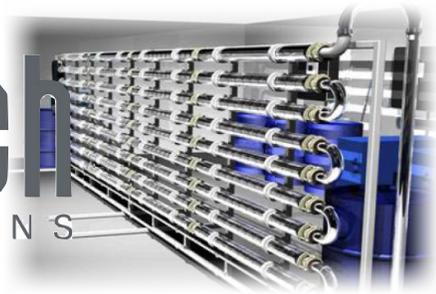
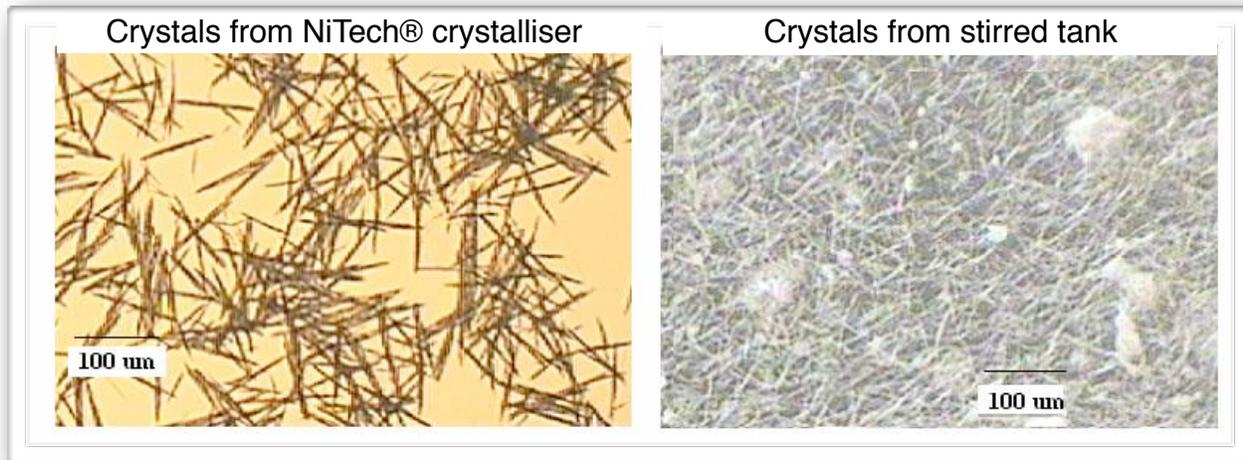




NiTech
SOLUTIONS



Continuous Crystallization of Pharmaceuticals Using NiTech® Continuous Crystalliser – Delivering Consistent Crystal Quality



Delivering consistent crystalline product requires significant process understanding and control over critical processing parameters. While traditional batch processes yield acceptable results, the ability to develop precise control over a process lifetime presents a unique challenge, with changing equipment, scalability, and process transfer.

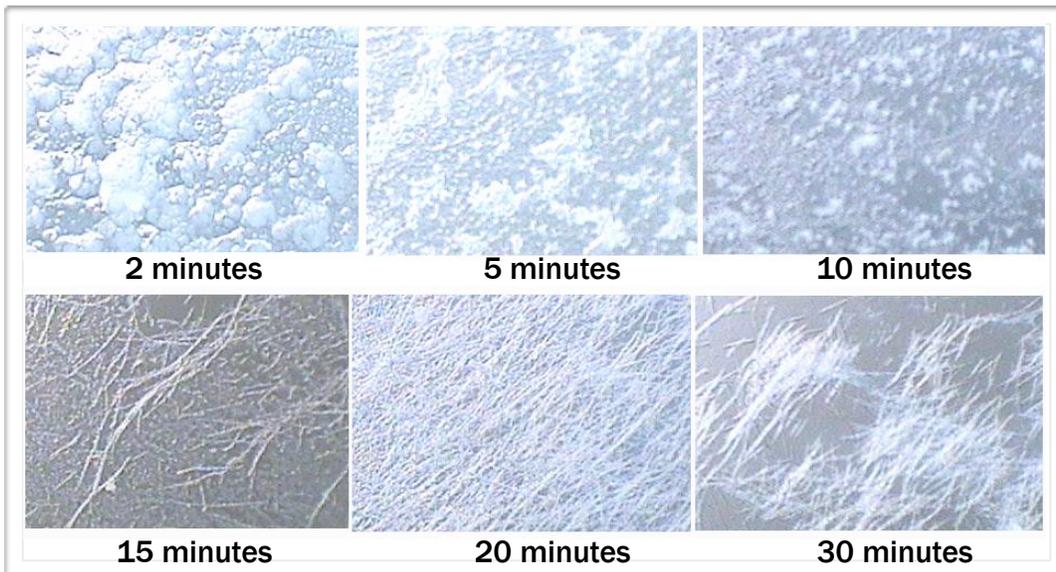
NiTech® plug flow crystalliser offers consistent fluid mechanical conditions and superior heat transfer rates, provides a highly reliable, repeatable and consistent environment for nucleation and crystal growth, leading to consistent crystal properties and significantly reduced process time. Furthermore, the scale up of NiTech® crystalliser is linear and all process analytical tools routinely used in lab environment can directly be applied to industrial crystallizations without modification, ensuring direct and smooth transition from lab to full scale of operations.

