

Controlling Fenofibrate Crystal Size in a Solid Dispersion Using MeltDose® Technology

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Introduction:

This study examines the effect of formulation and process parameters on fenofibrate particle size. MeltDose® controlled agglomeration is a proprietary technology for incorporating a drug into an amphiphilic polymer vehicle by spraying the drug dissolved in the melted vehicle onto carrier particles in a fluid bed. The resulting granular product containing the drug in a solid dispersion or solid solution is applicable for direct tablet compression. Poorly soluble fenofibrate dissolved in a melted PEG/Poloxamer matrix gives improved oral bioavailability and eliminates food effect. Fenofibrate recrystallizes in a solid dispersion partly as sub-micron particles.

Methods:

The impact on fenofibrate crystal size of carrier particle size, vehicle feed rate, product temperature, vehicle temperature, and degree of vehicle atomization was investigated in a half-fraction experimental design with four center points. The fenofibrate crystal size distribution in the produced granules was determined by laser diffraction in an aqueous suspension dissolving the remaining constituents.

Results:

Solid dispersions with a median fenofibrate crystal size in the range of 1.1-2.5 µm were manufactured. The statistically significant process variables controlling fenofibrate crystal size were product temperature ($p < 0.0008$) and vehicle feed rate ($p < 0.01$). This indicates the cooling time of the sprayed material being the critical factor for the fenofibrate crystal size in the solid dispersion. These process variables controlling the fenofibrate crystal size are also the main process parameters controlling the size of the granulate product.

Conclusion:

The recrystallization of fenofibrate in a MeltDose® based solid dispersion is controlled by only two process parameters, both influencing the cooling rate of the drug solution.