22.0 min
20	> 60 min	not tested
25	> 60 min	
30	> 60 min	29.5 min
35	> 60 min	not tested
40	> 60 min	
45	> 60 min	34.5 min
50	> 60 min	not tested
55	> 60 min	
60	> 60 min	29.5 min

Trial 2		
Sample time	Disintegration time in SGF (n=6)	Disintegration time in SIF (n=6)
0	> 60 min	27.0 min
5	> 60 min	not tested
10	> 60 min	
15	> 60 min	37.0 min
20	> 60 min	not tested
25	> 60 min	
30	> 60 min	31.5 min

Trial 3		
Sample time	Disintegration time in SGF (n=6)	Disintegration time in SIF (n=6)
0	> 60 min	28.0 min
5	> 60 min	not tested
10	> 60 min	
15	> 60 min	29.6
20	> 60 min	not tested
25	> 60 min	
30	> 60 min	27.0 min

Trial 3: End of process		
Sample location in the pan	Disintegration time in SGF (n=6)	Disintegration time in SIF (n=6)
Front (in feed side)	> 60 min	22.0
3 feet from front	> 60 min	18.0
6 feet from front	> 60 min	24.5
9 feet from front	> 60 min	26.0
Final discharge	> 60 min	25.0

Figure 4 shows the appearance of the Nutrateric coated softgels after 60 min. in SGF compared to the uncoated softgels in SGF after 5 minutes.

**Figure 4. Softgel Appearance After Exposure to SGF**



**Uncoated** after 5 minutes  
in simulated gastric fluid



**Nutrateric Coated** after 60 minutes  
in simulated gastric fluid

## CONCLUSIONS

Consistent enteric performance was achieved for each trial with all softgels passing disintegration testing irrespective of whether they were sampled from start-up, continuous mode or shut-down modes in the process. This is in contrast to historical continuous film coating processes where some products had to be discarded during start-up and shut-down stages of the process. Improvements in the continuous coater design with automatic sequencing of spray guns and additional control mechanisms ensured uniform and consistent coating for all softgels from start to finish, minimizing the potential for product loss.

The Nutrateric coating system provided gastric resistance at as low as 3.5% weight gain with a throughput of 200 kg/hour.

The Nutrateric coating provides a GRAS/approved DR system, in contrast to acrylic type polymers, which are not typically approved for nutritional applications.

This ADS has been adapted from the following Supply Side West poster:  
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