plasdone™ S630 ultra copovidone

improved processability and stability

description

Plasdone™ S630 Ultra is a new and improved version of copovidone. Designed to provide better performance in tablet formulations, hot melt extrusion (HME) and continuous processing, it offers superior benefits compared to the original Plasdone™ S630 copovidone.

Like the original, Plasdone™ S630 Ultra copovidone is a 60:40 random, linear copolymer produced by the free radical polymerization of N-vinyl-2-pyrollidone and vinyl acetate (Figure 1). Both monomers impart important properties that define the polymer's performance characteristics. The pyrrolidone ring is responsible for excellent water solubility, adhesion, film forming and solubilization properties, while the vinyl acetate monomer reduces glass transition temperature (Tg) and hygroscopicity compared to homopolymers of pyrrolidone (PVP). Well-known in the industry as a multipurpose excipient, copovidone functions as a binder, solubilizer/solid dispersion carrier and film former in a variety of pharmaceutical formulations.

key features and benefits

- excellent for oxidative sensitive APIs with greater long-term stability.
- efficient, high throughput, energy saving **binder/solubilizer/carrier** for hot-melt extrusion and continuous processes with enhanced processability and stability.
- versatile solid dispersion **solubilizer/carrier** for enhanced bioavailability in both spray-drying and hot-melt extrusion processes.
- superior **binder** for direct compression and dry granulation resulting in hard, non-friable tablets.

Our solvers set out to improve the peroxide stabiltiy and processing ease of original copovidone in HME applications. They successfully created an excipient that has lower peroxide content and growth rate, better powder flowability, extrudates lower in color and improved energy efficiency and throughput.

superior processing efficiency

As a spray dried powder, Plasdone™ S630 Ultra copovidone is well suited for direct compression, dry granulation, continuous processing and HME. Particles are spherical (Figure 1), with a d50 value of 80 to 160µm and a narrow particle distribution (Figure 2).

figure 1: scanning electronic microscopy of Plasdone™ S630 Ultra copovidone

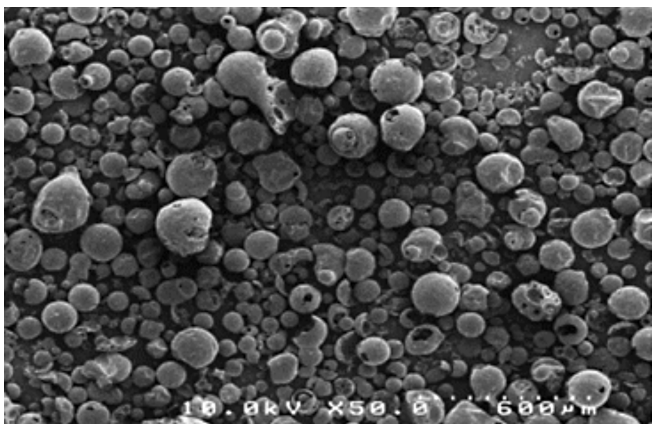
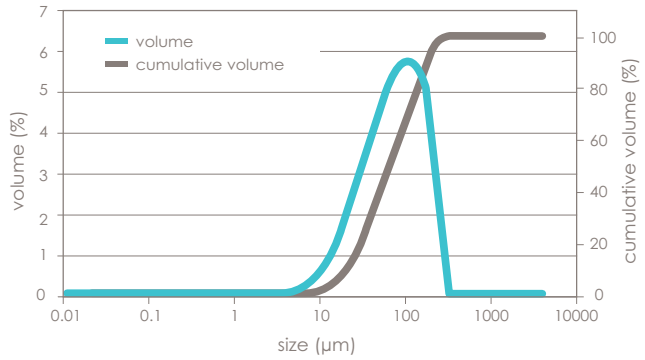


Figure 2: Plasdone™ S630 Ultra particle size and distributon



The spherical particle morphology of Plasdone™ S630 Ultra copovidone improves powder flow characteristics compared with the original copovidone as indicated in Figure 3. Improved powder flow results in a more efficient manufacturing process and minimizes or eliminates feeder clogging and prevents manufacturing stoppages.

Additionally, Plasdone™ S630 Ultra copovidone has lower melt viscosity(Figure 4) resulting in less energy consumption and better throughput.

