Polyplasdone™ crospovidone superdisintegrants

Product Overview

More than just an excellent tablet disintegrant

Superdisintegrants perform differently because they possess different chemical structures, particle morphologies and powder properties. Polyplasdone crospovidones are synthetic, insoluble, crosslinked homopolymers of N-vinyl-2-pyrrolidone (Figure 1) that differ by particle size (Table 1). Due to their nonionic nature, pyrrolidone chemistry and porous particle morphology, Polyplasdone crospovidones are the disintegrants of choice for rapid disintegration, enhanced rate of drug dissolution and robust tablets.

Table 1
Chemical structure of Polyplasdone crospovidone

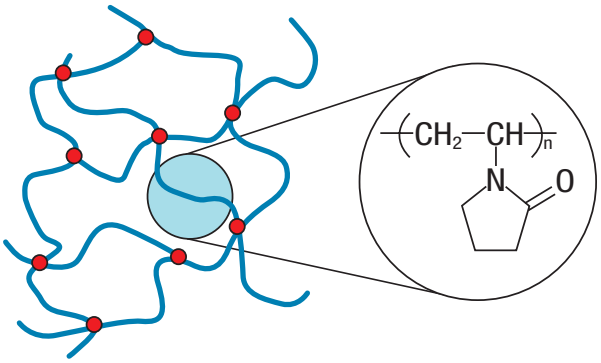


Table 1
Ashland offers several chemically identical Polyplasdone crospovidone polymers

Grade	Typical Average Particle Size (Microns)	Peroxide Specification (ppm)	Bulk Density (g/cm^{-3})	Tap Density (g/cm^{-3})
Ultra[a]	110–140	30 Max	0.3	0.4
XL[a]	110–140	400 Max	0.3	0.4
Ultra-10[b]	25–40	50 Max	0.3	0.5
XL-10[b]	25–40	400 Max	0.3	0.5

[a] Ph. Eur. crospovidone monograph type A
[b] Ph. Eur. crospovidone monograph type B

Benefits

Combines multiple mechanisms to achieve disintegration at low use levels (2-5 wt%)

Swells without forming gels that can slow tablet disintegration or dissolution

Provides rapid disintegration in wet and dry granulations and direct compression tablet processes. Can be added intra- or extra-granularly

Increases tablet breaking force and reduces friability

Enhances the dissolution of poorly soluble drugs

Available in two particle sizes

Polyplasdone Ultra and Ultra 10 crospovidone grades provide the same great performance with low peroxide levels

ASHLAND®
With good chemistry great things happen.™

Polyplasdone crospovidones use multiple mechanisms for disintegration

Unlike other superdisintegrants, which rely principally on swelling for disintegration, Polyplasdone crospovidones use a combination of mechanisms to provide rapid disintegration. Although Polyplasdone crospovidones swell by 95% to 120% upon contact with water, swelling is not the only mechanism for tablet disintegration. Swelling or swell volume is mainly a measure of the change in volume of the disintegrant after it is introduced to an aqueous solution and the system has reached equilibrium. However, swell volume does not measure the rate at which a disintegrant absorbs water and swells, or the pressure generated by swelling. Polyplasdone crospovidones, with their porous particle morphology (Figures 2 and 3), rapidly absorb water (wicking) via capillary action. In addition, during tablet compaction, the highly compressible Polyplasdone particles become extremely deformed. As the deformed Polyplasdone particles come in contact with water that is wicked into the tablet, the Polyplasdone particles recover their normal structure and then swell, resulting in rapid volume expansion and high hydrostatic pressures that cause tablet disintegration.

