

FMC is the world leader in quality excipients for pharmaceuticals and supplements.

As the world's foremost manufacturer of high-quality pharmaceutical and supplement excipients, FMC has vast experience in the areas of formulation and processing. When customers use Ac-Di-Sol[®], they get the benefit of this unparalleled experience, in the form of exceptional technical support.

FMC's technical service professionals perform a number of vital tasks for customers, including conducting functionality, stability, and other tests, helping customers find solutions to their processing problems, conducting training for customer personnel, and providing access to comprehensive reference libraries.

For further information on FMC's outstanding products and services, contact us at 1-800-526-3649 or go to our website at www.fmc.com

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FMC BioPolymer



Why settle for super
when you can have superior?



FMC BioPolymer



 Ac-Di-Sol[®]
The superior disintegrant.

High-quality Ac-Di-Sol® offers all the advantages of a superior disintegrant.

Ac-Di-Sol® croscarmellose sodium is an internally cross-linked sodium carboxymethyl cellulose (NaCMC) that aids in the disintegration and dissolution of pharmaceutical and dietary supplement tablets, capsules, and granules.

Originally created to solve formulators' problems and improve bioavailability of a drug via faster disintegration and dissolution, Ac-Di-Sol® is now widely recognized as the standard by which today's superdisintegrants are judged.

Ac-Di-Sol® exhibits consistent disintegrative functionality due to its excellent water uptake and rapid swelling properties. The result is a high-quality superdisintegrant whose faster disintegration and dissolution at low use levels and unmatched stability and functionality make it today's superior superdisintegrant.

 **Unmatched Purity**

 **Lower Use Levels**

 **Enhanced Long-Term Stability**

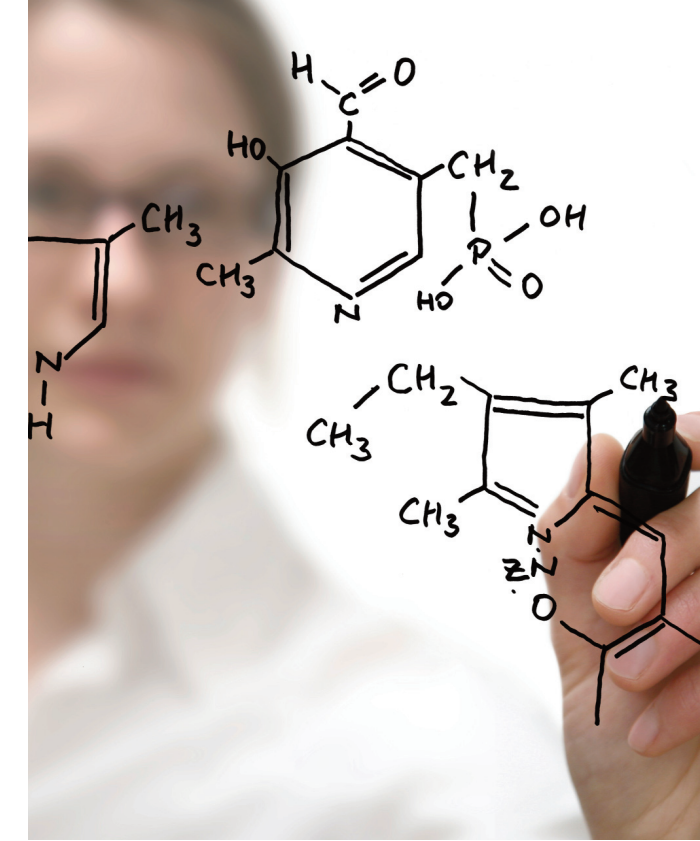
 **Broader Functionality**

FMC's quality standards help ensure the product purity of Ac-Di-Sol®

FMC's benchmark quality initiatives comply with recognized global quality standards, helping to ensure the unsurpassed product purity of Ac-Di-Sol® and its uniform, batch-to-batch consistency.

Ac-Di-Sol® croscarmellose sodium meets NF standards as published by the USP, and the standards of the European Pharmacopoeia (Ph. Eur) and the Japanese Pharmacopoeia (JP).

Ac-Di-Sol® is manufactured under cGMP conditions at two ISO registered manufacturing sites in the United States and Ireland. These plants produce consistent Ac-Di-Sol® that meets given physical and chemical specifications. Functional properties are systematically evaluated to assure that the product from each manufacturing site is equivalent chemically, physically, and functionally.



