



## The Effect of STARCH 1500® On The Stability of Aspirin Tablets Stored Under Accelerated Conditions

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### Objectives

Aspirin is a moisture sensitive drug and can hydrolyze into acetic and salicylic acids. Hydrophilic excipients can have adverse effects on aspirin under accelerated stability conditions. This study examines the effect of Starch 1500, partially pregelatinized starch, in combination with microcrystalline cellulose and two hydrophilic superdisintegrants on the stability of aspirin 81 mg tablets.

### Materials and Equipment

Aspirin 1040, (Aspirin USP 40-mesh crystals) from Rhodia was used in the study. The excipients included in the study were partially pregelatinized corn starch, Starch 1500®, Colorcon; Microcrystalline Cellulose, Emcocel® 50m, Penwest; Sodium starch glycolate, Explotab®, Penwest; Croscarmellose sodium, Ac-Di-Sol®, FMC; Stearic acid N.F., Purified vegetable grade powder, Oleotec Ltd.

The tablets were packaged for stability using 85cc foil-sealable HDPE bottles, Drug Plastics and Glass Co.

The ingredients were dry blended in an 8-qt. twin-shell blender (Patterson-Kelley Co.). The tablets were compressed on an instrumented 10-station Piccola rotary press (Riva Co.) with 7.1mm standard concave tooling. Tablet Hardness was measured using a Multichek™ tester (Erweka). A Dissolution Test station, VK7010, apparatus I, (VanKel) with a UV spectrophotometer (Varian) was used for drug release testing. An Alliance 2690 HPLC (Waters Corp.) was used for free salicylic acid determinations.

### Methods

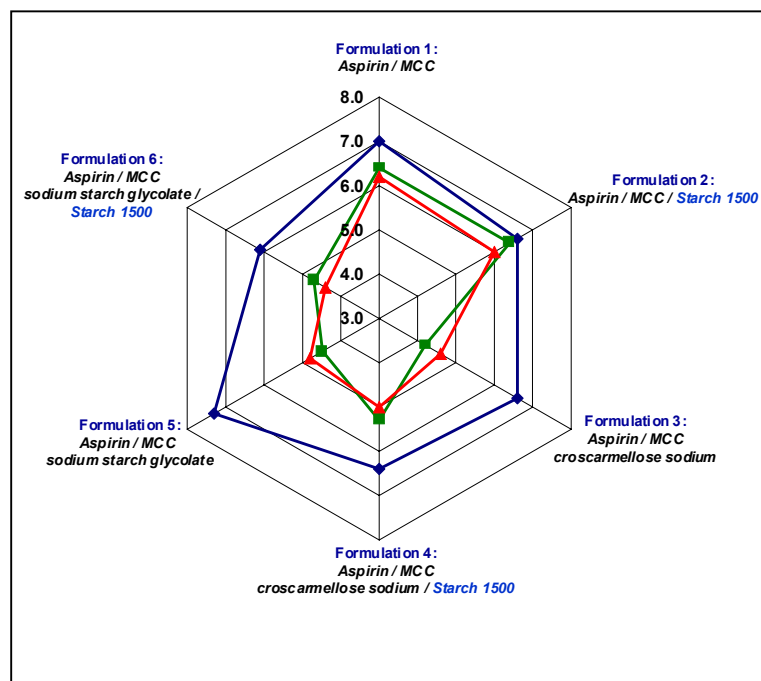
The following six formulations were dry blended for 15 minutes in the twin-shell blender. Each formulation was then compressed to 162.0 mg total tablet weight with a tablet breaking force target of 6 - 7 kp.

Ingredients	Formulations (% w/w)					
	1	2	3	4	5	6
Aspirin	50.0	50.0	50.0	50.0	50.0	50.0
Stearic acid	0.5	0.5	0.5	0.5	0.5	0.5
Microcrystalline cellulose	49.5	29.5	46.5	26.5	46.5	26.5
Starch 1500	-	20.0	-	20.0	-	20.0
Croscarmellose sodium	-	-	3.0	3.0	-	-
Sodium starch glycolate	-	-	-	-	3.0	3.0

Samples of the resultant tablets were packaged in foil-sealed HDPE bottles and stored in a 40 °C/75% RH chamber for six months.

## Stability Results

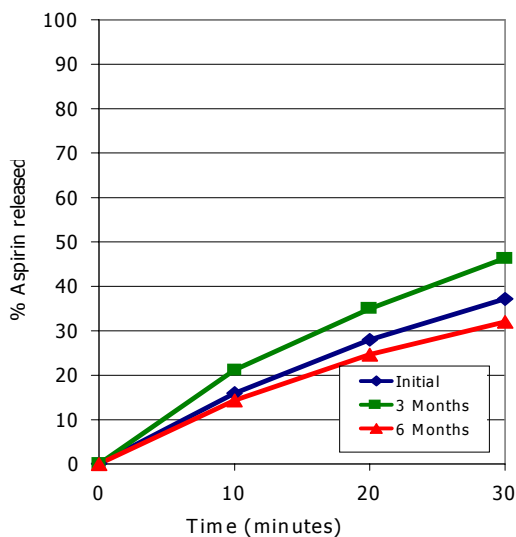
### Tablet breaking force (kp)



