

Comminution of ibuprofen to produce nano-particles for rapid dissolution.

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Abstract

A critical problem associated with poorly soluble drugs is low and variable bioavailability derived from slow dissolution and erratic absorption. The preparation of nano-formulations has been identified as an approach to enhance the rate and extent of drug absorption for compounds demonstrating limited aqueous solubility. A new technology for the production of nano-particles using high speed, high efficiency processes that can rapidly generate nano-particles with rapid dissolution rate has been developed. Size reduction of a low melting ductile model compound was achieved in periods less than 1h. Particle size reduction of ibuprofen using this methodology resulted in production of crystalline particles with average diameter of approximately 270nm. Physical stability studies showed that the nano-suspension remained homogeneous with slight increases in mean particle size, when stored at room temperature and under refrigerated storage conditions 2-8°C for up to 2 days. Powder containing crystalline drug was prepared by spray-drying ibuprofen nano-suspensions with mannitol dissolved in the aqueous phase. Dissolution studies showed similar release rates for the nano-suspension and powder which were markedly improved compared to a commercially available drug product. Ibuprofen nano-particles could be produced rapidly with smaller sizes achieved at higher suspension concentrations. Particles produced in water with stabilisers demonstrated greatest physical stability, whilst rapid dissolution was observed for the nano-particles isolated in powder form.

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