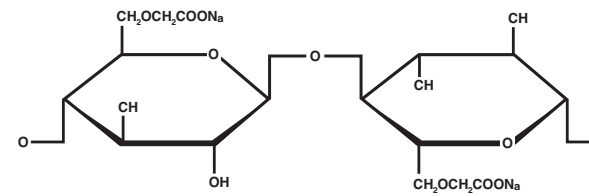
Higher quality and unmatched purity make Ac-Di-Sol® superior.

Ac-Di-Sol® has a dual mechanism for rapid disintegration and dissolution.

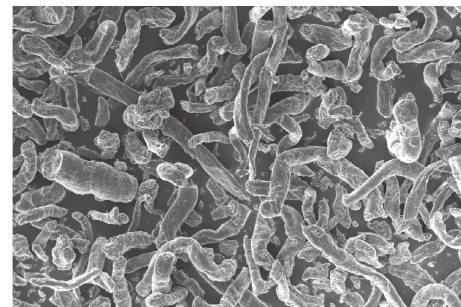
Water wicking and swelling are the two most important mechanisms of disintegrant action for Ac-Di-Sol®. Water wicking is the ability to draw water into the tablet matrix. Both the extent of water uptake and the rate of water uptake are critically important. Exposure to water can cause ingredients to swell and exert pressure against surrounding tablet or capsule ingredients, causing existing bonds between particles to break.

The fibrous nature of Ac-Di-Sol® provides many sites for fluid uptake and gives it excellent water wicking capabilities. The cross-linked chemical structure of Ac-Di-Sol® creates an insoluble, hydrophilic, and highly absorbent excipient that results in exceptional swelling properties.

Ac-Di-Sol® Chemical Structure



Ac-Di-Sol® Morphology



The product purity of Ac-Di-Sol® assures optimal performance.

There is growing concern about impurities in excipients, such as ethanol, methanol, and phosphorus, because they can cause an interaction with the active pharmaceutical ingredient (API) of a drug and compromise its efficacy and safety.

To prevent such an interaction, FMC adheres to the highest global quality benchmarks to produce Ac-Di-Sol®, a superdisintegrant whose unmatched purity enables it to deliver optimal performance.

A recent study compared Ac-Di-Sol® with four other brands of commercial superdisintegrants and clearly revealed the superior product purity of Ac-Di-Sol®

**Purity:
Ac-Di-Sol® vs. Other Superdisintegrants**

	Ethanol %	Methanol mg/kg	Phosphorous mg/kg	# of lots
Ac-Di-Sol®	0	0 ~ 1	<10	4
XL-CMC A	0 ~ 0.01	4 ~ 10	<10	2
XL-CMC B	2.5 ~ 3.2	2	<10	2
XL-CMC C	0.12 ~ 1.3	0 ~ 1	<10	4
XL-CMC D	0 ~ 0.01	339 ~ 791	90 ~ 130	5

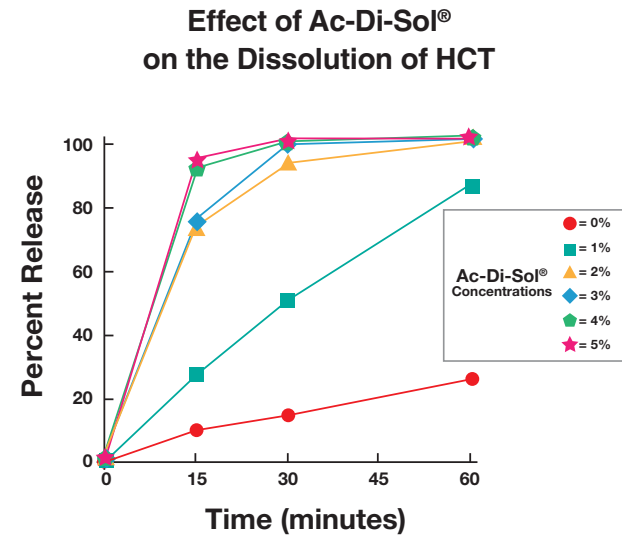
Ac-Di-Sol® shows superior product purity when compared to other superdisintegrants.

Ac-Di-Sol® shows faster disintegration at lower use levels.

Various studies have shown that Ac-Di-Sol® can be used at very low levels to achieve desired disintegration results.

Sakr, et al* studied the effectiveness of Ac-Di-Sol® in a direct compression hydrochlorothiazide (HCT) tablet.