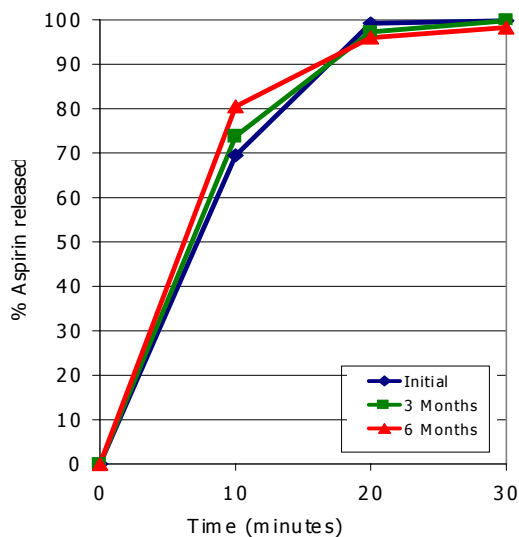
At six months, the tablets containing just aspirin and MCC lost 11.43% in tablet breaking force while the tablets containing the Starch 1500 / MCC combination showed the least decrease in breaking force with just a 9.0% loss. The use of either the croscarmellose sodium or sodium starch glycolate in combination with MCC resulted in a 30.3% and 34.24% loss in tablet mechanical strength respectively. When the same levels of superdisintegrant were used in the tablets that combined Starch 1500 and MCC, the % loss in tablet breaking force was reduced.

## Dissolution Stability

Formulation 1:  
Aspirin / MCC



Formulation 2:  
Aspirin / MCC / Starch 1500

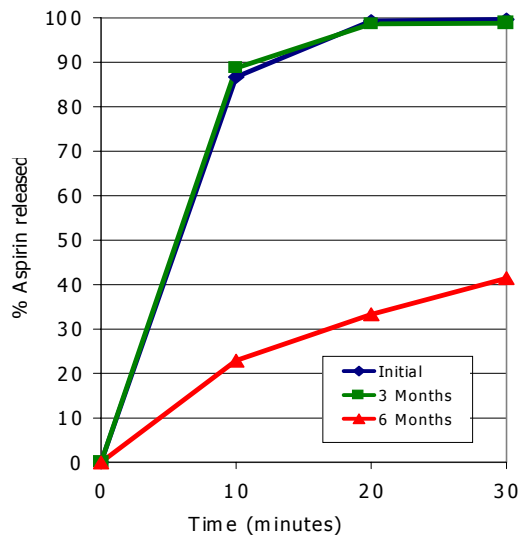


The tablets containing only microcrystalline cellulose (MCC) and aspirin exhibited slow dissolution initially and at the three and six month time points. The tablets failed the USP release criteria of not less than 80% aspirin released in 30 minutes. No significant change in release characteristics was observed over the 6 month stability period.

The addition of Starch 1500 to the formulation resulted in dissolution that exceeded the USP requirements at all time points.

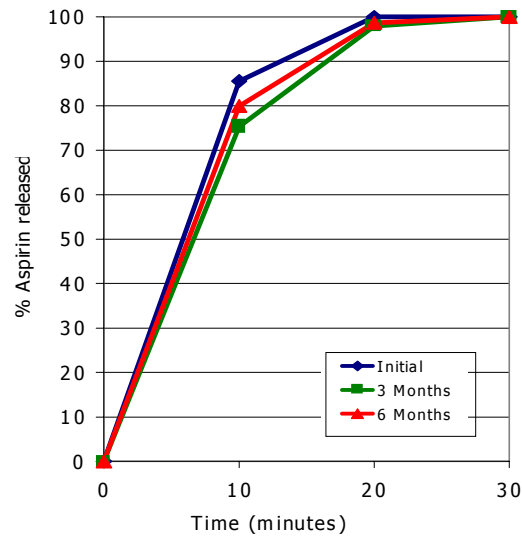
### Formulation 3:

Aspirin / MCC  
croscarmellose sodium



### Formulation 4:

Aspirin / MCC  
croscarmellose sodium / **Starch 1500**

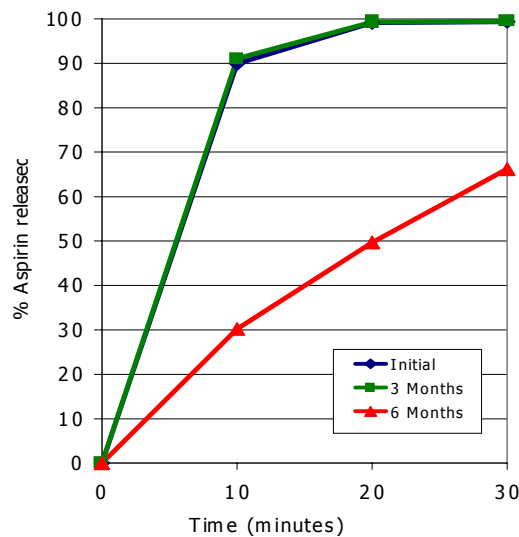


The tablets containing aspirin and MCC with croscarmellose sodium exhibited significantly slower release at six months compared to the initial and three month time points. Undispersed tablet fragments were found in the baskets upon completion of the dissolution test indicating a reduction in disintegrant effectiveness.

