



## Effect of PEO Particle Size Distribution on CR Tablets by Direct Compression Method

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Presented at the 2002 AAPS Annual Meeting and Exposition  
Toronto, Ontario, Canada  
November 10-14, 2002

## INTRODUCTION

- Polyethylene oxide (PEO) is a hydrophilic polymer, which is widely used as a rate-controlling excipient in CR matrix tablets.
- The spherical shaped POLYOX™ Water-Soluble Resins have good flow property
- POLYOX Water-Soluble Resins NF grade are available in various particle size grades, in addition to various molecular weight grades.

**Figure 1. SEM of Polyethylene Oxide (POLYOX WSR)**



## OBJECTIVE

To study the effect of particle size distribution of POLYOX Water Soluble Resins on properties of CR tablets prepared by direct compression method. The properties that were studied included the flow properties of bulk powder mixtures, tensile characteristics of the compressed tablets, and the drug release profiles.

## METHODOLOGY

### Materials

POLYOX WSR Coagulant NF grade,  
MW=5,000,000 (The Dow Chemical Company)  
Theophylline anhydrous, sieved through 20 mesh  
(BASF Pharma)  
Avicel PH-102 (FMC)  
Magnesium stearate, NF (Mallinckrodt)

### Fractionating POLYOX Particles

Commercially available POLYOX WSR Coagulant NF was sieved through a 20 mesh (0.841 mm) and 60 mesh (0.250 mm) screen respectively to obtain two batches of sieved samples. These were used throughout the study and were compared with non-sieved material.

### Mixing POLYOX and Other Ingredients

All the ingredients in the tablet formulations (Table I) except magnesium stearate were mixed on a V-blender (Blend Master C41850, Paterson-Kelly) for 10 min. The flow properties of the powder mixtures were measured using a powder flowability analyzer (Aeroflow, Amherst Process Instrument Inc.). Mixing was continued for one more minute after magnesium stearate was added.

## Table 1 Compositions of Three Blends for Direct Compression

<u>Blend 1</u>	
POLYOX (non-sieved)	500 g
Avicel PH 102	500 g
Theophylline	835 g
Magnesium stearate	9.2 g

<u>Blend 2</u>	
POLYOX (thru 20 mesh)	500 g
Avicel PH 102	500 g
Theophylline	835 g
Magnesium stearate	9.2 g

<u>Blend 3</u>	
POLYOX (thru 60 mesh)	500 g
Avicel PH 102	500 g
Theophylline	835 g
Magnesium stearate	9.2 g

## Tablet Preparation

Tablets were prepared on an instrumented press (Manesty Beta Press) equipped with 10.3 mm flat-faced, bevel-edged tooling. The maximum compression force was set at 4000 lb. The press was operated at 100 tablets/min when 8 stations were actually used. The target tablet weight was 500 mg.

## Tablet Properties Testing

Tablets were tested for thickness and hardness. Tablet thickness was measured using a Mitatoyo thickness gauge. Tablet hardness was measured by a tablet hardness tester (VanderKamp VK 200). A total of 10 tablets for each sample were measured. Tablet friability was measured using a Vankel Friabilator.

## Drug Dissolution

Dissolution testing of six tablets from each sample was performed using USP type 2 apparatus (Distek Model 2100B) with UV detector (HP 8452A diode array spectrophotometer).

