Kollidon® CL-Grades

Kollidon® CL
Kollidon® CL-F
Kollidon® CL-SF
Kollidon® CL-M

Super disintegrants and dissolution enhancers

Global Technical Marketing

Pharma Solutions

BASF
The Chemical Company

Background

- Tablet disintegration can be regarded as the initial step in terms of bioavailability and pharmacological action of the active substance.
- To achieve rapid disintegration, a disintegrant normally has to be added to the tablet formulation.
- The disintegrant swells rapidly upon contact with water and explodes the tablet from within.
- Disintegration should take place within seconds.
- The further uptake of water into the tablet core should not be impeded by increased viscosity resulting from a dissolution of the disintegrant.

Introduction

Kollidon® CL, the crosslinked PVP, is one of the three “super-disintegrants”.

Kollidon® CL accelerates the dissolution and bioavailability due to its power to form complexes with many insoluble actives.

- The insoluble grades of Kollidon® are widely used in the pharmaceuticals industry for this purpose.
- Their use as excipients is triggered by their ability to:
  - Hydrophilize insoluble drugs
  - Stabilize suspensions
  - Form complexes

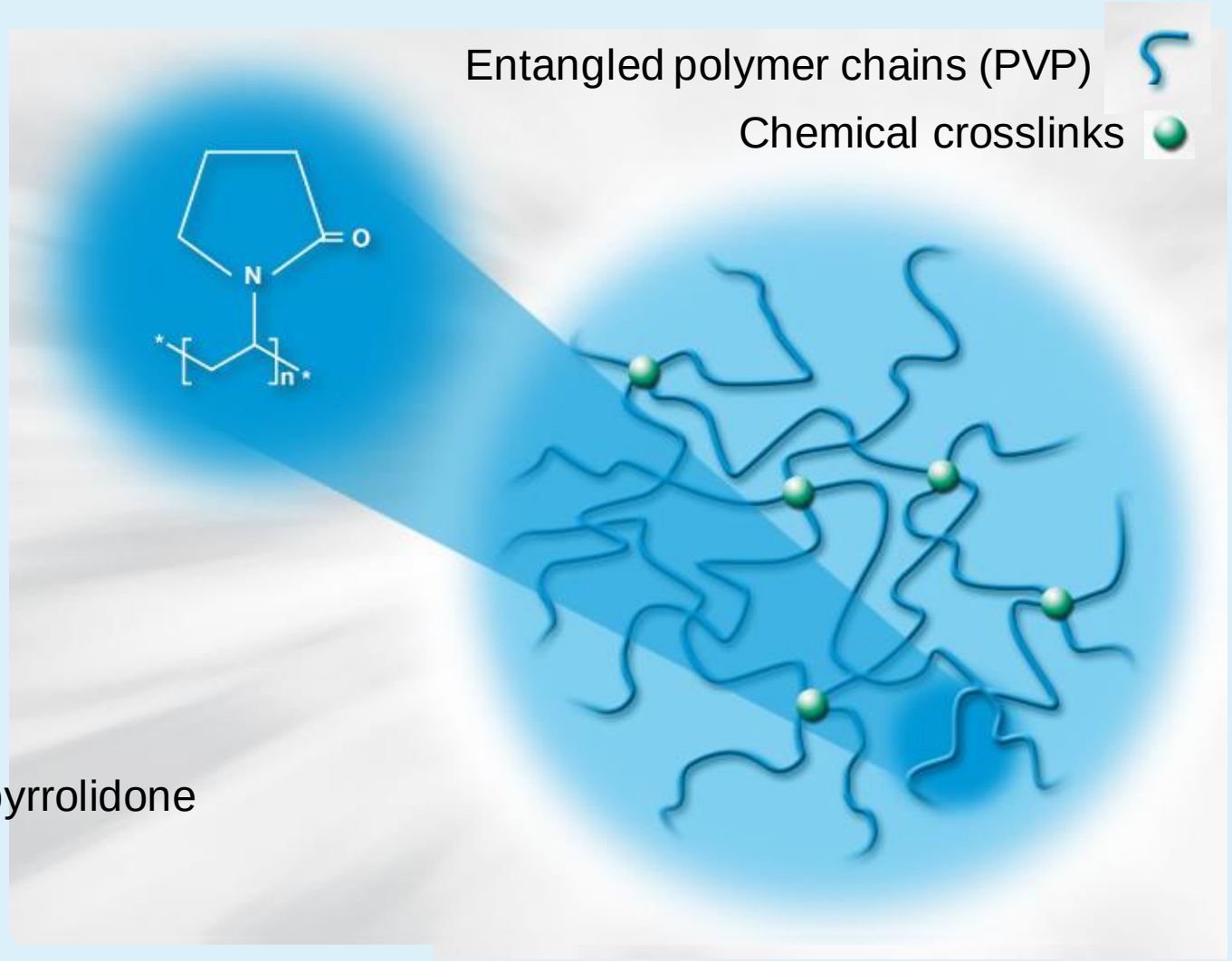
Kollidon® is well known as a universal excipient range since more than 60 years.