Ac-Di-Sol® was evaluated at concentrations of 1 to 5%. At an optimum concentration of 2%, Ac-Di-Sol® was found to exhibit appreciably low disintegration time with the percent release of HCT in compliance with USP requirements. The hardness and friability of the tablet was not adversely affected by the increased concentration of the disintegrant.



*Sakr, et al, Comparative Effectiveness of Super Disintegrants on the Characteristics of Directly Compressed Triamterene Hydrochlorothiazide Tablets. Pharm, Ind. 1993, 55 (nr.10) p. 953-957.

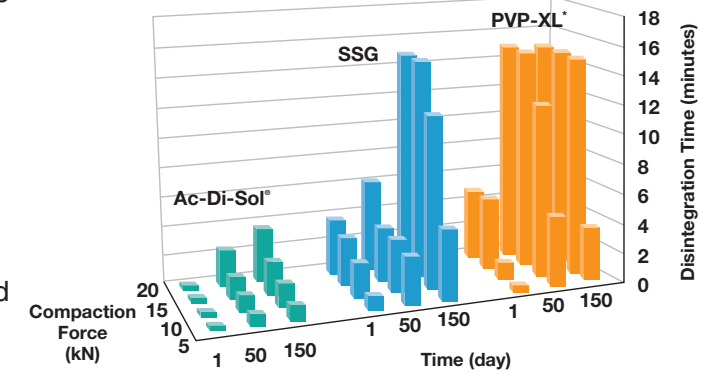
Ac-Di-Sol® assures long-term stability in disintegration.

Ac-Di-Sol® does more than show superior performance in initial disintegration and dissolution. Ac-Di-Sol® also imparts exceptional long-term dissolution stability in comparison to other superdisintegrants.

A comprehensive study by Dr. Yeli Zhang of FMC tested the long-term stability of Ac-Di-Sol®, SSG (Sodium Starch Glycolate) and PVP-XL (Crospovidone).

Results reveal that Ac-Di-Sol® provides much faster initial and over-storage tablet disintegration in comparison to the other commercial superdisintegrants, in all ranges of studied tablet compaction forces.

Stability of Commercial Superdisintegrants (DCP model & at 0.5% disintegrant level)



500 mg tablet, 7/16" standard concave tooling
*Small particle size

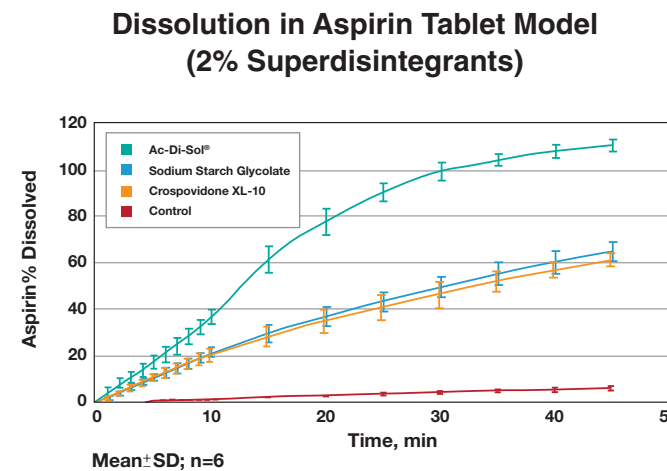
Lower use levels and greater long-term stability make Ac-Di-Sol® superior.

Ac-Di-Sol® offers greater dissolution at lower use levels.

Tablet disintegration is essential for the fast release of active ingredients, but dissolution is the most important criterion.

The dissolution efficacy of Ac-Di-Sol® compared to other superdisintegrants was tested in the study by Augsberger et al*, "A Contribution to Understanding Dissolution Functionality Based on a Comparison of Disintegration and Dissolution of Model Aspirin Tablets."

The results show that Ac-Di-Sol® allows a greater level of dissolution of tablets prepared by direct compression than other superdisintegrants evaluated at a 2% use level.



