Polymers for Solid Dispersions

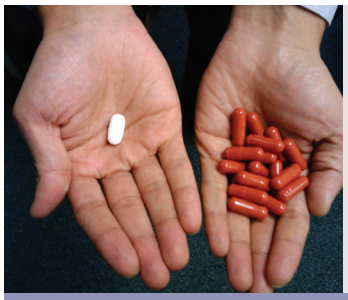
Ingredients, Process Technology Services, and Expertise for Drug Solubility Enhancement

A broad range of solutions for enhancing active pharmaceutical ingredient (API) solubility and bioavailability

Poorly soluble APIs pose development challenges, as common techniques for improving API solubility, such as salt formation and particle size reduction, do not always result in sufficient bioavailability required for therapeutic efficacy. As a result, there is increasing interest in the use of solid dispersion technology to improve the aqueous solubility and enhance the bioavailability of poorly soluble APIs. Multiple methods for preparing solid dispersions have been reported. Currently, the methods of most interest are melt extrusion and spray drying.

Ashland's Plasdone™ povidone polymers are widely used in preparing solid dispersions by melt extrusion and spray drying, as the inhibitory effect of povidone and copovidone on crystallization of drugs is well known. The thermoplastic property of Klucel™ hydroxypropylcellulose enhances processability in melt extrusion. Benecel™ hydroxypropylmethylcellulose is used in spray drying for its stability and to enhance bioavailability.

Application	Products	Benefits
Hot-melt Extrusion	Plasdone K povidone and Plasdone S-630 copovidone	Desirable thermal/rheological properties. Strong hydrogen bond acceptor. Enhances thermodynamic and kinetic stability of solid dispersions. Chemically inert. Non-pH dependent dissolution. Excellent safety profile with clinical precedence.
	Polyplasdone™ crospovidone	Extrudate is in the form of particles that can be used for direct compaction to simplify tablet preparation.
	Benecel™ HPMC	Hydrogen bond acceptor and donator. Superior stabilizer and supersaturation inhibitor. Chemically inert. Non-pH dependent dissolution. Excellent safety profile with clinical precedence.
	Klucel™ HPC	Superior thermal plasticity. Enhances processability and can be used as process aid in hot-melt extrusion.
Spray-dried Dispersions	Plasdone K povidone and Plasdone S-630 copovidone	Excellent solubility, stability and low viscosity in a wide range of solvents. Strong hydrogen bond acceptor. Enhances thermodynamic and kinetic stability of solid dispersions. Chemically inert. Non-pH dependent dissolution. Excellent safety profile with clinical precedence.
	Benecel™ HPMC	Hydrogen bond acceptor and donator. Superior stabilizer and supersaturation inhibitor. Chemically inert. Non-pH dependent dissolution. Excellent safety profile with clinical precedence.



Let us help you improve the performance of your poorly soluble APIs to do the following:

Reduce development timelines and costs

Develop delivery technologies for life-cycle management

Bring new products to market—faster

Improve safety and efficacy

Enhance patient compliance

Create new methods to rejuvenate failed/ discontinued products

ASHLAND®

With good chemistry great things happen.™

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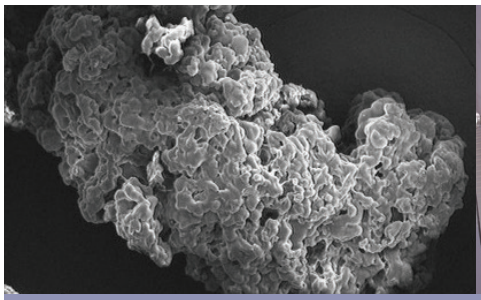
ASHLAND®

Experience with over 100 APIs

Ashland scientists have developed spray-dried dispersion formulations for over 100 APIs for over 50 pharmaceutical and biopharmaceutical clients worldwide. Our objective is to help you bring your drug products to market; therefore, Ashland pays close attention to the performance of the product, its stability, manufacturing efficiency and fit with finished dosage formulation and production. It is not unusual for pure crystalline drugs that are converted to amorphous forms to revert back to the crystalline form. However, when properly formulated, a drug-polymer solid dispersion can have a high level of amorphous stability and, in many cases, a relatively high drug load.

More ingredient solutions for poorly soluble APIs

Solution	Characteristics
Polyplasdone™ crospovidone	A unique disintegrant with high interfacial activity: improves the dissolution of poorly soluble drugs in a way that is not possible with other disintegrant technologies.
Plasdone™ C polymers	Inhibit API crystallization in injectable dosage forms.
Cavamax*, Cavasol*, and Cavitron™ cyclodextrins	Through the formation of cyclodextrin-API inclusion complexes, cyclodextrins improve the bioavailability of drugs in solid, liquid, and parenteral dosage forms.
Pharmasolve™ and 2-pyrol solubilizers	Formulation solvents increase the solubility, rate of solubilization and stability of drugs in aqueous solutions.



Solid dispersion development services from Ashland include the following:

Feasibility or proof-of-concept studies and optimization of spray-dried dispersions

Accelerated kinetic stability models to predict long-term physical stability

Kinetic solubility profiles to predict in vivo performance

Scale-up and manufacturing process development of spray-dried dispersions

Oral solid dosage formulation development and film coating

Manufacture of clinical trial materials in our cGMP facility

Projects can be conducted under R&D or cGMP protocols

Full cGMP documentation and analytical support

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