The Products

- In contrast to many other disintegrants, the Kollidon® CL grades are non-water-soluble.
- Crospovidones act as disintegrants by absorbing water and swelling.
- However, the speed of disintegration is not only based on the swelling; it is a combination of many factors such as:
  - The speed of swelling
  - The swelling volume of the disintegrant
  - The swelling pressure of the disintegrant
  - The hydrophilic behavior of the disintegrant
  - The pore sizes within the tablet
  - The mechanical properties of the tablet

The Chemical Structure

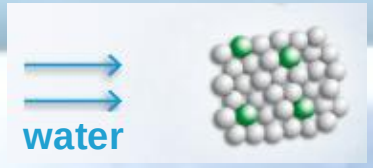
Structure
A highly (mainly physically) crosslinked polymer-matrix

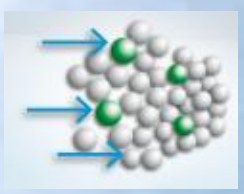


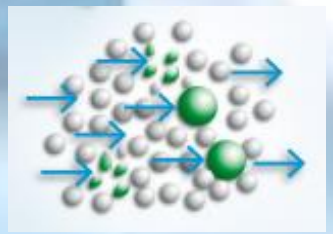
Chemical names
- Crospovidone
- Crospovidonum
- Insoluble polyvinylpyrrolidone
- Crosslinked PVP
- PVPP

The Disintegration – Insights

Theory of Disintegration of a Tablet



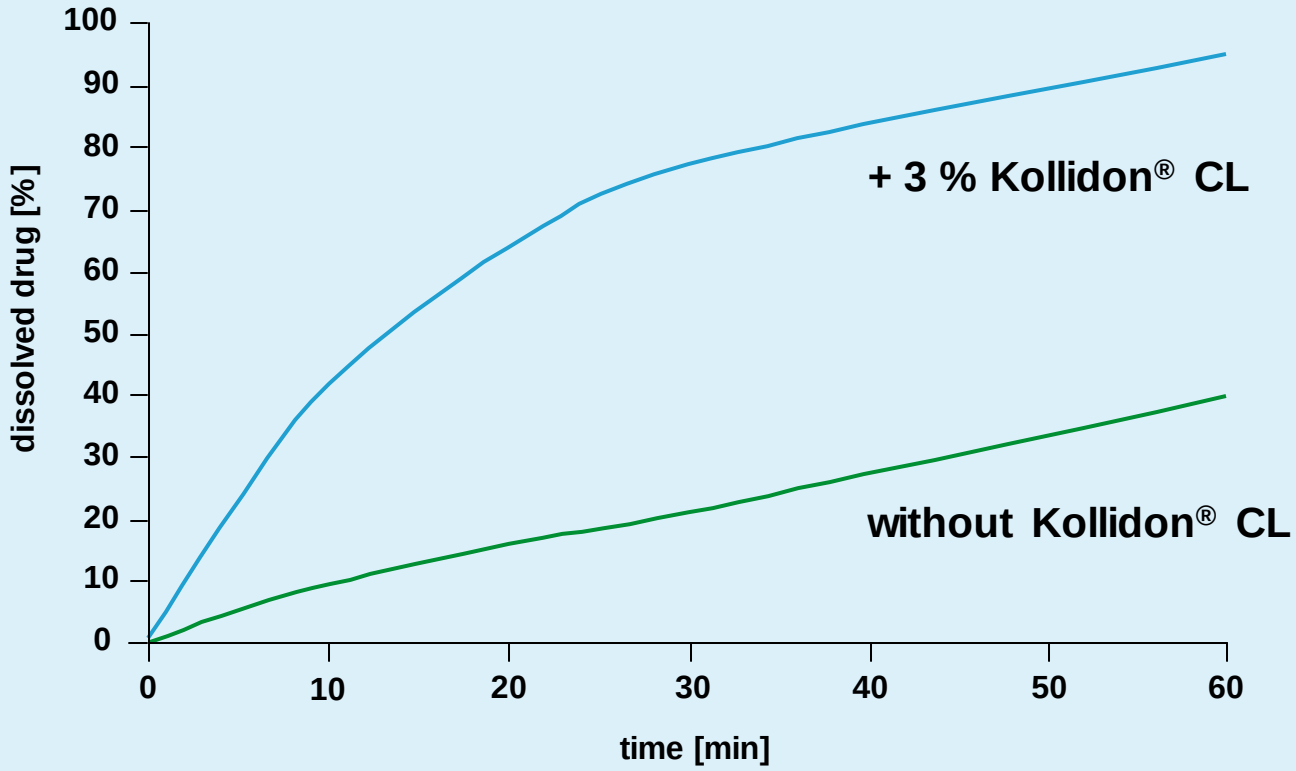




1. Disintegrants are very hydrophilic.
2. Spherical particles of disintegrant are uniformly distributed within the tablet.
3. They rapidly swell upon contact with water or other liquids.
4. They significantly increase volume and disintegrate the tablet.

