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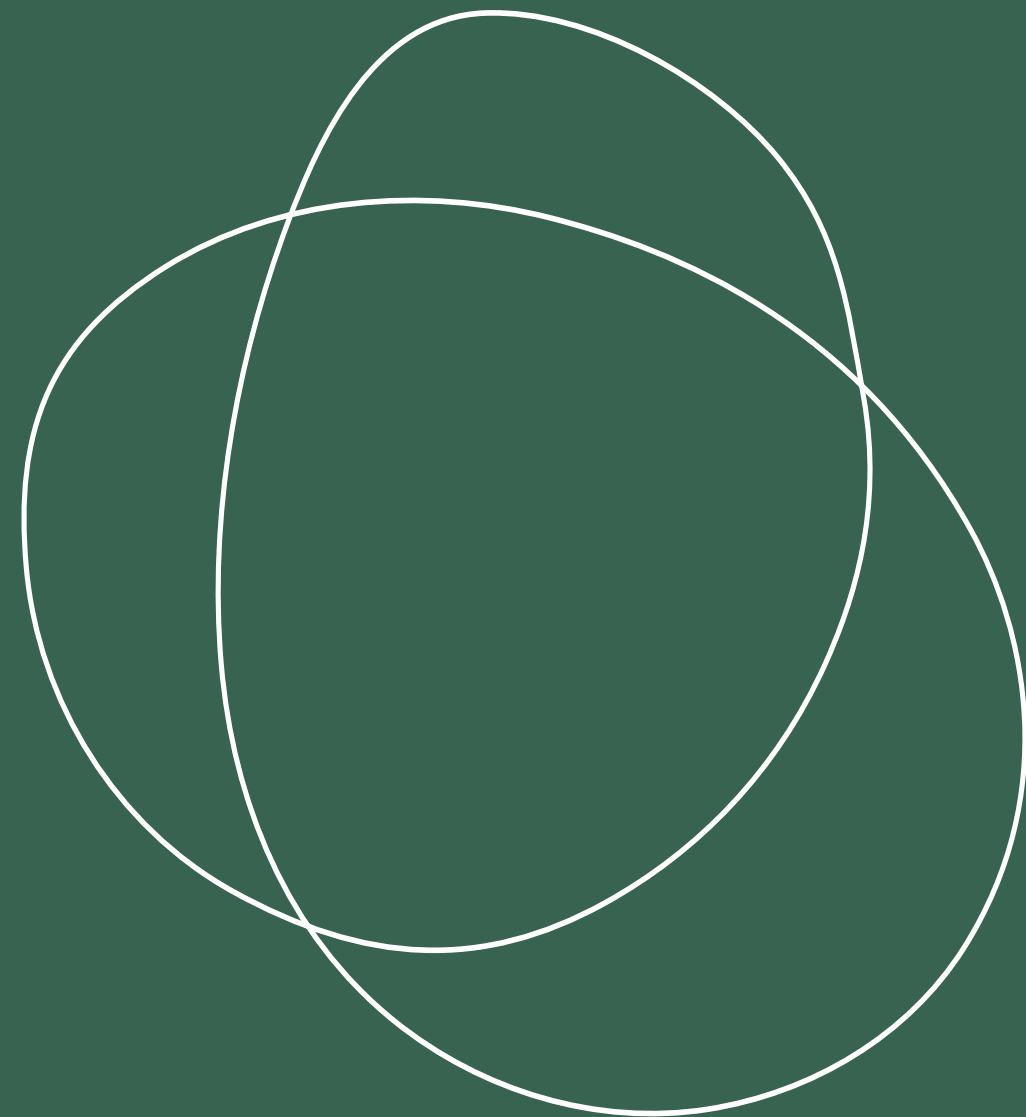
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TECHNICAL BULLETIN

Impact of cellulose source on properties and disintegration performance of croscarmellose sodium

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IMPACT OF CELLULOSE SOURCE ON PROPERTIES AND DISINTEGRATION PERFORMANCE OF CROSCARMELLOSE SODIUM

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Introduction

Croscarmellose sodium (XL-CMC) is a widely used superdisintegrant in the pharmaceutical industry. Its role is to accelerate the disintegration rate of oral solid dosage forms by wicking (water penetration into the tablet through capillary action) and swelling (expansion of particles through water absorption). The effectiveness of the wicking and swelling mechanisms is related to the molecular weight (MW) of the croscarmellose which is dependent on the MW of the cellulose source.

The two most common sources of commercial cellulose are cotton linters and wood pulp. Croscarmellose sodium products have traditionally been based on cotton linters since they yield cellulose with a higher MW compared to wood pulp. Since most cotton comes from genetically modified seeds, it is not feasible to certify cotton linters as a non-GMO source of cellulose. Wood pulp is a non-GMO raw material, so it is exempt from GMO labeling requirements. Wood pulp is therefore the preferred cellulose source for finished products needing non-GMO regulatory status.

Objective

The objective of this study was to evaluate croscarmellose sodium grades made from cotton linters and wood pulp. Key physical properties like water uptake capacity and water soluble content are compared. Performance of each grade as a superdisintegrant in model drug formulations is also evaluated to determine whether differences in physical characteristics impact functionality.