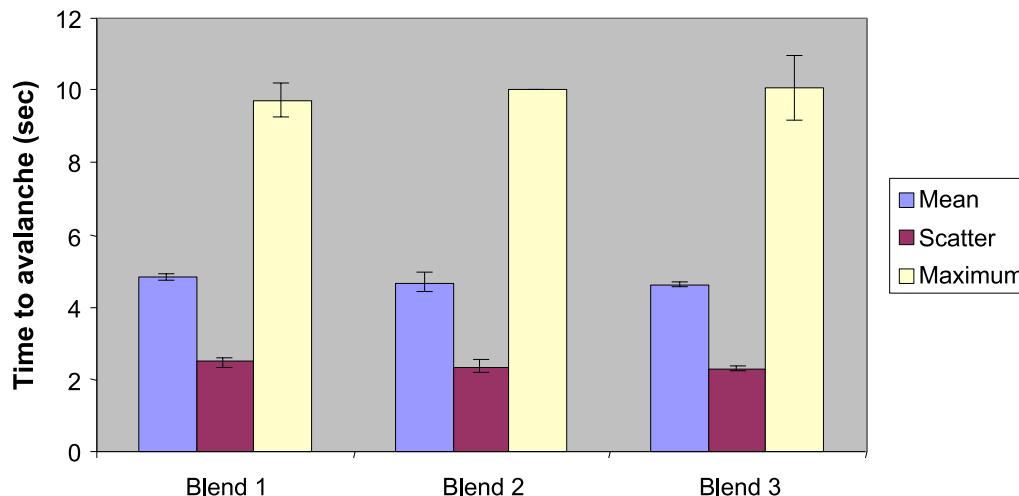
## RESULTS

### Table 2 Fractionation of POLYOX WSR Coagulant NF by Size

<u>Particle Size</u>	<u>Weight%</u>
>20 mesh	0.6
20 ~ 60 mesh	18.5
<60 mesh	80.9

**Figure 2. Flow Properties of Three Blends**

**Aeroflow Data - POLYOX Formulations**



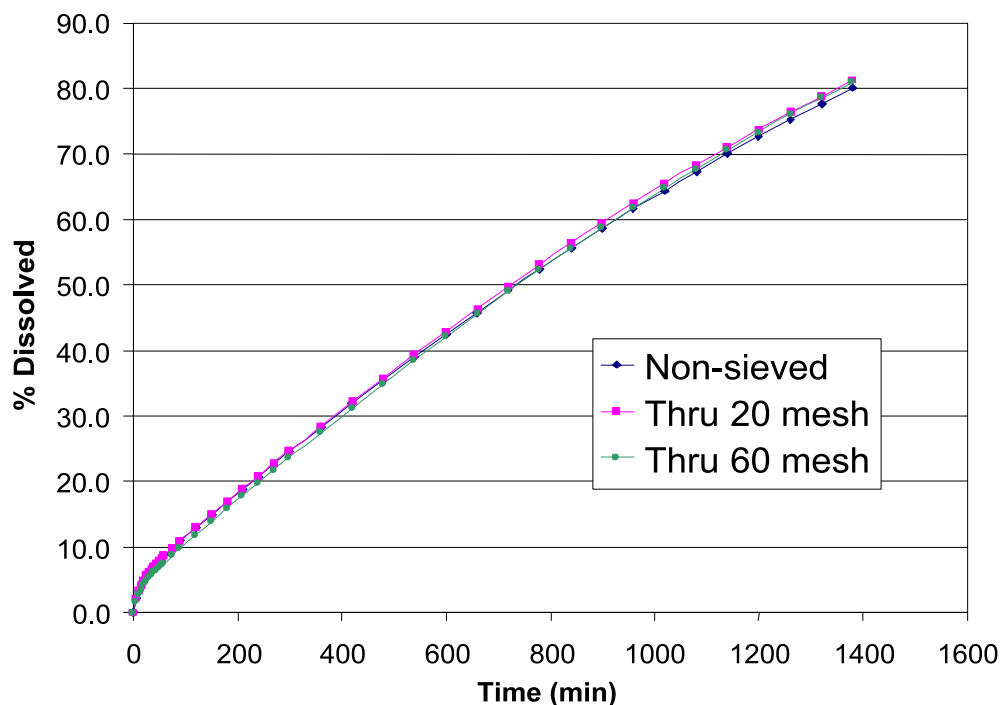
The flow properties of all three blends were identical. All powder mixtures flowed very well during the tableting process.

**Table 3  
Tablet Hardness**

Formulation	Average Hardness	Std. Deviation
Blend 1	23.3 kp	0.817
Blend 2	24.4 kp	0.822
Blend 3	25.8 kp	1.03

The thickness and friability were identical for tablets prepared from all three blends. Tablets prepared from Blend 3, which contained only <60 mesh POLYOX particles, were slightly harder than tablets made from Blend 1 and 2, which contained coarser POLYOX particles.

**Figure 3. Dissolution of Theophylline Tablets  
Effect of POLYOX Particle Sizes**



### Dissolution Results

- All tablets prepared from three blends gave similar drug dissolution profiles.
- Blend 3, which contained only <60 mesh POLYOX resins, showed slightly slower release rate at initial 30 min.
- Based on  $f_2$  similarity factor, the tablets containing non-sieved or <20 mesh POLYOX resins were identical ( $f_2 > 96$ ) throughout the 24 h testing period; while tablets containing <60 mesh or <20 mesh POLYOX resins were slightly different during the first 30 min ( $71 < f_2 < 90$ ), but became identical during the rest of dissolution period ( $f_2 > 90$ ).

### CONCLUSIONS

- Powder blends based on POLYOX Water-Soluble Resins and microcrystalline cellulose showed good flow properties and were suitable to prepare DC tablets.
- POLYOX particle size distribution had little effect on the physical properties of bulk powder mixtures and resulting compressed tablets.
- The impact of POLYOX particle size distribution on the dissolution rate of theophylline (the drug release mechanism was expected to be both erosion and diffusion controlled) was negligible.

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Published November 2002

