



## The Influence of Starch<sup>®</sup> on Drug Release from HPMC Matrices

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### Purpose

To investigate the influence of partially pregelatinized starch (Starch 1500<sup>®</sup>, Colorcon), in comparison to microcrystalline cellulose (MCC) and lactose, on drug release from hydroxypropylmethylcellulose (HPMC) sustained release matrix formulations.

### Materials and Methods

A model formulation was developed containing:

- 30% drug, 49.25% filler
- 20% HPMC (Methocel<sup>®</sup> K4M, The Dow Chemical Company, Midland, MI, USA)
- 0.5% fumed silica (Aerosil<sup>®</sup> 200, Degussa AG, Dusseldorf, Germany)
- 0.25% magnesium stearate (Peter Greven, Venlo, Netherlands)

Theophylline (Knoll AG, Ludwigshafen, Germany), poorly water-soluble and chlorpheniramine maleate (Avocado Research Chemicals Ltd., Lancas., UK), freely water-soluble, were used as model drugs.

Starch 1500<sup>®</sup> inclusion into HPMC matrices was evaluated against other commonly used fillers such as MCC (Avicel<sup>®</sup> PH102, FMC, Brussels, Belgium), water-insoluble, and lactose (Fast-Flo<sup>®</sup> #316, Foremost Farms, Wisconsin, USA), water-soluble.

Tablets (333 mg) containing 100 mg drug were compressed using a Piccola rotary 10-station tablet press, with 9 mm concave tooling.

Dissolution tests were performed using 6 tablets of the same mechanical strength (10-14 kp) in a Caleva ST7 dissolution tester, USP apparatus II (paddle), in water or buffer (pH = 7.4) at 100 rpm.

### Results

#### Ejection Force and Tablet Weight Variation

All formulations, regardless of type of excipient, had good flow and tablet weight variations for all tested batches were found to be less than 1%.

Table 1 shows the ejection forces for the formulations containing theophylline (TP) or chlorpheniramine maleate (CPM). Formulations with lactose produced the highest ejection forces. On the other hand, Starch 1500 due to its inherent lubricity produced the lowest ejection forces.

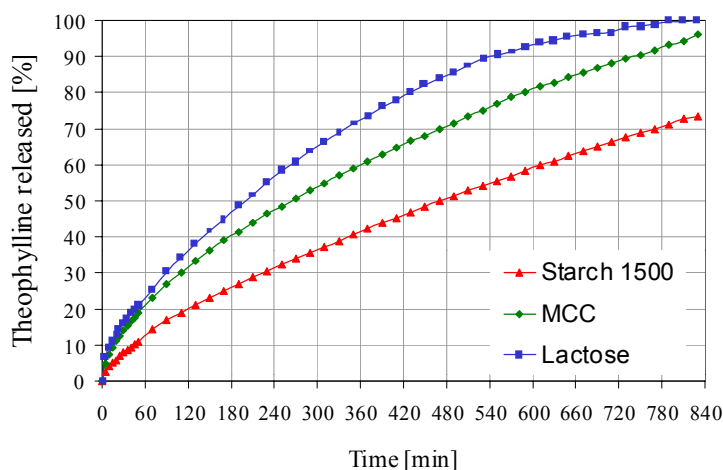
**Table 1 - Ejection Forces**

Drug	Filler	Ejection Force (N)
TP	Starch 1500	82 ± 3
TP	lactose	238 ± 9
TP	MCC	96 ± 4
CPM	Starch 1500	374 ± 22
CPM	lactose	1079 ± 48
CPM	MCC	530 ± 27

