



# Development of a Controlled Release Matrix Tablet Containing a Water-Soluble Drug Utilizing Hypromellose and Ethylcellulose

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

## Purpose

To develop a controlled release matrix tablet containing a very water-soluble drug utilizing a combination of hypromellose (HPMC) and finely milled ethylcellulose (EC).

## Introduction

- Matrix tablets containing hydrophilic polymers are a common and commercially successful means of prolonging oral drug delivery.
- A common problem observed with hydrophilic matrix systems containing very water soluble drugs is an initial burst release of the drug.
- To overcome this problem, a finely milled hydrophobic polymer (ETHOCEL\* ethylcellulose FP resin) was added to the matrix system.

## Experimental Methods

### Materials

Material	Lot Number	Source	Concentration in the formulation
METHOCEL* K100 LV Premium (Polymer)	PA27012N22	The Dow Chemical Company	30%
ETHOCEL 10FP Premium	LE06013T10	The Dow Chemical Company	15% and 25%
ETHOCEL 100FP Premium	LD21013T11	The Dow Chemical Company	15% and 25%
Impalpable lactose (Diluent)	MRP686315	Sheffield Products	24.5% to 49.5%
Naproxen sodium	9SY004	Pharmaceuticals Fine Chemicals, S.A.	40%
Aspirin	RD0944	Spectrum Chemicals	40%
Diphenhydramine HCl	55070	Kongo Chemical Company	20%
Magnesium stearate (Lubricant)	2256KTM4	Mallinckrodt	0.50%

**Table I. Experimental Conditions for Granulation Studies**

Granulated Formulations:				
<sup>1</sup> binder added using fullcone spray nozzle at 30 g/min and aim droplet size of 20 micron				
Formulations	Experiment	Post Added Material	Water added (grams)	Torque (n-m) End Point
Diphenhydramine HCl	1A	ETHOCEL 10FP (15%)	300	2.2
	2A	ETHOCEL 10FP (25%)	330	2.5
	1B	ETHOCEL 100FP (15%)	300	2.2
	2B	ETHOCEL 100FP (25%)	220	2.5
Naproxen Sodium	1A	ETHOCEL 10FP (15%)	415	2.3
	2A	ETHOCEL 10FP (25%)	459	2.4
	1B	ETHOCEL 100FP (15%)	415	2.3
	2B	ETHOCEL 100FP (25%)	459	2.4
Aspirin	1A	ETHOCEL 10FP (15%)	395	2.2
	2A	ETHOCEL 10FP (25%)	383	2.5
	1B	ETHOCEL 100FP (15%)	395	2.2
	2B	ETHOCEL 100FP (25%)	383	2.5