Figure 2
Polyplasdone XL crospovidone particles are porous and granular to enhance wicking of liquid into the particle

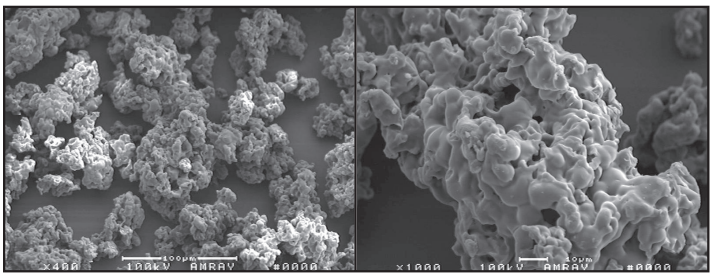
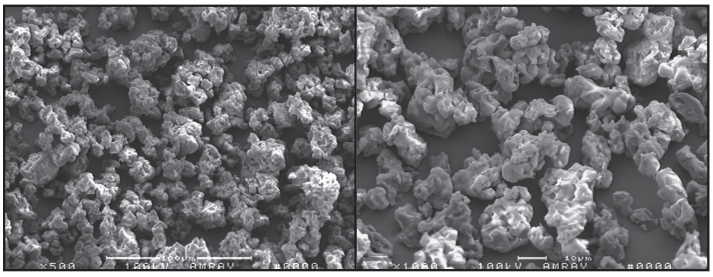


Figure 3
Polyplasdone XL-10 crospovidone particles are smaller, but also porous and granular

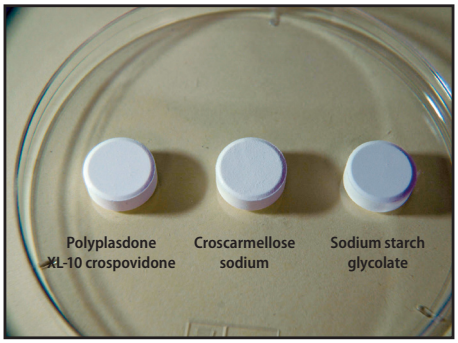


Swelling without gelling

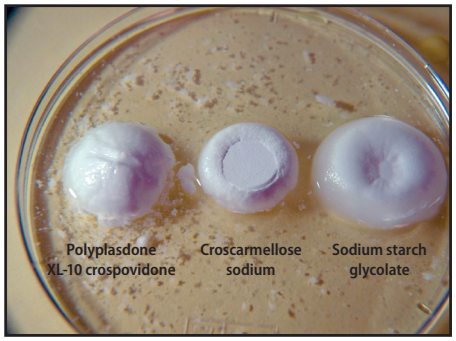
Characterized by high crosslink density, Polyplasdone crospovidones swell without gelling. Other superdisintegrants form gels when fully hydrated (Figure 4), particularly at high use levels required in some formulations to achieve desired tablet disintegration or drug dissolution. Gels can delay dissolution as the drug must first diffuse through the gel layer before being released into the body. Because Polyplasdone crospovidones do not gel upon wetting, they maintain their full disintegration efficiency, even after undergoing several wetting and drying cycles. For these reasons, Polyplasdone crospovidones are ideally suited for use in wet granulation tablet processes.