Figure 3: Flow function and conditioned bulk density of original copovidone and Plasdone™ S630 Ultra copovidone

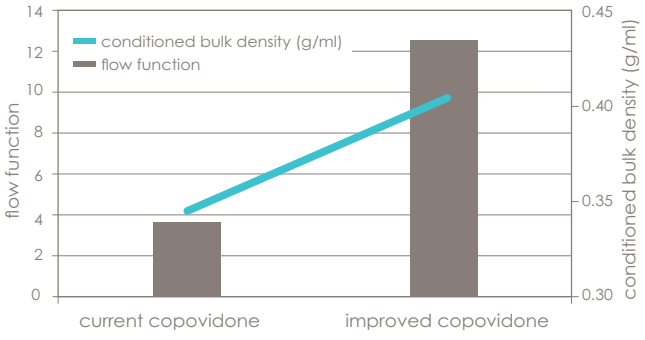
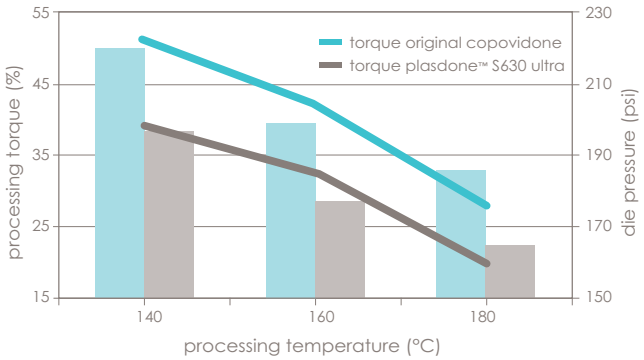


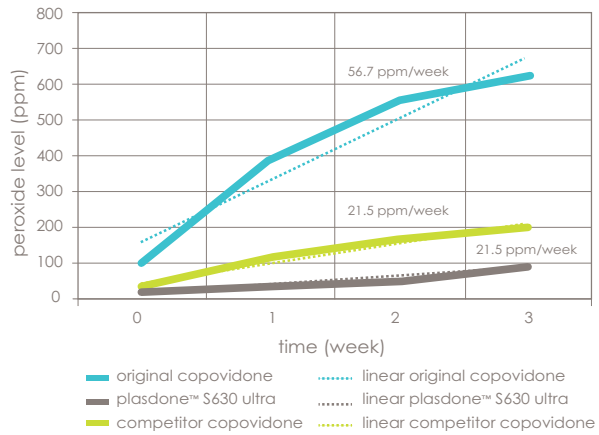
Figure 4. Processing torque and die pressure of original copovidone and Plasdone™ S630 Ultra copovidone at varied hot-melt extrusion process temperatures



greater stability

Monograph compliant copovidone contains peroxide levels less than 400 ppm. Even at this low level, APIs that are prone to oxidation may experience stability issues and HME extrudates tend to exhibit yellowish discoloration. Plasdone™ S630 Ultra copovidone exhibits significantly lower levels of peroxide (< 100 ppm), mitigating API instability as well as improving extrudate color. In Figure 5, initial levels of peroxide and its growth over a three-week period at ambient temperature is reported for the original copovidone, a competitor's product and Plasdone™ S630 Ultra copovidone.

Figure 5: Peroxide growth rate of original copovidone, Plasdone™ S630 Ultra copovidone and a competitor's copovidone



As seen in Figures 6 and 7, extrudates prepared with Plasdone™ S630 Ultra copovidone demonstrate a lower yellowness index and significantly lower peroxide levels compared to those prepared with original copovidone at various extrusion temperatures.