*L. Augsberger et al, 2004 AAPS Meeting, Baltimore MD

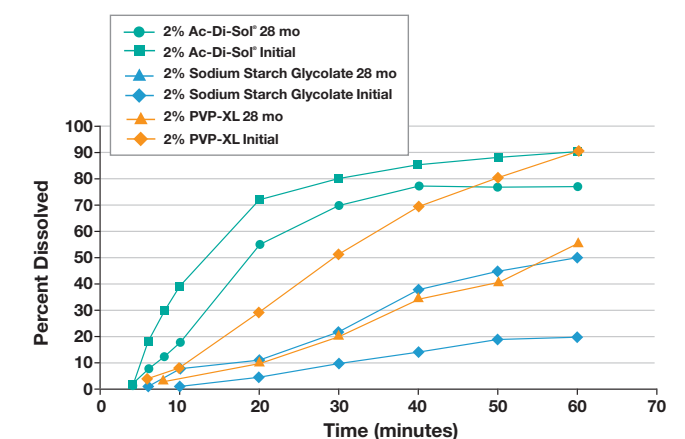
Ac-Di-Sol® assures long-term stability in dissolution.

In one key study, a hydrochlorothiazide (HCT) model drug system was evaluated in order to assess how the superdisintegrants Ac-Di-Sol®, SSG (Sodium Starch Glycolate), and PVP-XL (Crospovidone) perform over time.

HCT was selected since it is relatively water insoluble. HCT's insolubility in water creates interference effects relative to fluid uptake and penetration, resulting in slower tablet disintegration and dissolution.

The results indicate that wet granulated HCT tablets with Ac-Di-Sol® exhibit virtually no change in drug availability after being stored for 28 months at a controlled room temperature. Both SSG and PVP-XL showed significant drops in both initial dissolution rates and in HCT dissolution after storage.

Long-Term Stability of Commercial Superdisintegrants



Ac-Di-Sol® works effectively in direct compression formulations.

Ac-Di-Sol® can be used at very low levels to achieve desired disintegration results in tablets made by direct compression, which are a blend of active ingredients and excipients compressed without any granulation step.

The amount of Ac-Di-Sol® used depends on the tablet formulation. Solubility of the major tablet component, either the drug or filler, significantly affects the rate and mechanism of tablet disintegration. Tablets composed primarily of water-soluble ingredients tend to dissolve rather than disintegrate, resulting in much longer disintegration times. As the active ingredient or filler dissolves on the outer layer of the tablet matrix, the rate of fluid diffusion into successive layers is retarded, particularly if highly concentrated or viscous solutions are formed. Tablets containing insoluble drugs and filler often disintegrate rapidly if sufficient disintegrant is present.



Ac-Di-Sol® delivers excellent performance in roller compaction tablet formulations.

Used for many years by the pharmaceutical industry, roller compaction, or granulation by compression, is a process employed when the active ingredients in drugs are sensitive to moisture or heat or both. It is also used when formulations are found to resist compression when prepared by wet granulation methods.

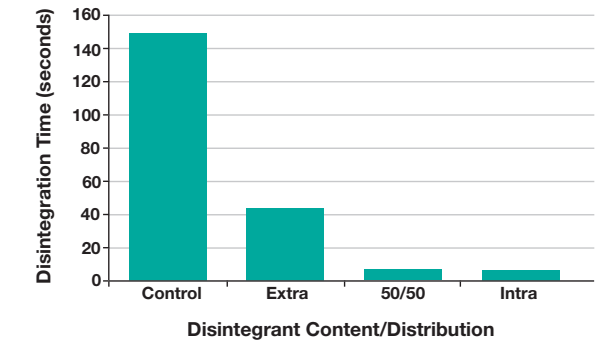
Studies at Purdue University have shown that Ac-Di-Sol® functions effectively as a disintegrant for tablets from granulations prepared by roller compaction. Avicel® PH-101 microcrystalline cellulose was roller compacted with 3% Ac-Di-Sol® added extragranularly, intragranularly, or distributed equally (50/50) and compressed into tablets.

The results show that for these study conditions, Ac-Di-Sol® is most effective when added intragranularly, or when distributed equally between the two phases.

Roller Compaction Studies: Ac-Di-Sol®/Avicel® PH-101 Mixtures in Tablet Form

	Hardness	Friability	Disintegration Time
0% Ac-Di-Sol®	12.8 kp	<0.10%	150 Sec.
3.0% Ac-Di-Sol® (outside)	11.7 kp	0.34%	45 Sec.
1.5% Ac-Di-Sol® (inside and outside)	11.6 kp	0.53%	6 Sec.
3.0% Ac-Di-Sol® (inside)	10.6 kp	0.58%	6 Sec.