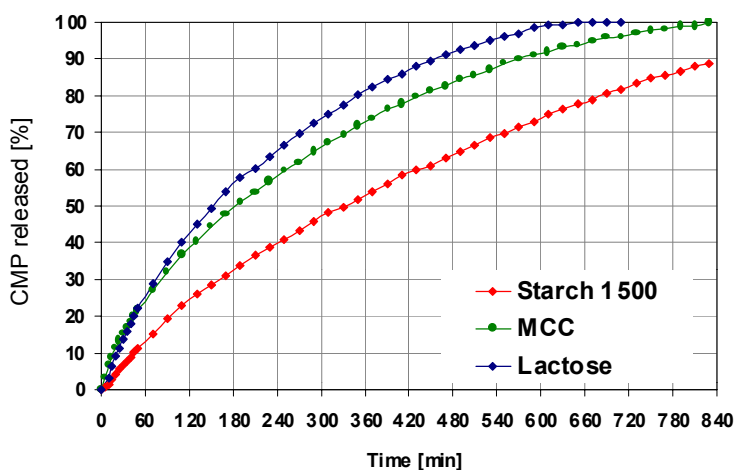
### Drug Release in Water

Figures 1 and 2 show that Starch 1500 addition resulted in a slower release of TP and CPM respectively as compared to MCC and lactose formulations.

**Fig. 1 - Effect of Different Fillers-Binders on TP Release from HPMC Matrices**



**Fig. 2 - Effect of Different Fillers-Binders on CPM Release from HPMC Matrices**



Dissolution profiles were compared using  $f_2$ , a similarity factor (Federal Register, 1995; Moore & Flanner, 1996). An  $f_2$  value between 50 and 100 suggests that the two dissolution profiles are similar.

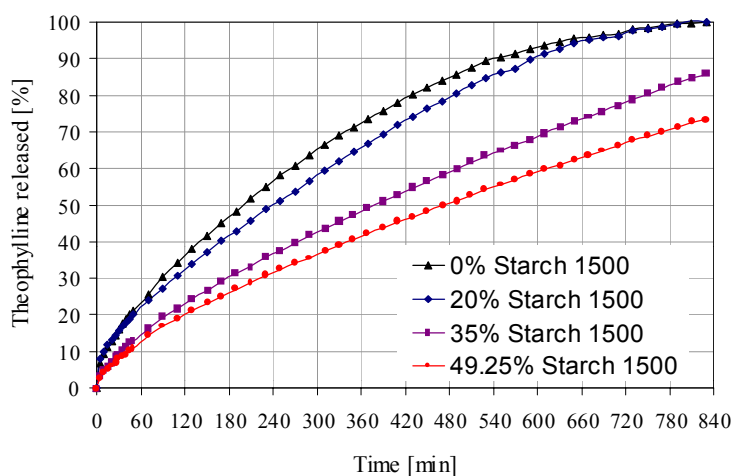
The results in Table 2 indicate that the release of both drugs from formulations containing Starch 1500 were different to those containing MCC or lactose.

Examination of dissolution curves (Figures 3 and 4) of the drugs TP and CPM with different Starch 1500 quantities shows that as the Starch 1500 fraction increases, the dissolution of the drugs significantly decreases.

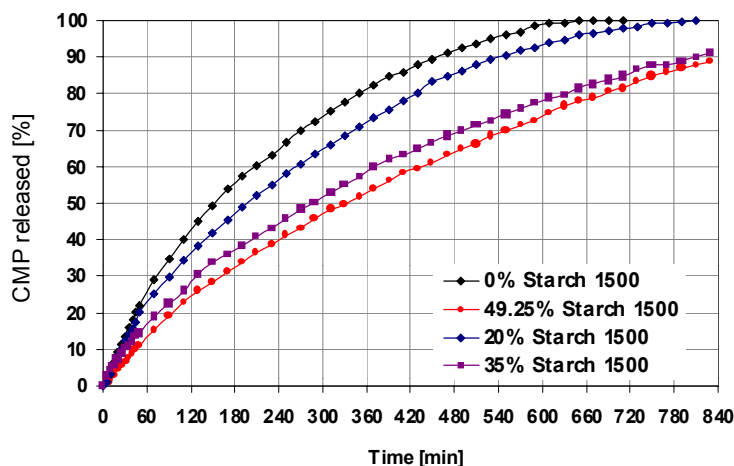
**Table 2 - F<sub>2</sub> values**

Drug	Filler		F <sub>2</sub>	Dissolution profiles
	Form. A	Form. B		
TP	Starch 1500	lactose	34	different
TP	Starch 1500	MCC	44	different
TP	lactose	MCC	54	similar
CPM	Starch 1500	lactose	36	different
CPM	Starch 1500	MCC	42	different
CPM	lactose	MCC	63	similar

**Fig. 3 - Effect of Starch 1500 levels on TP Release from HPMC Matrices**



**Fig. 4 - Effect of Starch 1500 levels on CPM Release from HPMC Matrices**



The study showed that using lactose in place of Starch 1500 in the formulations resulted in a faster drug release profile. Thus the effect seen with Starch 1500 is not just a spatial effect due to the presence of any filler, but Starch 1500 actively contributes to the dissolution kinetics.

