Crystal Design for the Optimal Performance of Solid Pharmaceuticals

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Purpose: The aim of this research was to clarify the effect of crystal shape (crystal habit) on the disintegration and dissolution properties of active pharmaceutical ingredient (API) on the basis of surface energy and packing energy of API.

Methods: The different crystal habits of API were prepared from the different crystallization solvents. The physicochemical properties of different crystal habits of API were evaluated by powder X-ray diffraction, scanning electron micrograph, surface free energy and calculation of packing energy. The disintegration of tablet and the dissolution study was performed in aqueous medium.

Results: From the contact angle measurements and packing energy calculation, it was found that (002) face of phenytoin was more hydrophilic and lower packing energy than any other faces of phenytoin crystal. The dissolution rate of phenytoin from (002) face was greater than any other faces of phenytoin crystal. So, it is important to control the crystal shape for the quality control of dissolution rate of API.
The crystal shape affected the water penetration to glycine crystal. Although the water penetration toα-from (water) was slow enough due to the hydrophobic properties of developed 002 plane, the disintegration ofα-from (water) was significant fast. On the other hand, water penetration toα-from (ethanol) was fast due to hydrophilic properties of developed 120 plane, however the disintegration was not occurred. For the disintegration properties, 002 plane is weakly attached, then, when a little water was penetrate into crystal, penetrated water promote the disintegration through the 002 plane. On the other hand, although the water penetration was fast forα-from (ethanol), developed 120 plane was strongly attached, then, the disintegration was not easily occurred.

Conclusions: The physicochemical characteristic of each crystal face was quantitatively evaluated by above analytical methods. It was found that microscopic analysis of API is important to control the disintegration and dissolution characteristics of API.