Experimental

Materials

Ac-Di-Sol® SD-711 is the standard grade of cotton linter-based croscarmellose sodium NF offered by FMC BioPolymer. Two lots of Ac-Di-Sol® SD-711 were evaluated along with 3 lots of Ac-Di-Sol® SDW-802, an optimized wood pulp grade of XL-CMC also from FMC BioPolymer.

Methods

Powder property analysis

- USP/NF required analysis – All tests required by NF monograph on XL-CMC, such as pH, loss on drying (LOD), total sodium chloride and sodium glycolate content, heavy metals, water soluble (WS), settling volume (SV), and degree of substitution (DS), were performed according to NF defined methods.
- Analysis beyond NF requirements – Other important physical-chemical properties of the products were also studied. This includes molecular weight, water uptake rate and capacity, and swelling characteristics.

Tablet preparation and characterization

- Tablet preparation – formulation and tableting information are shown in Figure 1 on the following page. In addition to these direct compression formulas, wet granulation formulas were also evaluated.
- Tablet characterization – tablet crushing strength along with tablet weight and dimensions were determined. Disintegration times of tablets were conducted at 37 +/- 0.5°C in a medium of distilled water. Dissolution testing was performed per USP reference standards.

Results and Discussion

Powder properties

Figure 2 shows the molecular weights (MW) of the samples. As expected, the MW results of Ac-Di-Sol® SD-711 samples are higher since the MW of the starting cellulose source is higher. Several other differences in powder properties can be directly attributed to the differences in MW of the two products.

Figure 3 shows water uptake rate and capacity. Soluble CMC becomes insoluble but swellable after crosslinking, the crosslinking density is indirectly reflected in DS level. At the same DS level, XL-CMC with higher MW (Ac-Di-Sol® SD-711) has slightly higher

Figure 1. Formulation and tableting information for direct compression formulations.

	Soluble		Matrix		Insoluble	
	API	Soluble	API	Soluble	API	Soluble
400 mg tablets Compression forces: 4, 8, 12, 16 kN	Lactose	q.s.	Dicalcium phosphate	q.s.	Alubra™ SSF	2%
	Alubra™ SSF	2%	Alubra™ SSF	2%	CPM*	1%
	CPM*	1%	CPM*	1%	Ac-Di-Sol®	2, 3, 5%
	Ac-Di-Sol®	2, 3, 5%	Ac-Di-Sol®	2, 3, 5%	Total (%)	100%
	Total (%)	100%	Total (%)	100%		
500 mg tablets Compression forces: 5, 10, 15, 20 kN	Lactose	q.s.	Dicalcium phosphate	q.s.	Alubra™ SSF	2%
	Avicel® PH-102	10.1%	Avicel® PH-102	10.1%	Alubra™ SSF	2%
	Alubra™ SSF	2%	Alubra™ SSF	2%	Ibuprofen DC85	47.1%
	Ibuprofen DC85	47.1%	Ibuprofen DC85	47.1%	Ac-Di-Sol®	2, 3, 5%
	Ac-Di-Sol®	2, 3, 5%	Ac-Di-Sol®	2, 3, 5%	Total (%)	100%
Total (%)	100%	Total (%)	100%			

*CPM is Chlorpheniramine Maleate, a soluble antihistamine.
Instrumented Stokes B2 Rotary Press, 7/16" standard concave tooling.

water uptake capacity than XL-CMC with lower MW (Ac-Di-Sol® SDW-802), but similar water uptake rate (or similar bursting power).

Figure 4 shows water solubles content. The lower MW of wood pulp material inherently generates CMC that has more water solubles. Therefore the water solubles % is generally higher for Ac-Di-Sol® SDW-802 than for Ac-Di-Sol® SD-711. All results were well below the compendia specification of 10.0% maximum.

Figure 5 shows degree of substitution. A higher level of cross-linking is required with Ac-Di-Sol® SDW-802 to reach the same total DS as Ac-Di-Sol® SD-711. The higher level of crosslinking results in a lower settling volume for the wood based material (Figure 6).

Figure 2. MW of croscarmellose samples.

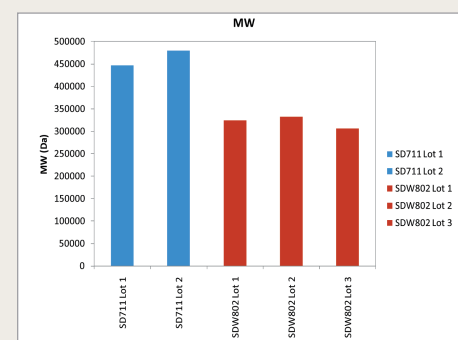


Figure 4. Water solubles content.

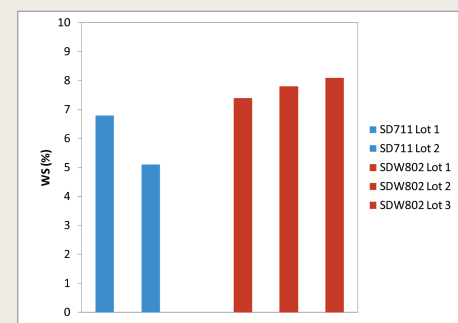


Figure 3. Water uptake rate and capacity.