The Effect of Disintegrants

Dissolution of acetylsalicylic acid tablets



Four for Your Needs

The four Kollidon® CL grades
can best be distinguished by their different particle sizes:

Kollidon® CL-Grade		Average particle size range [µm]
• Kollidon® CL	Standard	110–130
• Kollidon® CL-F	Fine	20–40
• Kollidon® CL-SF	Super Fine	10–30
• Kollidon® CL-M	Micronized	3–10

- All Kollidon® CL-grades are crosslinked, water-insoluble polyvinylpyrrolidones.
- Kollidon® CL grades meet the requirements of all existing monographs of the USP/NF, Ph.Eur. and JPE.
- The material has been granted an E-number (E1202) in Europe for use in food supplements and artificial sweeteners.

Their Specific Advantages

- **Kollidon® CL** shows strong disintegration power; this makes it especially suitable for use in large tablets. It has advantages due to its increased disintegration and dissolution speeds.

- **Kollidon® CL-F** has strong disintegration power in combination with fine particles. It is ideal for small tablets as it causes fewer content uniformity problems.

- **Kollidon® CL-SF:**
  - the finest grade for disintegration applications,
  - excellent disintegration power,
  - fewer defects on the tablet surface after storage.

  Perfect for fast dispersible tablets since the mouth feel is superior to the other grades. Strong ability to absorb water (e.g. in wet granulation).

- **Kollidon® CL-M** is mainly used as a stabilizer in suspensions. It is also used in some formulations as a pore former and disintegrant.

Customer Demand and Recommendation

	Customer requirements				
	Fast disintegration	Good mouthfeel (e.g. for fast dispersible tablets)	Smooth tablet surface	Hard tablets	Improved drug solubility and dissolution
Kollidon® CL	++	+/-	-	+/-	++
Kollidon® CL-F	+	+	+	+	+
Kollidon® CL-SF	+	++	+	++	+/-
Kollidon® CL-M	Mainly used as a suspension stabilizer				+

The Market Trends

- The market moves towards **highly potent actives** (HPAPI) and, as a consequence, towards **smaller tablets**.
- These smaller tablets require disintegrants of much smaller particle size to guarantee **content uniformity** and to prevent the tablets from showing **rough surfaces** after storage.
- In new drug delivery technologies such as oral dispersible tablets, fast disintegrants with **very smooth mouth feeling** are in strong demand.

The Application

Comparison of Disintegrants

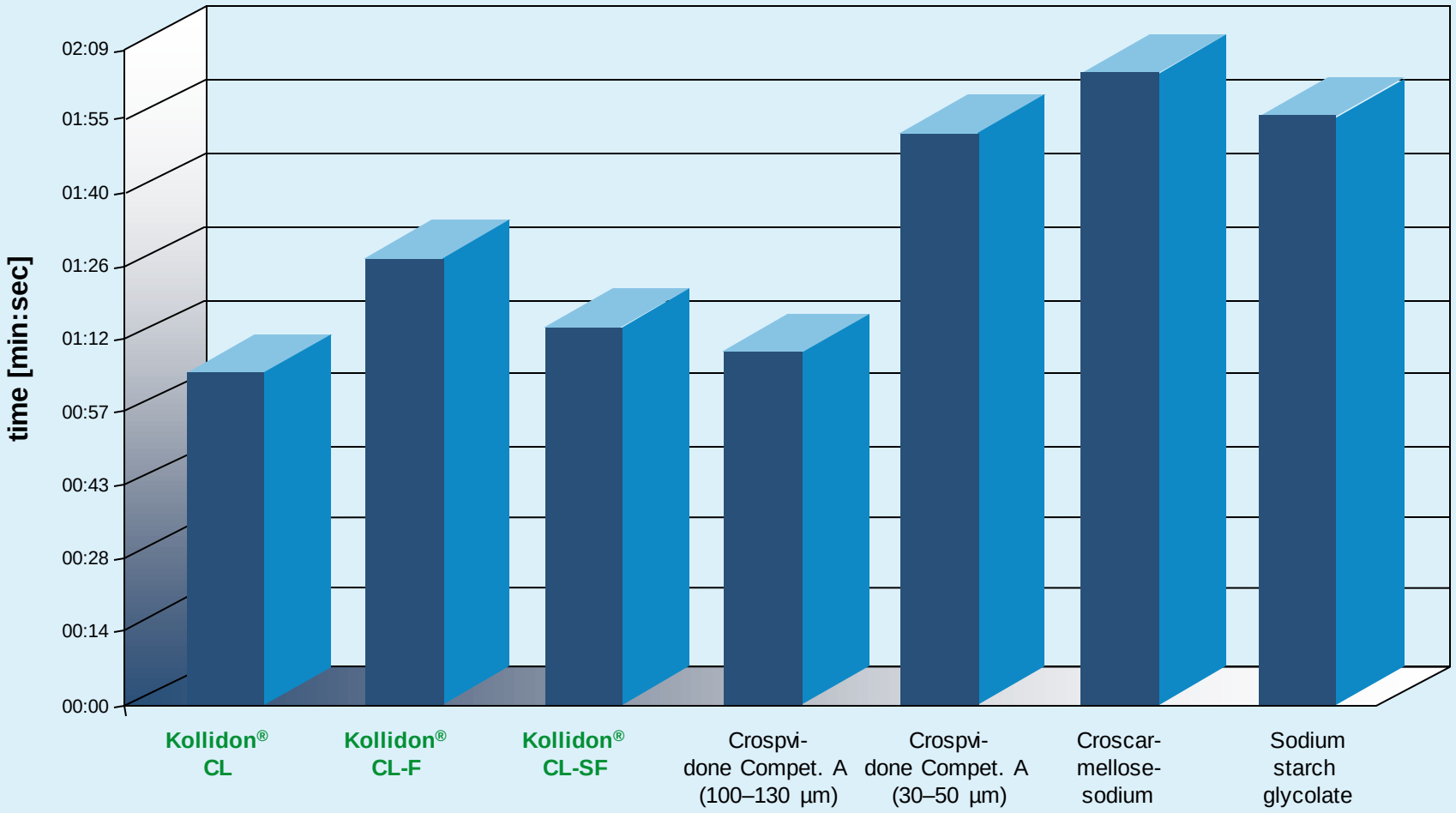
- Disintegration is strongly dependent on the formulation and properties of the tablet:
  - Porosity and Hardness
  - Method of manufacture
  - Type and amount of actives and other excipients.