Figure 4
Placebo tablets with Polyplasdone crospovidone in water do not gel

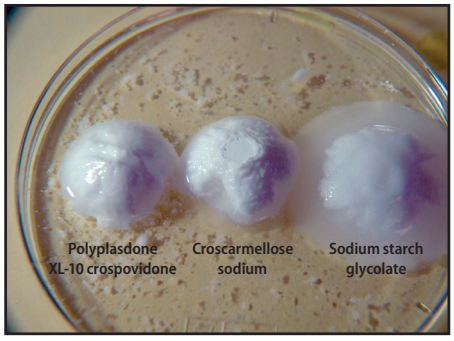
Placebo tablets at 0 minutes



Placebo tablets after 1 minute in water



Placebo tablets after 2 minutes in water

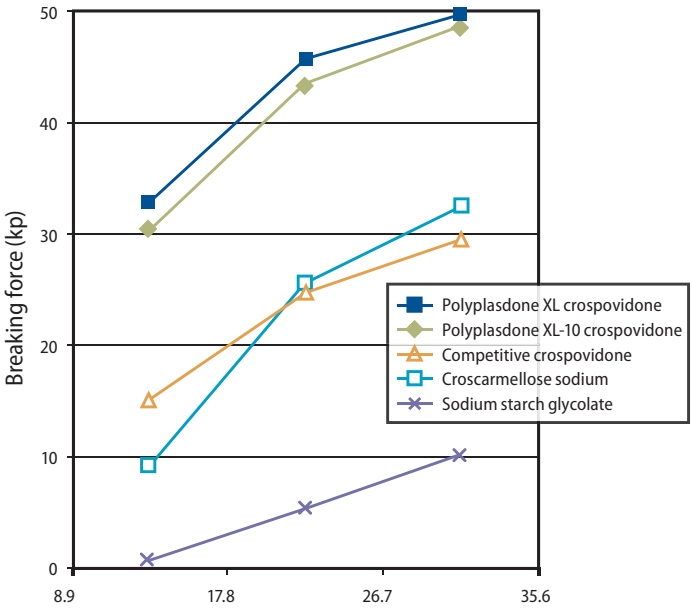


Good compressibility

Supplied as free-flowing white powders, Polyplasdone crospovidones are easy to handle during direct compression, as well as wet- and dry-granulation tablet manufacturing processes.

With unique particle morphology, Polyplasdone crospovidones are significantly more compressible than other superdisintegrants, allowing for tablets with high breaking force and low friability. The breaking force of pure compacts of several superdisintegrants tested at various compaction forces can be seen in Figure 5. The results show that Polyplasdone crospovidones possess significantly higher breaking force. Accordingly, Polyplasdone crospovidones are ideally suited for use with poorly compressible actives or in formulations such as orally disintegrating tablets that commonly use high levels of disintegrant.

Figure 5
Polyplasdone crospovidones are highly compressible, as demonstrated by the breaking force of pure compacts

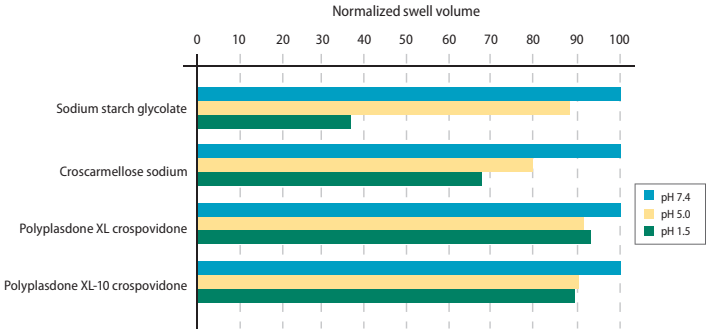


Non-ionic

An important formulation consideration is the potential interaction between drug actives and excipients. Anionic disintegrants like croscarmellose sodium and sodium starch glycolate may complex with cationic drug actives and slow dissolution. Polyplasdone crospovidones are nonionic and do not interact with cationic drug actives to retard drug release. Studies demonstrate that tablets formulated with Polyplasdone disintegrants and cationic drug actives give the fastest drug dissolution.[1]

Unlike other common superdisintegrants, the swell volume of Polyplasdone crospovidones is unaffected by changes in pH. The differences in swell volume under acidic and neutral conditions for Polyplasdone crospovidones and other common superdisintegrants is shown in Figure 6. For comparison, the swell volume for each disintegrant was normalized to pH 7.4. This demonstrates that the disintegration performance of Polyplasdone crospovidones will not be affected by the various pH changes within the gastrointestinal tract.

Figure 6
Swelling of Polyplasdone crospovidones is independent of pH



A history of use

Widely used in pharmaceutical and dietary supplements for over 20 years, Polyplasdone crospovidone conforms to the current USP/NF, Ph. Eur. and JPE monographs for crospovidone. As outlined in the European Pharmacopeia, Polyplasdone XL crospovidone complies to Crospovidone, Type A and Polyplasdone XL-10 crospovidone complies to Crospovidone, Type B. All of Ashland's Polyplasdone crospovidone products have received the United States Pharmacopeia (USP) Verified Pharmaceutical Ingredient Mark. This mark is awarded to companies and pharmaceutical ingredients that pass all USP verification requirements, including a comprehensive GMP audit by USP. Polyplasdone crospovidone is listed in the United States Food and Drug Administration's (U.S. FDA) Inactive Ingredient Guide. Ashland maintains a Drug Master File with the U.S. FDA.

A toxicity and safety profile for Polyplasdone polymer is available on request.