<sup>1</sup> - end point was determined by torque values

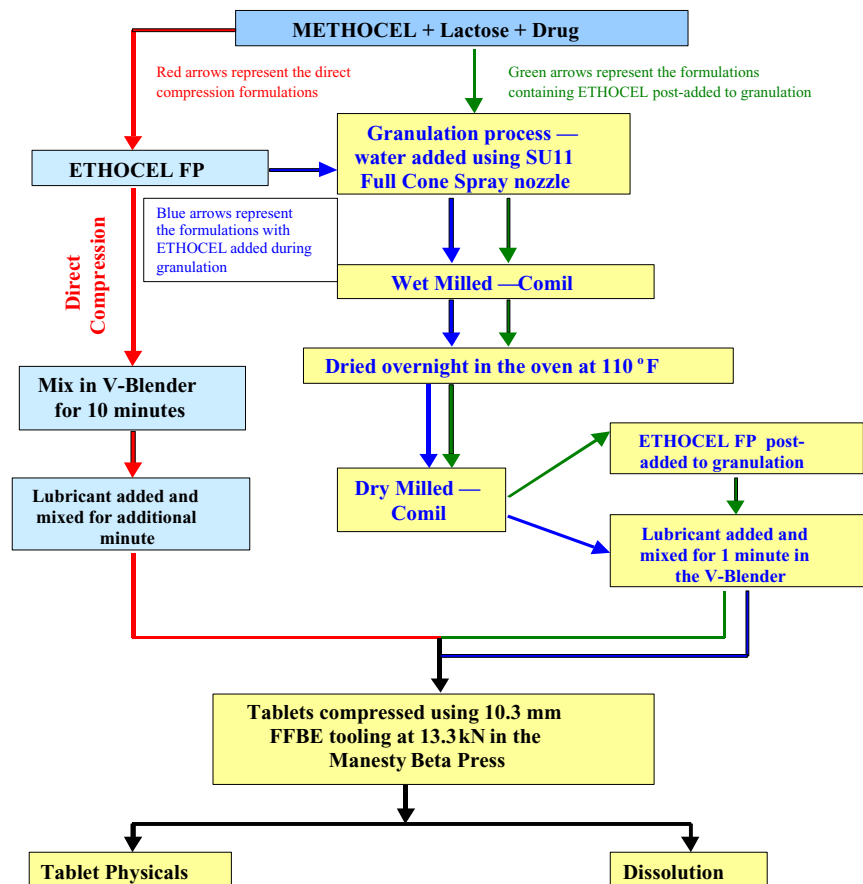
## Equipment

- Granulations were performed in a laboratory scale (6L) Powrex vertical high shear granulator model FM-VG-10.
- The nozzle SU11 Full Cone, was obtained from Spraying Systems Co., Wheaton, IL (Figure 1).
- Comil, Model #1975, Quadro Engineering Corporated
- Instrumental Manesty Beta press using 10.3 mm FFBE tooling at 13.3 kN.
- Dissolutions were performed using USP Type 2 apparatus (Distek Model 2100) with UV detection (HP 8452 diode array spectrophotometer).
- Key International Hardness Tester, Model– HT 500