The addition of Starch 1500 to this formulation resulted in tablets that exhibited rapid release of aspirin independent of storage times or conditions.

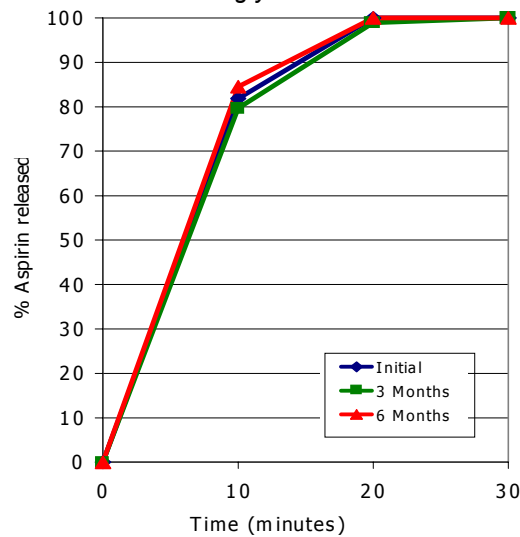
### Formulation 5:

Aspirin / MCC  
sodium starch glycolate



### Formulation 6:

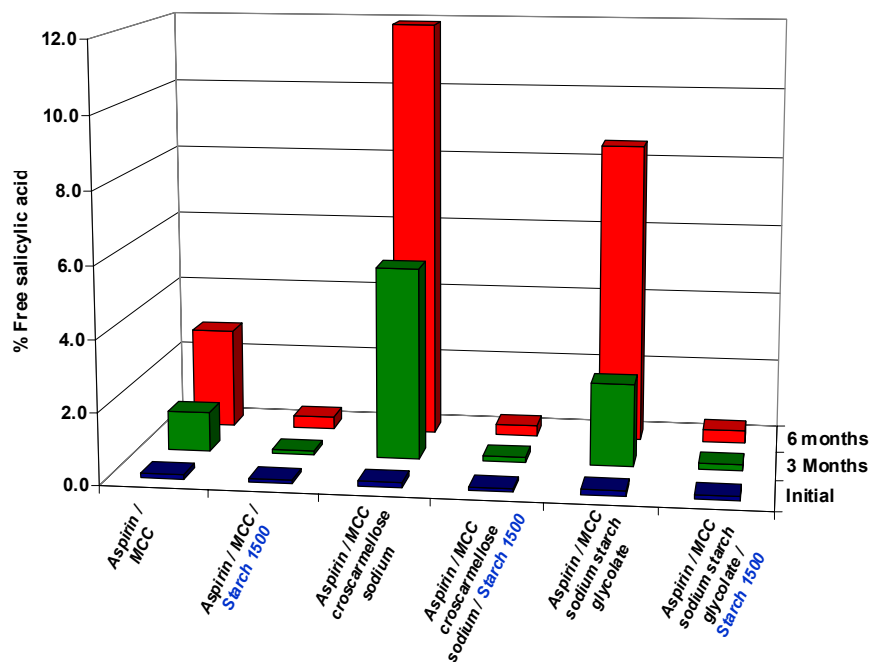
Aspirin / MCC  
sodium starch glycolate / **Starch 1500**



As with the tablets containing croscarmellose sodium, the tablets containing aspirin and MCC with sodium starch glycolate also exhibited rapid dissolution initially and at the three month time points. The release of aspirin from the tablets stored for six months was much slower and failed the USP release criteria. Again, undispersed tablet fragments were found in the baskets upon completion of the dissolution tests for the six month samples.

The addition of Starch 1500 to this formulation also resulted in tablets that exhibited rapid release of aspirin independent of storage times or conditions.

## Free Salicylic Acid Stability



After 6 months, only the tablets that contained Starch 1500 in the formulation had acceptably low levels of free salicylic acid. The use of MCC alone with the aspirin or with either of the superdisintegrants resulted in substantial degradation.

### Conclusions

Starch 1500 has a lower propensity for moisture absorption than either croscarmellose sodium or sodium starch glycolate and does not rely solely on water uptake and swelling as a mechanism for disintegration. This may account for some of the positive effects seen with its use in these formulations. The data suggest that Starch 1500 may be inhibiting water activity within the formulation and retarding moisture interaction with the aspirin. The use of Starch 1500 provided for exceptional stability in this moisture sensitive application. Most noteworthy was the effect of Starch 1500 in reducing or eliminating the deleterious effects of other excipients in the study.

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