

New Product...

Application: Dissolution / Micronization— Groundbreaking Tool for Formulation of Poorly Soluble Drugs



Before

- Crystalline API particle in water
- Average particle size > 200um
- Large pieces, clumping

After

- Average particle size < 10um
- Improved homogeneity
- Tighter distribution

Covaris AFA Process Technology (bench-top system)

Flow Systems

- Improves quality of DMPK Pharmacokinetic studies
- Enhances bio-availability
- Dramatic reduction in API degradation
- Standardizes repeatable protocols
- Improves process efficiency

SITUATION

While the number of poorly soluble APIs is rapidly increasing the current formulation technologies constrain and limit appropriate preclinical evaluation studies. New drugs face multiple challenges in formulation development:

- Solubilization adjuncts impair rapid pharmacologic assessment.
- Dissolution procedures are generally complex, difficult to control, time consuming. . .and ultimately very costly.

CURRENT TECHNOLOGY LIMITS

Current Issues	Fundamental Limits/Constraints
Solvents	Risk of contamination
Surfactants / detergents	Risk of added toxicity
Stirring / agitation	Adds heat and degrades API
Operator error / high subjective content	Non-repeatable and inconsistent dosing
Uncontrolled shear stresses	Super saturation / crash / inconsistent dosage
Heat	Molecular modification and damage

COVARIS SOLUTION

Key Features	Benefits
■ Rapid	✓ Reduces or eliminates additives, simplifies formulations (little or no surfactants)
■ Reproducible	✓ Standardized application of industry-proven AFA technology ✓ Eliminates subjective operator influence / automated processing
■ Scalable	✓ Scales from small scale bench-top screening through clinical studies (microliters to 1,000+ liters)
■ Isothermal	✓ Eliminates molecular damage by maintaining isothermal sample temperatures
■ Closed non-contact	✓ Minimizes impurities or risk of contamination with disposable wetted surfaces



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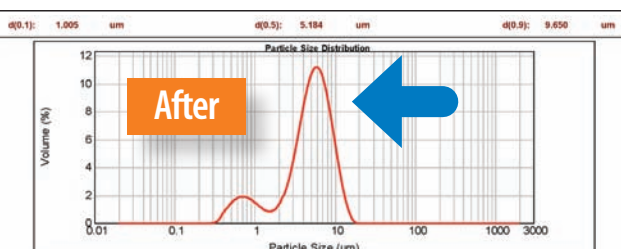
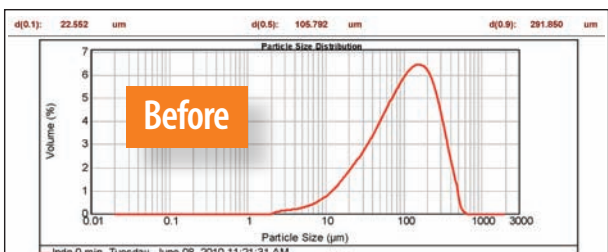
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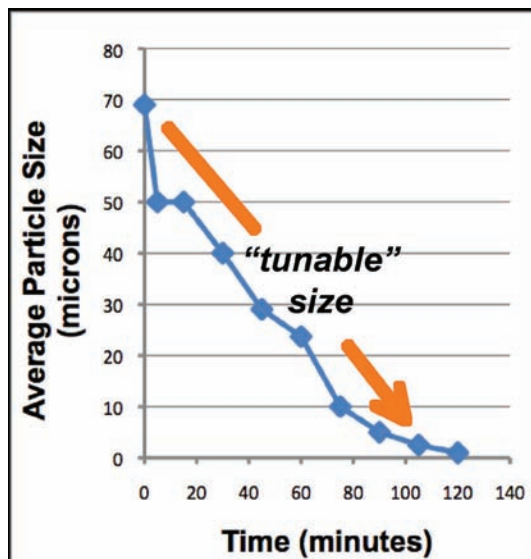
Industry-proven Covaris AFA™ (Adaptive Focused Acoustic) dissolution/micronization technology is now available for high volume processing with Covaris Flow Systems

IMPROVED PARTICLE SIZE REDUCTION—efficient, tunable particle size reduction to 100nm.

Indomethacin (water, no surfactants)



250 ml Quercetin (water, no surfactants)



	Current method (homogenizer)	Focused Acoustics
D90	45µm	9.65µm
D50	25µm	5.2µm
D10	15µm	1.0µm

Breakthrough

IMPROVED SOLUBILITY PERFORMANCE—Covaris AFA dramatically reduces processing time requirements from 2 days to less than 3 minutes, AND improves purity by up to 15X over current methods.

ID	Poorly Soluble Medias	Approx Target	Covaris			Current Technology				Covaris		
			Total Solubility	Best Current Tech	% Improvement	API Conc.	API Conc.	Degrade d API Conc.	Degrade d API Conc.	% Degrade d API	% Degrade d API	% Purity Improvement
A	Cavitron, PEG300, Water, API	10+	2.0	1.31	53%	1.9	0.852	0.2	0.456	9.0	34.9	388%
B	Cavitron, Propylene Glycol, Water, API	10+	1.7	1.14	49%	1.5	0.736	0.2	0.407	13.0	35.6	274%
C	Cavitron, Glycerin, Water, API	10+	2.0	1.37	46%	1.8	0.916	0.2	0.456	8.0	33.2	415%
D	Cavitron, Sorbitol, Water, API	10+	2.5	1.47	70%	2.3	1.01	0.2	0.458	7.0	31.2	446%
E	Cavitron, Water, PVP K29/30, API	10+	2.9	2.34	24%	2.7	1.76	0.1	0.575	5.0	24.6	492%
F	Cavitron, Water, API	10+	2.9	1.52	91%	2.8	1.05	0.2	0.474	6.0	31.1	518%
G	Cavitron, EtOH, 50mM pH7 Citrate Buffer, API	10+	10.5	9.81	7%	9.8	3.96	0.6	5.85	6.0	59.6	993%
H	Cavitron, PEG300, 50mM pH7 Citrate Buffer, API	10+	10.4	9.53	9%	9.8	3.8	0.6	5.73	6.0	60.1	1002%
I	Cavitron, Propylene Glycol, 50mM pH7 Citrate Buffer, API	10+	10.1	9.51	6%	9.5	3.78	0.5	5.73	5.0	60.3	1206%
J	Cavitron, Glycerin, 50mM pH7 Citrate Buffer, API	10+	10.1	9.55	6%	9.6	3.71	0.5	5.84	5.0	61.2	1224%
K	Cavitron, Sorbitol, 50mM pH7 Citrate Buffer, API	10+	11.1	10.5	6%	10.6	4.11	0.5	6.37	4.0	60.8	1520%
L	Cavitron, 50mM pH7 Citrate Buffer, PVP K29/30, API	10+	9.6	9.25	4%	9.2	3.68	0.4	5.57	4.0	60.2	1505%
M	Cavitron, 50mM pH7 Citrate Buffer, API	15+	14.8	14.4	3%	14.0	5.67	0.8	8.7	5.0	60.5	1210%

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	Current Technology	Covaris AFA
Time Required	2 Days	160 Seconds
% Impurity	> 60%	4-13 %

Breakthrough