

Nano Milling for Enhanced Bioavailability

Nanocrystalline drug products offer an alternative to amorphous dispersions for some compounds that require enhanced bioavailability. A nanocrystal approach is preferred for APIs that rapidly crystallize from an amorphous state, exhibit temperature-dependent chemical instability, or are poorly soluble in common solvents used for spray drying.

DRIED NANOCRYSTAL FORMULATIONS

Formulation
Screening



Process Development
and Scale Up



GMP

FORMULATION LOCK

DEMONSTRATION BATCH AND TECH TRANSFER

MANUFACTURING CAPABILITIES

10 - 20 mL batches
1 - 2 g API per batch

≤ 3 - 25 L batches
0.3 - 5 kg API per batch

≤ 3 - 200 L batches
0.3 - 40 kg API per batch

Milling
Equipment



Material Sparing Vials



WAB Dynomill
MultiLab



Netzsch Labstar
Zeta

Spray Drying
Equipment



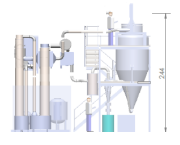
SD-45



SD-90



SD-180



SD-720

Benefits of Nano Milling

- ✓ Alternative to amorphous dispersions
- ✓ Bioavailability enhancement for poorly soluble compounds
- ✓ Reach high doses required for pre-clinical toxicological studies
- ✓ Increased dissolution rates

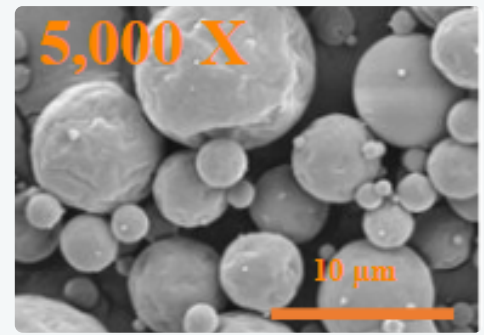
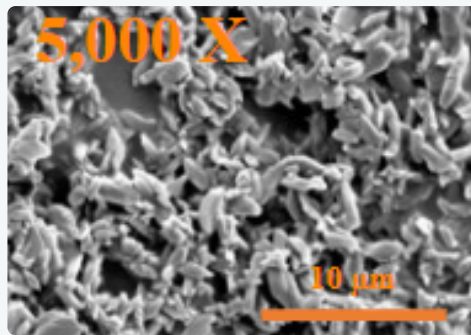
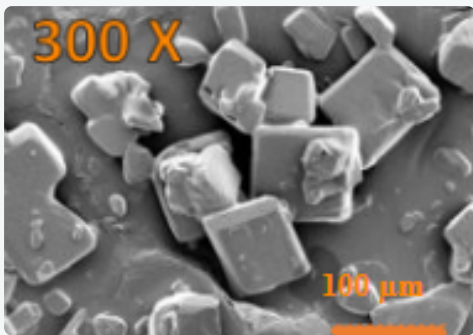
Drug Product Options

Nanocrystals ranging from 100-300 nm in diameter are incorporated into a drug product either as a liquid suspension or as a dry powder. Common dry nanocrystalline products include capsules, tablets, multiparticulate beads, powder for reconstitution, and dry powder inhalers for pulmonary and nasal delivery.

Better formulation and processes achieved **early in product life cycle.**

Primary bioavailability enhancement results from an increased dissolution rate relative to micronized API crystals. When dissolution rate limits bioavailability, reducing crystal size from 20 μm to 200 nm increases dissolution rate 100-fold. Increased solubility is a secondary benefit whereby strong interfacial curvature of the nanoparticle may boost solubility up to 2-fold relative to micronized API for nanocrystals < 200 nm.

INGOING API  MILLED NANOCRYSTALS  SPRAY-DRIED PARTICLES



Nanoparticle size distribution is a CQA

- ✓ In-line measurements of nanocrystal size are made during the manufacturing process using spatially-resolved DLS. Unlike traditional in-process measurements, this new technique does not require sampling and dilution from the process stream, leading to instantaneous and direct process monitoring.
- ✓ Off-line, Serán complements DLS using resistive pulse sensing to construct the shape of the particle size distribution by measuring large numbers of particles one-by-one. By quantifying the large and small tails of the particle size distribution, better formulation and process choices are made early in the product life cycle.

There's a Science to **Success**™

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Serán is a world leader in drug development and manufacturing. Utilizing a foundation of physical and chemical science, Serán designs robust formulations and engineering solutions to some of the industry's toughest drug product problems.