## Influence of the Dissolution Medium on Drug Release

Figures 5 and 6 show that drug release from matrices containing Starch 1500 in phosphate buffer (pH=7.4) was slower than when lactose or MCC was used.

Fig. 5 - TP Release from HPMC Matrices

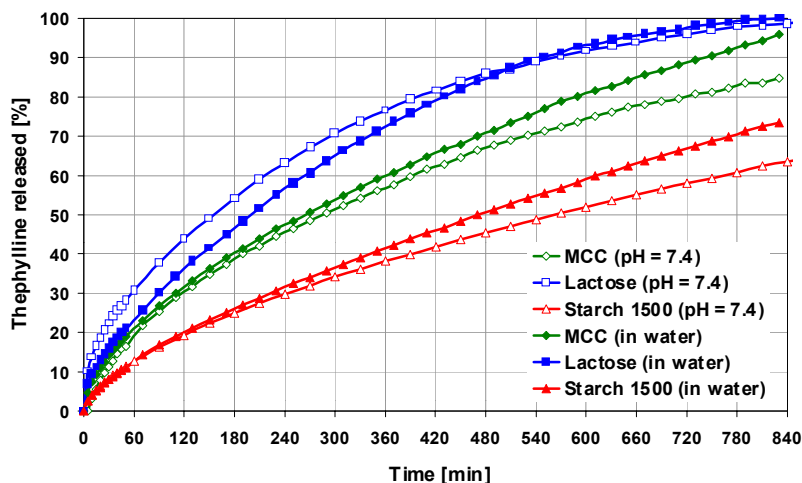
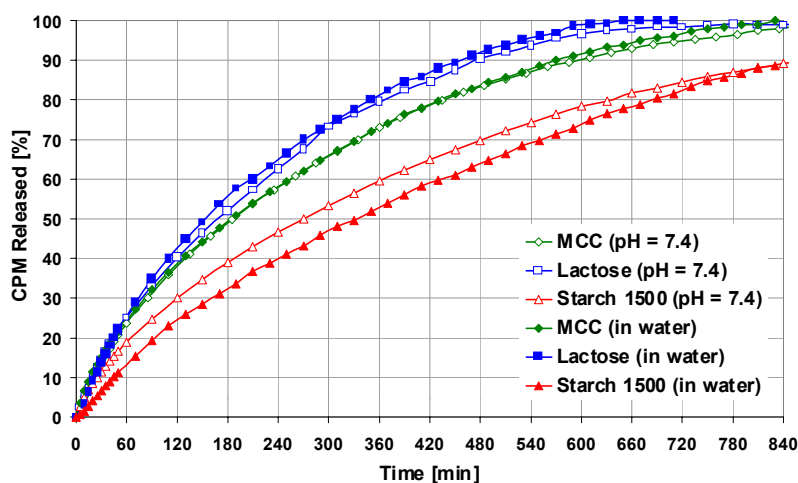


Fig. 6 - CPM Release from HPMC Matrices



## Conclusions

- All matrix formulations regardless of type of filler resulted in a slow drug release for both drugs. However, when Starch 1500 was used, drug release was significantly decreased compared to formulations containing MCC or lactose.
- These results may suggest that Starch 1500 is not an inert filler in HPMC matrices, but it actively contributes to the mechanism of drug release causing a decrease in drug release rate.
- It was shown that for both drugs, increasing concentrations of Starch 1500 (20, 35 and 49.25%w/w) in the formulations caused a decrease in their release profiles.
- Drug release from matrices containing Starch 1500 in phosphate buffer (pH=7.4) was slower than when lactose or MCC was used.

## References

- Federal Register, Food and Drug Administration, Vol.. 60, No.230, 1995, p.61642.
- Moore, J.W. and Flanner, H.H., *Pharm. Tech.*, 20(6) (1996) 64-74.

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