Figure 6. Appearance of original copovidone and Plasdone™ S630 Ultra copovidone post HME

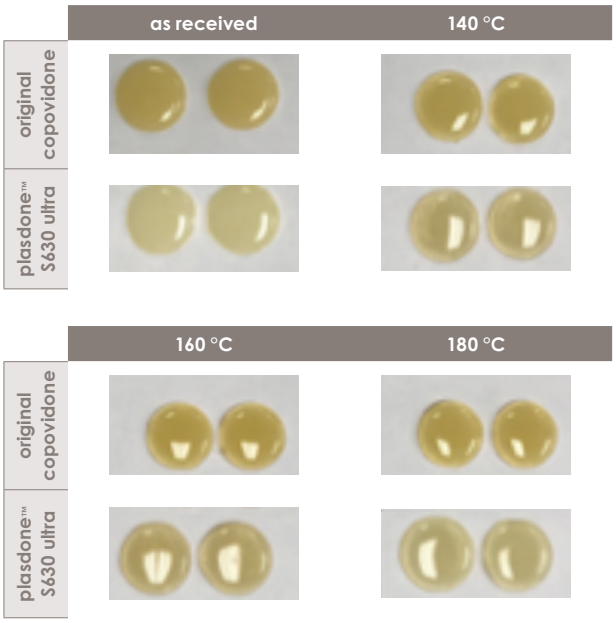
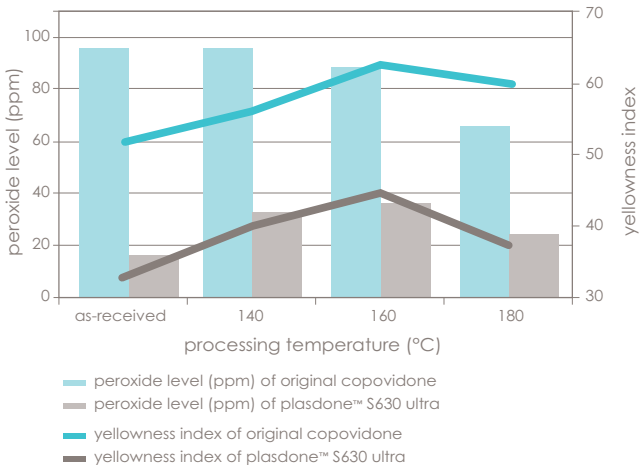


Figure 7: Yellowness index and peroxide level of original copovidone and Plasdone™ S630 Ultra copovidone post HME



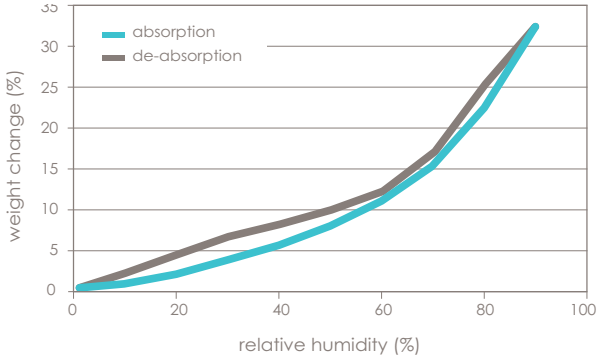
excellent binder for direct compression and dry granulation processes

Plasdone™ S630 Ultra copovidone is an excellent binder for direct compression and dry granulation processes (such as roller compaction) because it can be compressed to a higher degree than other polymers. The combination of pyrrolidone and vinyl acetate results in a copolymer with a relatively low Tg and upon compression it undergoes plastic deformation. This results in a slew of benefits starting with higher quality tablets — harder and non-friable — and reduced tablet punch wear due to lower compression forces.

lower hygroscopicity improves stability in high humidity

When formulating moisture sensitive actives, the low hygroscopicity of Plasdone™ S630 Ultra copovidone makes it an excellent excipient choice. The moisture adsorption profile (Figure 8) indicates that at 50% relative humidity, Plasdone™ S630 Ultra copovidone gains less than 10% moisture.

Figure 8: Plasdone™ S630 Ultra copovidone moisture absorption and desorption profile