- The principle property of the disntegratnts is to shorten the disintegration time of tablets.

- Kollidon® CL-F and Kollidon® CL-SF show excellent performance and avoid some of the drawbacks of Kollidon® CL due to their much smaller particle sizes.

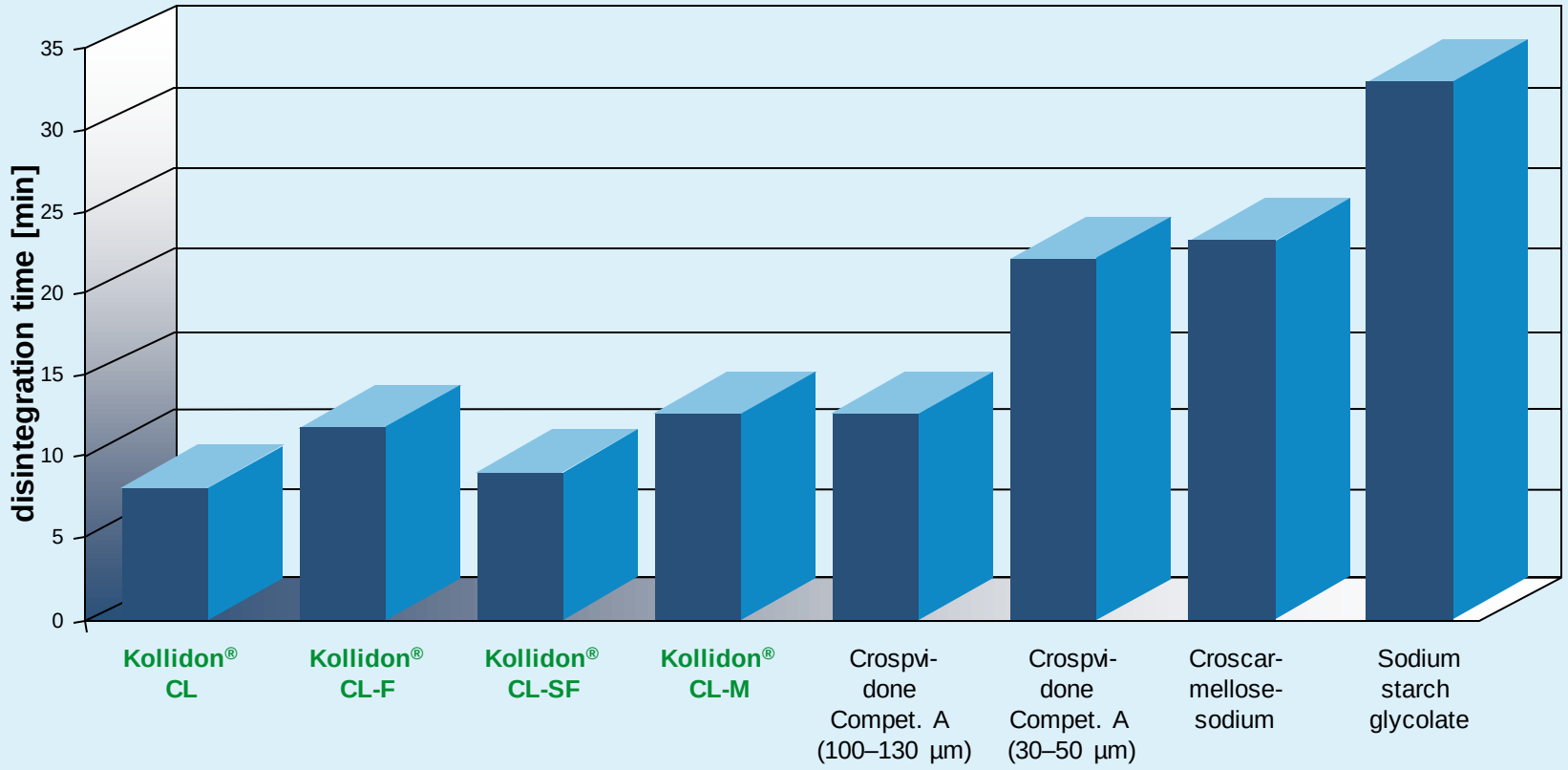
The Application

Disintegration time of direct compressed tablets (6 % disintegrant in Ludipress® LCE, compressed at 18 kN)



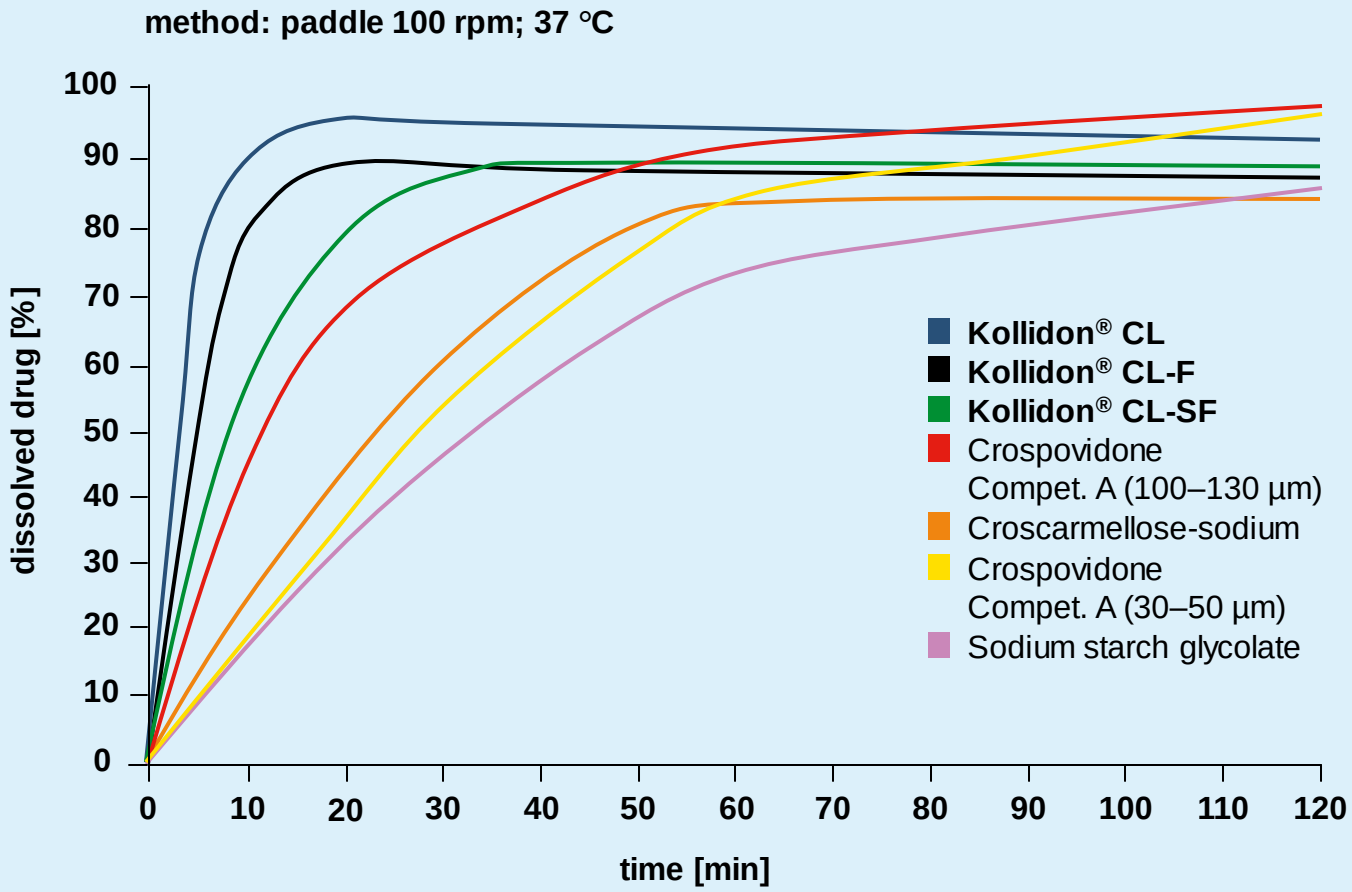
The Application

Disintegration of tablets made of granules
(2,7 % disintegrant extragranular use, compressed at 18 kN)



The Application

Dissolution of acetaminophen in deionized water
(2.7 % disintegrant, wet granulated formulation, compressed at 18 kN)



Disintegration Speed and Dissolution

- Kollidon® CL shows the fastest disintegration, closely followed by Kollidon® CL-F and Kollidon® CL-SF.
- The crosspovidone of a competitor with comparable particle size to Kollidon CL is much slower than even Kollidon CL-SF.
- Starch or cellulose derivatives tend to increase the viscosity of the dissolution and thus slow down water uptake and disintegration time.
- Kollidon® CL-grades are insoluble and thus do not slow down the dissolution of an oral dosage form. They even can increase the release of the active ingredient.

