

Investigating crystallization mechanism of celecoxib nanocrystals in presence of mannitol

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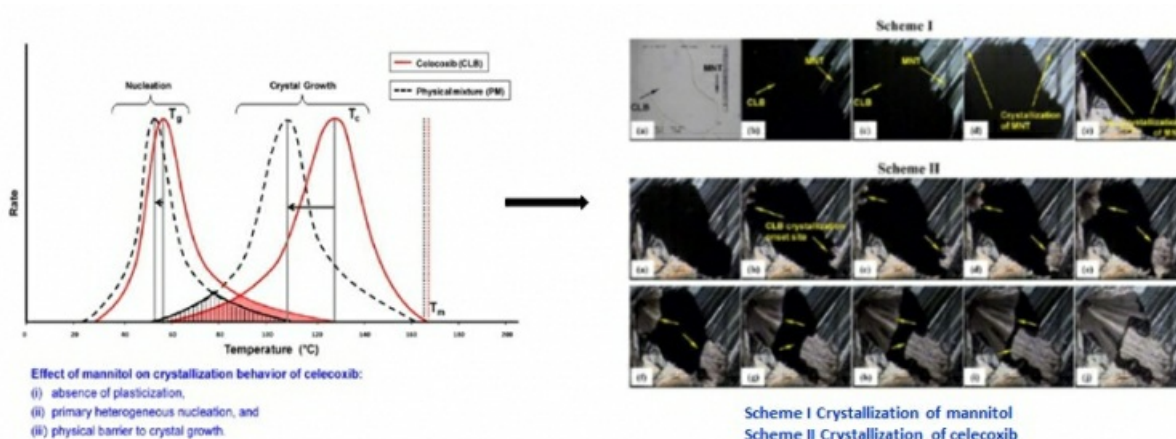
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Mannitol acts as crystallization inducing excipient in novel bottom up NanocrySP technology developed in our lab. The objective of this work was to investigate crystallization inducing mechanism of mannitol for generation of celecoxib (CLB) nanocrystals during spray drying process. Nanocrystalline solid dispersion (NSD) of CLB was obtained by spray drying the solution of CLB: mannitol in 1:1 ratio with average crystallite size of 214.07 ± 45.27 nm. In NanocrySP technology, nanocrystals are formed via intermediate amorphous form of the drug. In earlier work we have reported plasticization of amorphous drug hesperetin in presence of mannitol. In present case, DSC studies revealed the glass transition temperature (T_g) of amorphous CLB at 56.8 °C and there was negligible change (54.8 °C) in presence of mannitol negating the role of plasticization of amorphous drug by mannitol. However, DSC data suggested the crystallization inducing potential of mannitol by reducing the crystallization temperature of amorphous CLB. Amorphous CLB alone was crystallizing at 128.28 °C while it was crystallizing at 109.74 °C in presence of 25 % mannitol. To further investigate, polarized light microscopy-simple and reliable method for visual observation of crystallization, was explored. Mannitol facilitated heterogeneous nucleation of amorphous CLB at CLB-mannitol interface as evidenced by polarized light microscopy images. Transmission electron microscopy revealed inhibition of crystal growth of CLB. In conclusion, though mannitol did not plasticize amorphous CLB, it induced crystallization by (i) heterogeneous nucleation at CLB-mannitol interface (ii) reducing crystallization temperature and (iii) providing physical barrier to crystal growth.

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