By changing the distance and frequency of oscillation, mixing intensity in the NiTech crystalliser can be precisely controlled throughout the entire continuous reactor. This uniform mixing and temperature control allows for a much more uniform environment for crystals to nucleate and grow.

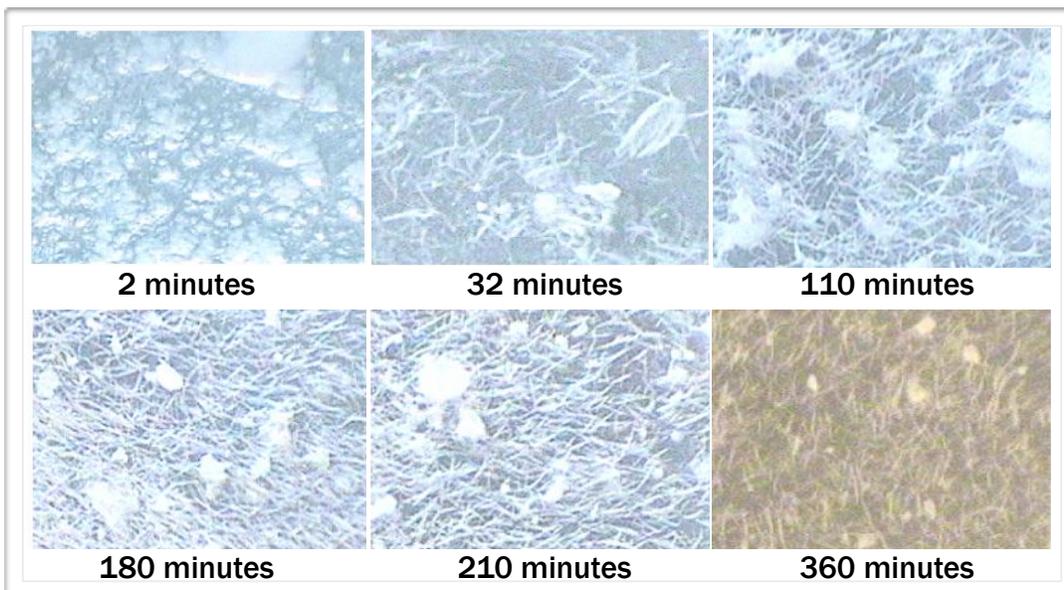
Using a well known API that exhibits problematic polymorph behaviour, we produced consistent polymorph (left picture) by just changing the mixing intensity alone, while keeping the chemistry the same (no changes to solvent, concentration or salt form). In the process **we** eliminated the amorphous form obtained from traditional batch operation. The moisture content was reduced to 50% (target 55%) from 65% and the overall process time was reduced from 8 hours to 30 minutes!



NiTech crystal growth



Batch crystal growth



As can be seen from the pictures above, providing uniform mixing using COBR results in less entrainment of amorphous material, fewer agglomerates, and much more consistent crystalline product.

Cost benefits include reduced filtration times, and higher polymorphic purity. Moreover, heat transfer in jacketed tubes is much more efficient, mimicking lab scale processes and resulting in dramatic reduction in overall energy use and space while increasing process intensity.