Additional Value
of Kollidon CL-F and Kollidon CL-SF

- Because the Kollidon® CL grades are very hydrophilic, they tend to absorb water and thus produce a rough surface due to swelling.
- In the case of film tablets, this might cause cracks in the film.
- A requirement of many customers is that the tablets show a smooth surface after storage in multidose containers.
- To fulfill these needs, BASF has developed crospovidones with much smaller particle sizes, but comparable disintegration properties: Kollidon® CL-F and Kollidon® CL-SF.
- Tablets produced with the super-disintegrants Kollidon® CL-F and Kollidon® CL-SF offer very smooth surfaces and an excellent mouth-feel.

Kollidon® CL

SEM

- Kollidon® CL is used as the standard disintegrant for all kinds of fast dispersible tablet formulations.
- Kollidon® CL shows a very quick disintegration and fast dissolution of active ingredients.
- Kollidon® CL is insoluble and does not slow down the dissolution of an oral dosage.
- Kollidon® CL is especially suitable for porous tablets and when an extremely high tablet hardness but quick disintegration is required.
- Kollidon® CL shows a medium uptake of liquids. For wet granulation with large amounts of solvent, Kollidon® CL-F or Kollidon® CL-SF are highly suitable replacements.

Kollidon® CL-F

SEM

BASF
The Chemical Company

- Kollidon® CL-F is the perfect alternative when formulators are looking for a disintegrant with strong disintegration power and a smooth tablet surface.
- Kollidon® CL-F is the disintegrant of choice for the development of small tablets. Its small particle size avoids content uniformity problems.
- Tablets with Kollidon® CL-F show dramatically reduced surface roughness and and smooth and plaesant mouth-feel.
- Kollidon® CL-F is able to absorb large amounts of liquids, and thus is highly suitable for wet granulation with large amounts of solvent

Capsules filled with microtablets (capsule size 00–4)

Kollidon® CL-SF

SEM

BASF
The Chemical Company

- Unique properties which makes it the disintegrant of choice
- Offers an excellent disintegration power with its small particle size
- Tablets can be obtained with extremely smooth surfaces.
- Best mouth-feel for applications such as oral dispersible tablets
- Offers the highest uptake capacity for water and other solvents of all the crospovidones produced by BASF
- Ideal for wet granulation processes using large amounts of solvent.

Kollidon® CL-M

SEM

BASF
The Chemical Company

- Kollidon® CL-M is an inert material, suitable for the stabilization of oral or topical suspensions.
- Kollidon® CL-M achieves this by increasing the volume of the sediment and reducing the sedimentation rate.
- Redispersing the sediment by shaking is eased without increasing the viscosity of the dispersion and prevents the formation of a cake.
- Kollidon® CL-M also has been used as a binder, a dissolution enhancer and as disintegrant.

Kollidon® CL-Grades at a Glance

BASF
The Chemical Company

	Benefits for manufacturers	Benefits for patients	Main applications
Kollidon® CL	The super-disintegrant, very fast disintegration	Fast drug absorption for most APIs	Disintegrant for standard tablets
Kollidon® CL-F	No content uniformity problems especially in small tablets	Easy to swallow due to tablet size	Small tablets, tablets stored under high humidity
Kollidon® CL-SF	Perfect for fast dispersible tablets, excellent tablet surface	Best mouthfeel	Fast dispersible tablets, intragranular disintegrant for wet granulation
Kollidon® CL-M	Stable dispersions	Easy to redisperse	Suspensions

Summary

Depending on the desired

- disintegration time,
- dissolution rate,
- particle sizes,
- mouth-feel,
- tablet smoothness,
- solvent uptake capacity or
- dispersion ability

Kollidon® CL
Kollidon® CL-F
Kollidon® CL-SF
Kollidon® CL-M

our customers can select

THE EXCIPIENTS OF CHOICE

from our comprehensive product range.

Questions?

BASF
The Chemical Company

“BASF experts around the world can enable your business to gain competitive advantage. Why not take a look at some of these innovative products?”

BASF
The Chemical Company

■ Ludiflash®	For orally fast-disintegrating tablet
■ Ludipress® Ludipress® LCE	Direct compression excipient with and without disintegrant
■ Kollidon® VA64 Fine	Dry binder: Fine Grade
Kollidon® VA64	Standard Grade
■ Kollidon® SR	Matrix polymer for sustained release formulations
■ Kollidon® CL-grades	Disintegrants
Kollidon CL / CL-F / CL-SF	Standard / Fine / Super fine grade
■ Kollidon CL-M	Micronised; Suspension Stabilizer etc.