Smooth tablets

Polyplasdone XL-10 crospovidone provides a very smooth tablet surface. In some cases when uncoated tablets with larger particle size crospovidone, Type A, are stored at high humidity, visible surface roughness may occur. With the smaller particle size Polyplasdone XL-10 crospovidone, tablets are smooth. In one study, 300 mg placebo tablets containing 2% Polyplasdone XL-10 crospovidone; 97.4% lactose monohydrate and small amounts of lubricant (0.5 wt %) and glidant (0.1 wt %), were compressed at 15 kN compaction force on a compaction simulator. The tablets were stored in an open container at 40°C and 75% relative humidity for 3 hours and then evaluated for surface roughness using a light-scanning profilometer. Representative surface roughness images of the tablets before and after exposure are shown in Figure 7. The images indicate a smooth surface with no imperfections before and after exposure. The photograph (Figure 8) also shows a visibly smooth surface after exposure. Under the same conditions, tablets containing larger particle size crospovidone, Type A, show an increase in roughness from 1.7 to 4.6 µm. Thus, smaller particle size Polyplasdone XL-10 crospovidone is preferred for a smoother tablet surface.

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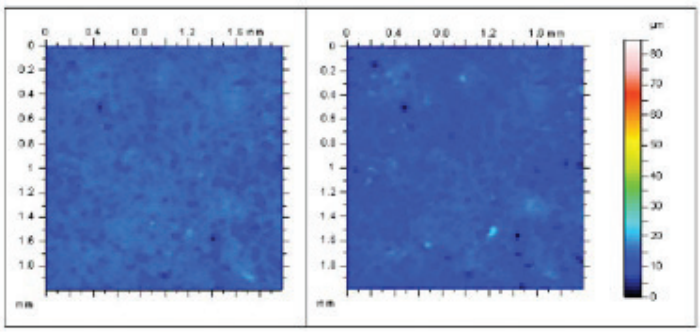
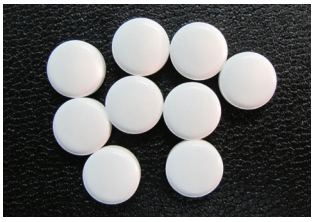
Figure 7
Tablets containing Polyplasdone XL-10 crospovidone show no increase in surface roughness when exposed to high humidity



A. Before exposure B. After exposure

Figure 8
A placebo tablet with Polyplasdone XL-10 crospovidone is visually smooth after exposure to high humidity



Applications

Polyplasdone polymers provide rapid disintegration in oral solid dosage formulations. With its unique particle morphology, Polyplasdone crospovidone is the disintegrant of choice in the following applications:

- In wet-granulation tablet processes, Polyplasdone XL-10 crospovidone, with its small average particle size, is highly effective at rapid disintegration when used intragranularly.
- Polyplasdone disintegrants are highly compressible, thus they are ideally suited for use with poorly compressible drug actives and in direct-compression tablet processes.
- As Polyplasdone crospovidones are non-ionic, they will not form complexes with ionic drug actives that would slow drug release. Recent data show Polyplasdone crospovidones provide fastest dissolution with cationic drug actives in a model tablet formulation.[1]
- Polyplasdone XL-10 crospovidone is well suited for orally disintegrating and chewable tablet formulations. It provides rapid disintegration, smooth mouthfeel and high tablet breaking force with low friability.[2]
- With poorly soluble drugs, Polyplasdone XL-10 crospovidone increases the rate and extent of dissolution.[3]

References:

[1] J. Balasubramaniam, et al., "Effect of Superdisintegrants on Dissolution of Cationic Drugs," *Dissolution Technologies*, 15 (2), 18-25 (2008).
[2] W. Camarco, R. Dipan, A. Druffner, "Selecting Superdisintegrants for Orally Disintegrating Tablet Formulations," *Pharm Tech Supplement*, S28-S37 (2006).
[3] J. Balasubramaniam, T. Bee, "Influence of Superdisintegrants on the Drug Dissolution from Oral Solid-Dosage Forms," *Pharm Tech Excipient Supplement*, S4-S14 (2009).