Avicel® PH-101 Roller Compacted Tablets with 3% Ac-Di-Sol®



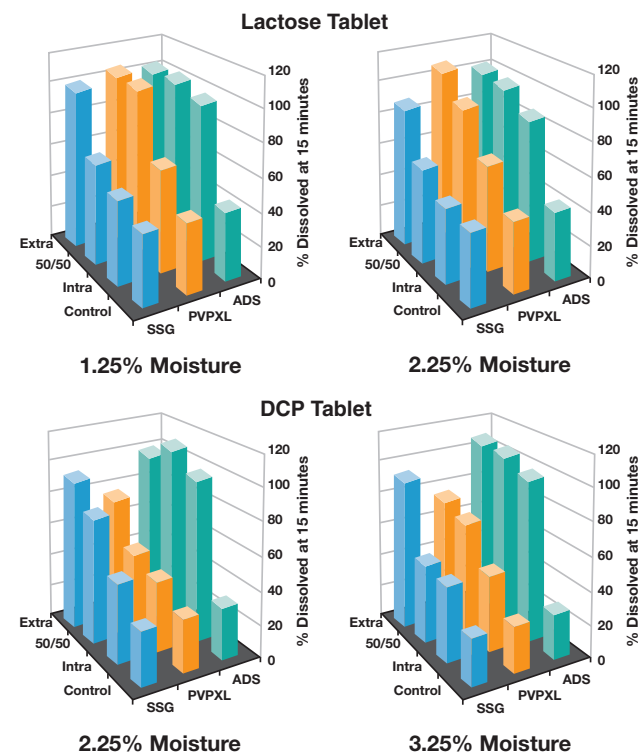
Broader functionality and efficacy make Ac-Di-Sol® superior.

Ac-Di-Sol® shows greater efficacy in wet granulation applications.

The disintegrant is usually added to the formulation both intragranularly and extragranularly. Tablets prepared by wet granulation disintegrate into granules because of the extragranular disintegrant. The granules then disintegrate further into fine particles due to the intragranular disintegrant. Ac-Di-Sol® is very effective when used in wet granulation at a 2% concentration with respect to the granulation mix. A 1 to 2% extragranular concentration with respect to the formulation produces tablets with excellent disintegration properties.

Gordon et al (1993) investigated the effect of mode of disintegrant incorporation on dissolution in wet granulated tablets. Three modes of incorporation (intragranularly, extragranularly, and in both phases) were studied using Ac-Di-Sol®, SSG (Sodium Starch Glycolate), and PVP-XL (Croscopvidone). Results indicated the superior functionality of Ac-Di-Sol® in wet granulation forms.

Comparison of Superdisintegrants in Wet Granulation Applications

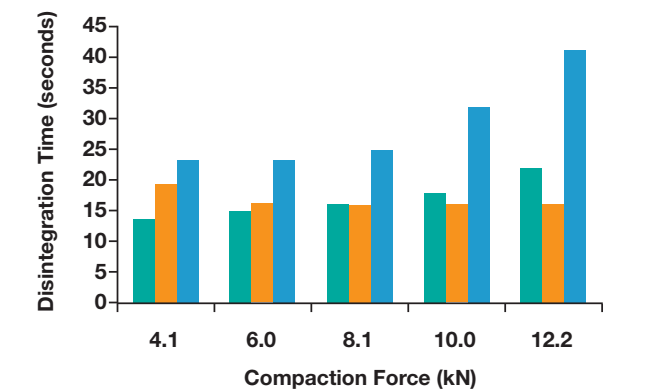


Ac-Di-Sol® ensures the rapid disintegration of orally disintegrating tablets (ODTs).

Orally disintegrating tablets (ODTs) have gained much attention as a preferred alternative to conventional oral dosage forms such as tablets and capsules. Recent studies show that more than half of the patient population prefers ODTs to other dosage forms. In addition, several business needs are driving ODT technology development and the commercialization of new ODT products, such as the need for expanded product lines, improved life-cycle management, extended patent life, and marketing advantages.

A superdisintegrant is crucial to achieve rapid disintegration of an ODT. FMC evaluated Ac-Di-Sol®, PVP-XL (Croscopvidone), and SSG (Sodium Starch Glycolate) when used in ODT applications within a common ODT tablet hardness range. Results revealed that Ac-Di-Sol® is a highly effective superdisintegrant at low use levels.

Comparison of Superdisintegrants in ODT Applications



400 mg tablet, 7/16" standard concave tooling
*Small particle size