Additional Information

Additional Information

Disintegrants on the market

	Required %	Disinte-gration power 1: low/10: high	Hardness of the tablets	Issues during storage at high humidity
Starches	3–15	3	Low	*
Starch derivatives				
Sodium starch glycolate	2–8	4	High	Brown spots
Cellulose derivatives				
Carmellose-sodium	1–6	5	Medium	*
Croscarmellose-sodium	0.5–5 (most cases 2–3)	7	High	Brown spots
Carmellose-calcium	5–15	5	Medium	*
HPC	5–25	5	High	*
Crospovidone grades				
Compet. A (100–130 µm)	2–5	8	High	Rough surface
Compet. A (30–50 µm)	2–5	7	High	Smooth surface
Kollidon® CL	2–5	9	Medium	Rough surface
Kollidon® CL-F	2–5	8	High	Smooth surface
Kollidon® CL-SF	2–5	7	Very High	Smooth surface

*: Not tested

Additional Information

Kollidon CL-M: Stabilisation of Vitamins

BASF
The Chemical Company

The effect of Kollidon® CL-M on the stability of vitamin B_1, calcium pantothenate and vitamin C was demonstrated in an accelerated storage test

Vitamin B_1:	1 month	2 months	3 months	5 months
Without Kollidon® CL-M	4 %	11 %	16 %	26 %
With Kollidon® CL-M	0 %	1 %	7 %	10 %

Vitamin C:	1 month	2 months	3 months	5 months
Without Kollidon® CL-M	17 %	18 %	40 %	49 %
With Kollidon® CL-M	0 %	2 %	13 %	19 %

Ca-Pantothenate:	1 month	2 months	3 months	5 months
Without Kollidon® CL-M	–	8 %	21 %	50 %
With Kollidon® CL-M	–	10 %	10 %	15 %

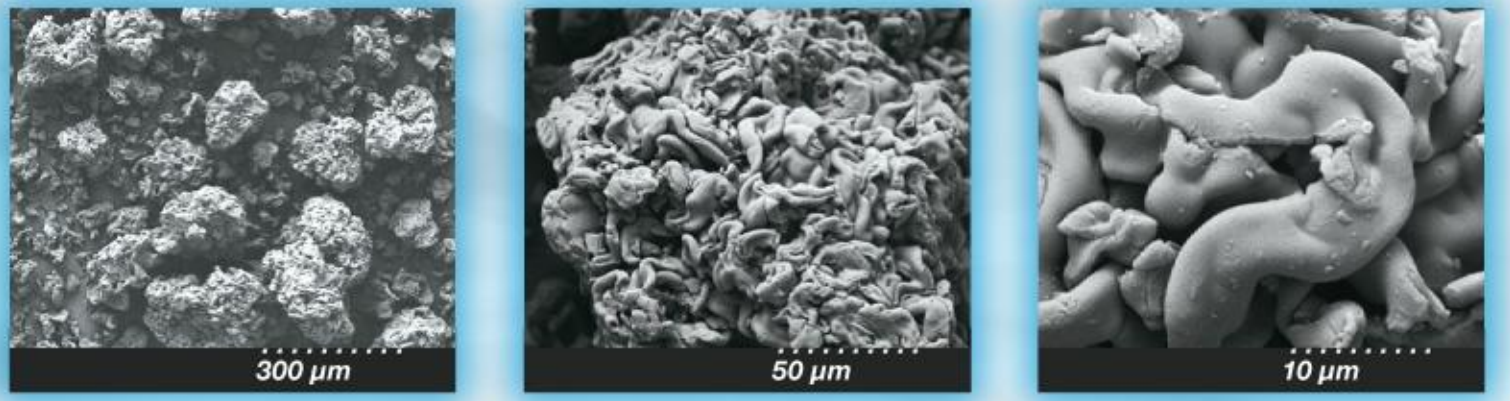
Vitamin degradation in multivitamin instant drink granules with and without Kollidon® CL-M (30°C/70 % relative humidity)

