# Concurrent crystallization of two active pharmaceutical ingredients using polymers

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Particle engineering of active pharmaceutical ingredients by crystallization is important and widely used to meet complex requirements. By adding a small amount of polymer during crystallization, various characteristics such as bioavailability, crystal stability, and drug release control may be controlled, and many advantages such as high efficiency and cost reduction may be obtained. Such polymer-directed crystallization can trigger crystal formation through non-classical crystallization pathways mediated by physical adsorption of long-chain molecules. We hypothesized that one polymer can link the crystals of two different drug molecules by polymer-directed crystallization. Complex drug crystals can be made into two drugs into one tablet to improve processability and stability, reduce the number of drug tablets, and reduce prices. The two drugs used in this study are valsartan (VAL) and amlodipine besylate (AMB), which treat hypertension. The polymer dissolved in the solution is adsorbed on the surface of the nucleus, and the crystals form a collection of crystals. Optical and scanning electron microscopy showed two different types of crystal habits. In addition, changes in crystallinity were observed through birefringence observation. As a result of measuring the melting point by the differential scanning calorimetry, it was found that the melting point of the two drugs changed significantly in the composite crystal, resulting in a significant change in the interaction between the drug and the polymer. Through powder X-ray diffraction, it was confirmed that the crystal shape changed according to the composition ratio of the drug. The proton nuclear magnetic resonance confirmed the composition ratio of the obtained crystal, and the result showed that the precipitation ratio was the same as the addition ratio. This new method of preparing composite crystals may provide new opportunities for convenient preparation of composite formulations and improved processability and stability.