297g Particle Design for Enhanced Dissolution Rates of Poorly Water Soluble Drugs

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For poorly water soluble drugs, the clinical utility of available pharmaceutical dosage forms can be limited. Novel processes have been developed to form amorphous nanoparticles of water insoluble drugs for enhanced dissolution rates: evaporative precipitation into aqueous solution (EPAS), spray freezing into liquid (SFL) and antisolvent precipitation processes. The goal is to combine pharmaceutical science with chemical engineering in order to design particles with high bioavailability. To minimize growth of the drug particles in EPAS, which would otherwise occur in the free jet expansion, the solution was sprayed into an aqueous solution containing a surfactant stabilizer. Drug levels as high as 37.9 mg/mL of 400-700 nm particles were achieved in a 5.0 wt. % surfactant solution. Strategies are reported for achieving high drug potencies up to 90%, yet with rapid dissolution rates. In these processes, the ability to arrest drug particle growth to achieve high surface areas results from rapid phase separation and stablization of the resulting particles with polymers and surfactants. The mechanisms of particle formation and stabilization, as well as the enhancement in dissolution rates, are discussed for various water insoluble drugs. Bioavailabilty resuts for mice, for oral and pulmonary administration are reported for particles made by various processes. These solution based approaches to produce nanoparticles offer several advantages over mechanical homogenization/milling processes including reduced handling of solids, high yields, ease of incorporation of stabilizing excipients, ease of scale-up, and control of crystallinity.