Additional Information

Kollidon CL: SEM-Pictures

back

BASF
The Chemical Company



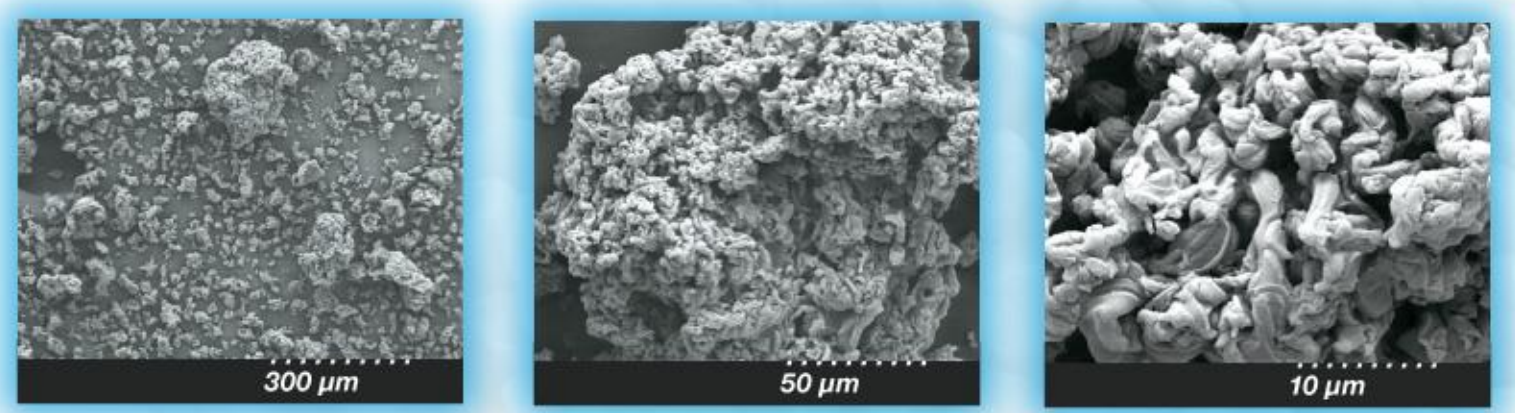
Kollidon® CL

Additional Information

Kollidon CL-F: SEM-Pictures

back

BASF
The Chemical Company



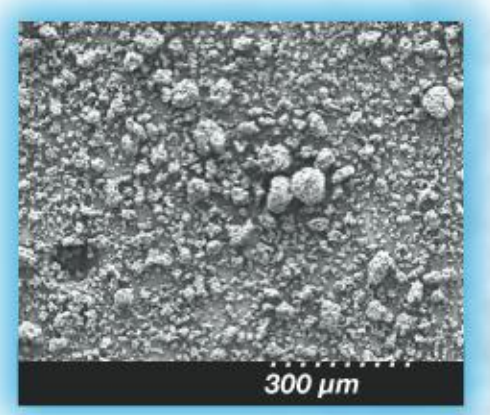
Kollidon® CL-F

Additional Information

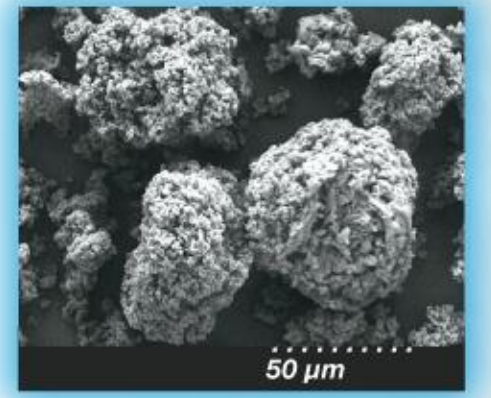
Kollidon CL-SF: SEM-Pictures

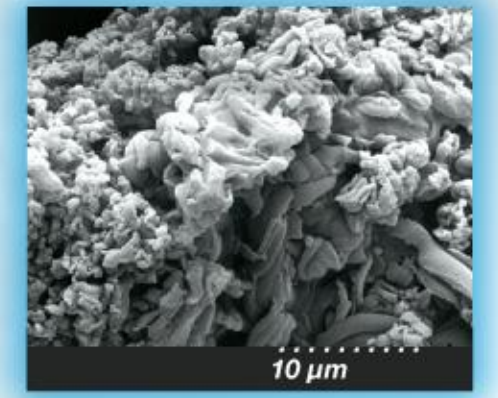
back

BASF
The Chemical Company



Kollidon® CL-SF



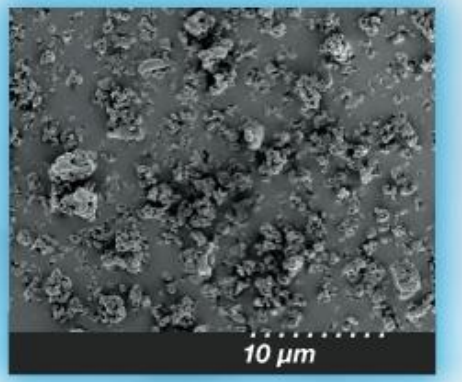


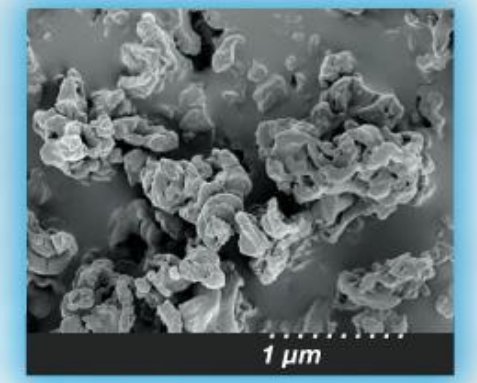
Additional Information

Kollidon CL-M: SEM-Pictures

back

BASF
The Chemical Company





Kollidon® CL-M