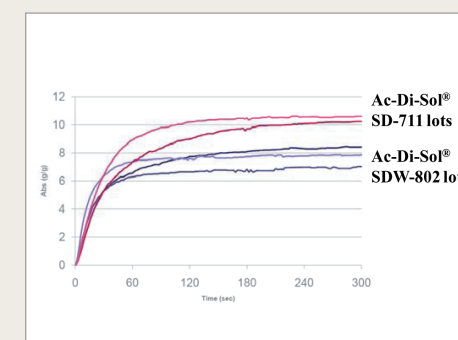
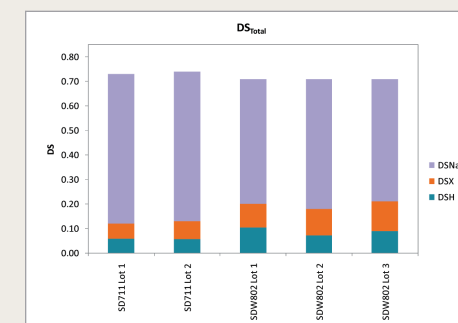


Figure 5. Degree of substitution.



Finally, Figure 7 shows pH results. To reach the same DS level, more acid is required in process to thermally crosslink wood pulp based CMC. This results in a lower pH for Ac-Di-Sol® SDW-802.

Figure 6. Settling volume.

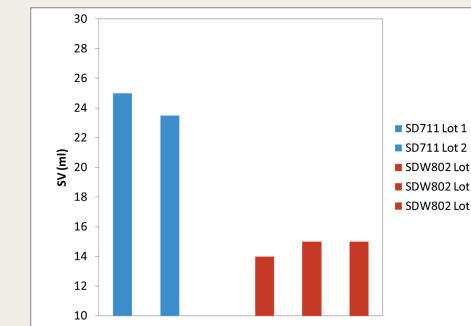
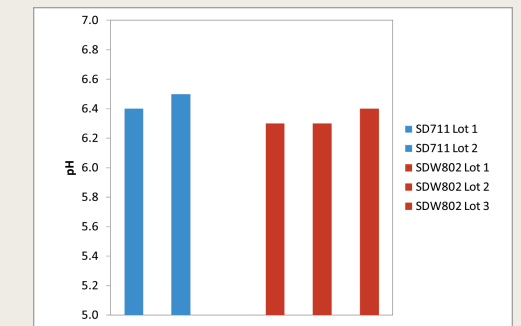


Figure 7. pH.



Tablet Properties

The data shown in the figures below is representative of results at all concentrations (0.5%-5%) and in all model formulations. Disintegration times (Figure 8) and dissolution (Figure 9) were similar between Ac-Di-Sol® SD-711 and SDW-802. The differences in physical characteristics had no noticeable impact on disintegration performance. Tablet hardness and friability were comparable in all formulations.

Figure 8. Disintegration time of lactose/CPM model.

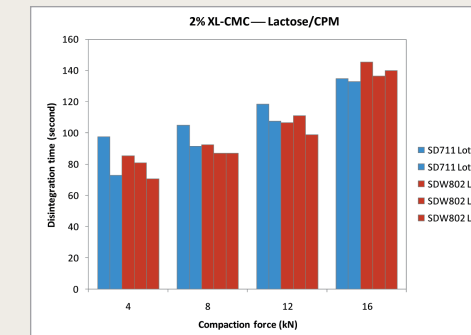
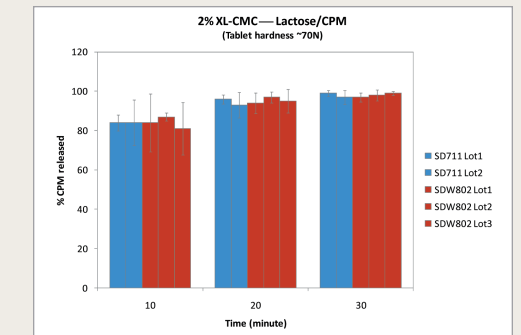


Figure 9. Dissolution of lactose/CPM model.



Conclusions

This study shows that croscarmellose sodium based on wood pulp has inherent physical differences compared to material based on cotton linters. These differences include lower molecular weight, increased water solubles, slightly decreased pH (due to more acid being required for cross-linking), decreased water uptake capacity and decreased settling volume (at the same DS level).

Despite these differences, Ac-Di-Sol® SDW-802 performs similarly to Ac-Di-Sol® SD-711 at standard usage levels in a variety of direct compression and wet granulation model formulations. This is likely due to the high disintegration bursting power that Ac-Di-Sol® offers, through optimization of product morphology and strict control of the manufacturing process.

It is also important to note that Ac-Di-Sol® SDW-802 utilizes only thermal cross-linking (as opposed to various forms of chemical cross-linking) in order to limit impurities and assure the highest levels of quality.

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