bioavailability enhancement

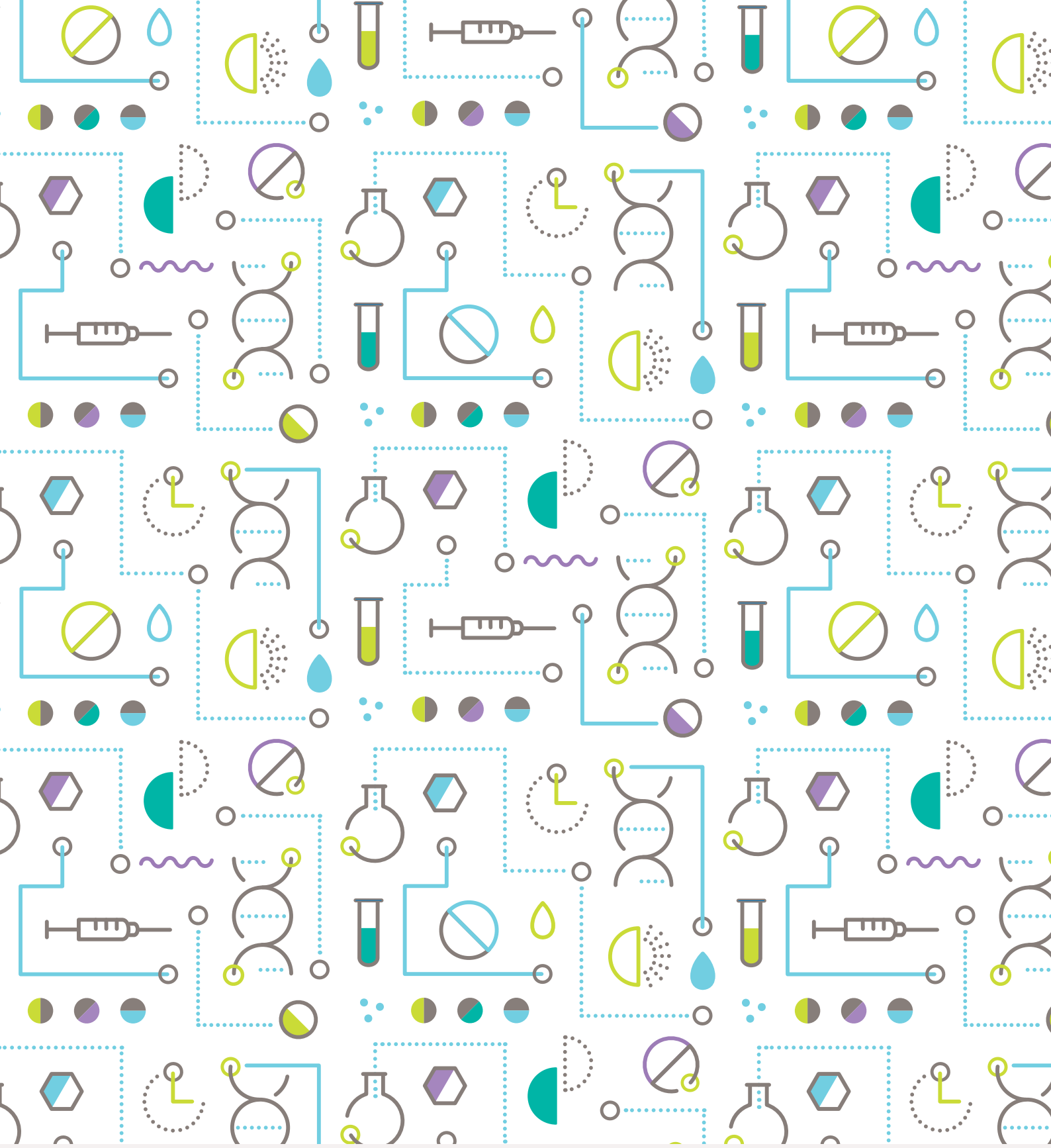
The unique combination of pyrrolidone and vinyl acetate monomers produces a copolymer with both hydrophilic and hydrophobic properties. This combination is perfect for increasing solubility and ultimately enhancing bioavailability. Plasdone™ S630 Ultra copovidone acts as a solubilizing agent, dispersant, and crystallization inhibitor. When used in spray drying and HME processes, copovidone transforms the API into amorphous nanoparticles or a solid solution. Plasdone™ S630 Ultra copovidone used in solid dispersion formulations prevents recrystallization during storage, facilitates dissolution and inhibits recrystallization *in vivo*.

tough and flexible films

Films made with Plasdone™ S630 Ultra copovidone possess low hygroscopicity, high elasticity, and low tack with a high substantivity to skin. When used in water-based sprays for topical applications, the films are clear and glossy.

monograph status

Plasdone™ S630 Ultra copovidone conforms to the current European Pharmacopeia (EP) and the National Formulary (NF) for copovidone as well as the Japanese Pharmaceutical Excipient standards (JPE) for copolyvidone.



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