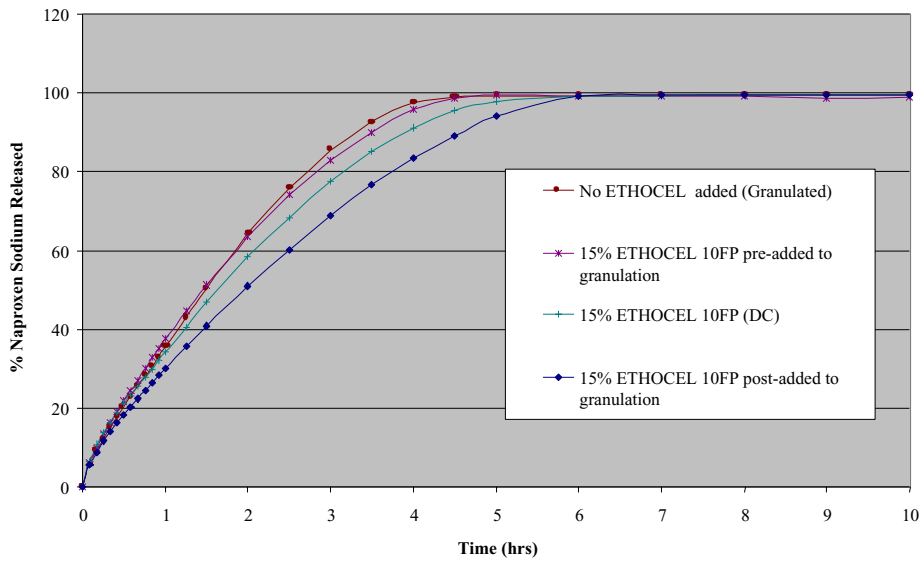
## Figure 1. Full Cone Nozzle



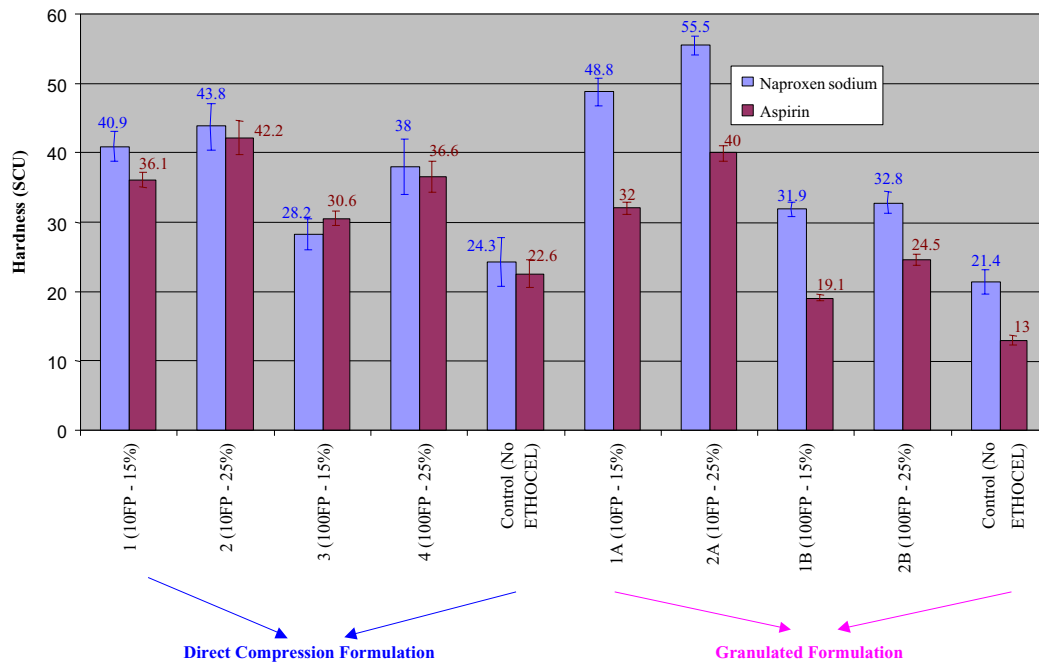
## Figure 2. Formulation Process



**Figure 3. Comparison of Release Profiles with ETHOCEL 10 FP Pre and Post-Added to Granulation**

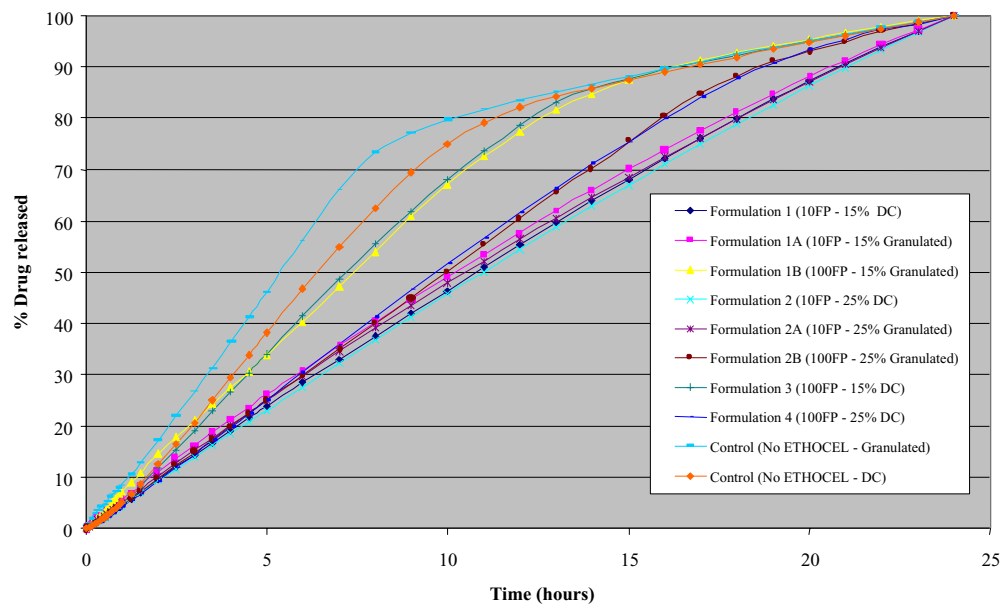


**Figure 4. Tablet Crushing Strength- Summary Naproxen sodium and Aspirin (40%), ECFP Post Added**

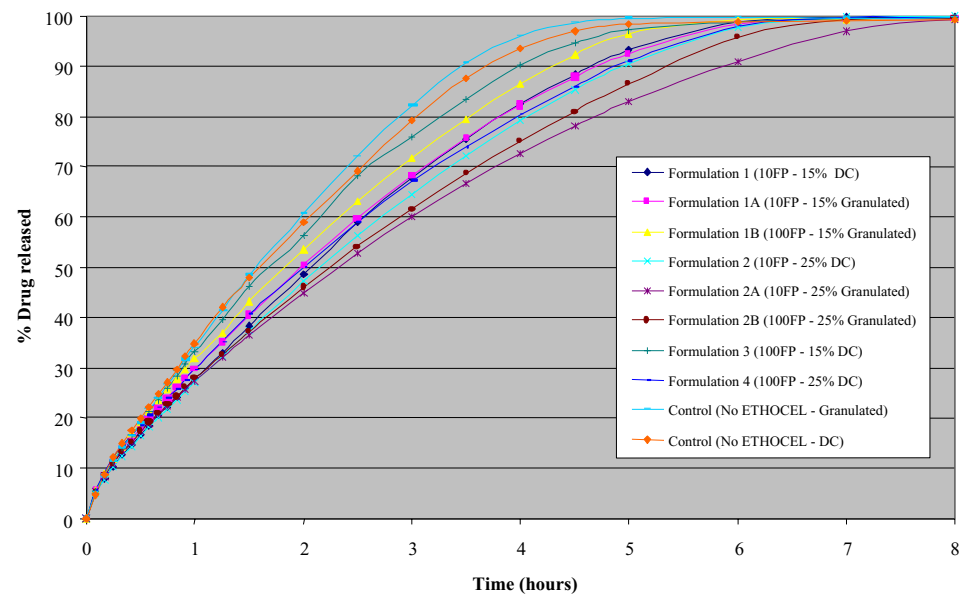




**Figure 7. Dissolution Data- Summary  
Aspirin (40%), ECFP Post Added**



**Figure 8. Dissolution Data- Summary  
Naproxen sodium (40%), ECFP Post Added**



## **Preliminary Experiments**

- The EC FP polymer was initially added with the other materials before granulating.
- The tablets did not have any improved performance compared to the control and thus the EC FP was post-added for the remaining experiments (Figures 2 and 3).

## **Conclusions**

- For all 3 water soluble drugs, the presence of the EC-FP increased the tablet hardness values and typically reduced the friability. EC STD 10 Prem. FP produced the hardest tablets at both polymer levels.
- The post addition of the EC STD 10 Prem. FP at 25% provided the slowest release for all three actives.

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Published November 2002

