

This has been demonstrated using a single stage MSMPR with a recycle loop in an effort to minimize waste and obtain a system where nucleation and growth kinetics could be estimated.¹⁴⁵ In this work the nucleation rate increased with increasing supersaturation and suspension density. It has also been shown that a two stage MSMPR cascade with a recycle loop can be used to better control the PSD utilizing kinetic parameters obtained from the single stage MSMPR process.¹⁴⁶ By changing the temperature profile across the two MSMPR stages the mean particle size can be controlled where a steeper temperature decrease and a shorter residence time results in smaller particles.

With regards to work that did not use recycle loops, one study looked at using antisolvent addition to generate a seed suspension in batch before implementing continuous flow in a single stage MSMPR and how this compares with the equivalent batch process.¹⁴³ It was found that the MSMPR crystallizer was able to access PSDs that were both smaller and larger compared with batch. Another study looked at cooling crystallization to generate the seed suspension in batch so that steady state operation was reached sooner after continuous flow began.¹⁴⁴ In this work it was demonstrated that the nucleation rate increased with increasing suspension density and this depends on the temperature profile. As well as having an MSMPR in the form of a stirred tank reactor there has been research into using a TCC as an MSMPR where continuous cooling crystallization takes place after the initial seed suspension is created in batch mode.¹⁴² The TCC operates by imposing the crystallization under a Taylor vortex flow induced in the cylinder gap by rotating the inner cylinder where the rotation speed can be altered in addition to the solution feeding strategy (number of feeding ports used). It was demonstrated that the PSD was controlled by the solution concentration, feeding strategy and the rotation speed of the inner cylinder as these factors controlled the supersaturation profile which determine primary and secondary nucleation rates.

1.4.8 High Shear Wet Mill in MSMPR Configuration

A wet mill can be used in an MSMPR configuration for the purpose of delivering high shear to a solution leading to continuous seed generation. The wet mill can either be placed inside the MSMPR^{100,147,148} or upstream of the MSMPR.^{147,148} The studies have demonstrated that whether the wet mill is used inside or upstream of the MSMPR, it acts both as a continuous seed generator and a size reduction tool in a continuous crystallization process. A clear conclusion from using the wet mill is that increasing the rotor speed decreases the mean particle size, as would be expected.¹⁰⁰ This decrease in particle size is due to increased secondary nucleation in addition to increased primary nucleation depending on the process. Furthermore, using wet milling has been shown to significantly enhance the yield of a process especially when used upstream of the MSMPR in the form of a high shear nucleator due to the increased nucleation rates.¹⁴⁷ Using the wet mill upstream has also