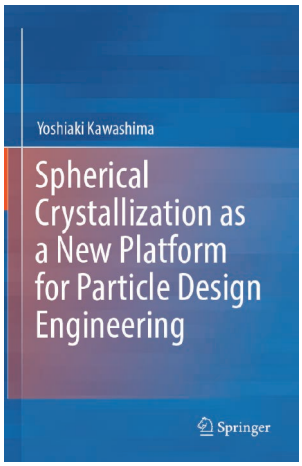

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Book Review

Introduction of a new book entitled "Spherical Crystallization as a New Platform for Particle Design Engineering" by Y. Kawashima

Traditional powder (KONA) technology has described successfully powder processing, i.e. powdered material handling, as a mass-unit operation system such as comminution, classification, agglomeration and others. A paradigm shift has been occurred in modern powder technology by looking at carefully individual particle's property itself such as surface topography and even internal structure at molecular level. As a result, a new concept of particle design engineering has been arisen to modify or change the property or function of the raw particulate material to produce more valuable product. In general, there are two ways for particle designing, classified as break-down and built-up methods. We proposed a new built-up particle-design method, called the "spherical crystallization process," which can open the door to unique crystallization engineering that could replace traditional micro- and nano-technology approaches. In this process, nano to micro crystals produced by crystallization are spherically agglomerated at the same time. Spherically agglomerated crystals can improve the micromeritic properties of original particles, which can be reliably formulated in pharmaceutical dosage forms. The paradigm shift of nano-to-microparticle design by spherical crystallization is overviewed by looking at the principle of spherical agglomeration in liquid and new particle design platform developed by the spherical crystallization system shown in the contents (**Table 1**).

In Chap. 2, it was described that the ultrafine crystals formed by antisolvent crystallization of an API (salicylic acid) are simultaneously self-agglomerated—spherically—by a small amount of bridging liquid produced from the crystallization solvent by phase separation. The agglomeration kinetics were described by a first order, followed to zero-order process with mass base after crystallization finished. In Chap. 3, the paradigm shifted pharmaceutical process provided by spherical crystallization is explained by direct-tableting API. The way how spherically agglomerated API crystals can be directly tableted without using a binder is explained owing to the paradigm shifted compaction behavior of spherically crystallized products appearing under static and dynamic compactions. In Chap. 4, it was explained how the spherical crystallization technique was developed as a novel particulate-design platform to create various functional particulate preparations. Spherical crystallization was originally carried out using a tri-solvent system, that is, a good solvent, a poor solvent, and a bridging liquid, in which the crystallized particles spherically agglomerated with the bridging liquid induced from the system simultaneously. It was recently found that if a good solvent solution is partially miscible in a poor solvent, the residual undissolved good solvent acts as a bridging liquid for the crystals, which can make the original spherical crystallization technique widely applicable to any other API. Ascorbic acid crystals, as poorly compressible model crystals, are spherically agglomerated using a binary-solvent system, enabling direct tableting without requiring a binder. To improve the physicochemical properties of APIs, such as their solubility or therapeutic performance, a multi-component system was developed by combining a surfactant or hydrophilic polymer with a dispersing (poor) solvent. The solubility of the formulated drug can be enhanced by adding a specifically interacting API to the formulation. The solubility of the anti-inflammatory drug indomethacin is enhanced by combining it with epirizole to form a new spherically

crystallized complex. Spherical crystallization using a double-component system such as theophylline and ethylene diamine can produce polymorphic aminophylline depending on the water content in the system. Polymeric spherical crystallization has been developed for preparing drug carriers (microspheres and microballoons) for novel DDSs. Interestingly, the spherical crystallization process can be widely applied as a platform technique for semi-solid materials such as vitamin E, which is transformed into a solid powder and can be filled in a capsule or tableted using colloidal silica. In Chap. 5, it was described how an ethanol solution of an acrylic polymer, such as Eudragit (RS, S or L), and an API dispersed in water or polyvinyl alcohol (PVA) forms quasi-emulsion droplets in which the API and the polymer are co-precipitated to form a spherical micro-matrix. A controlled drug-releasing system was developed by using this process, termed "emulsion solvent diffusion (ESD)" method. Hollow microspheres (microballoons), which are used for multiple floating-controlled drug-delivery systems, are developed by the polymeric spherical crystallization process. To quantitatively describe the floating behavior of the microballoons in the stomach, a novel radio-scintigraphical method using Technetium-99m has been developed. In Chap. 6, the development of biocompatible and biodegradable polymeric micro/nanospheres using poly (D,L-lactide-co-glycolide) (PLGA), loaded with a bioactive substance by the ESD method, is described. It is difficult to directly formulate nanospheres in their final pharmaceutical form due to their strong aggregation tendency. To overcome those problems, the PLGA nanospheres are transformed into solid dispersed nanosphere composites containing a water-soluble excipient, such as a sugar alcohol, which can reproduce the original fresh nanospheres (NSs) dispersed at the applied site. Preparing nanocomposite particles can allow to handle them in the same way for preparing solid-dosage forms, such as tablets, capsules, dry-powder inhalations (DPIs), and so on. PLGA nanospheres with chitosan-modified surfaces can improve the drug absorption at the target site due to a sustained stay and prolonged release of the drug. Transdermal DDSs containing PLGA-nanosphere composites have been developed for nanocosmetics, as discussed in Chap. 7. A whitening and anti-aging cosmetic containing ascorbyl tetraisopalmitate (VC-IP) loaded PLGA NSs, named "NanoCrysphere®," was launched in 2004 by Hosokawa Co. Ltd. In Chap. 8, future perspectives of the platforms for designing new DDSs and manufacturing them at industrial scale with a new continuous pharmaceutical process are described.

[Author: Kawashima, Yoshiaki]

Table 1 Contents

Author's Short Biography

Yoshiaki Kawashima

Yoshiaki Kawashima is an Emeritus Professor of Gifu Pharmaceutical University and a Contract Professor of Aichi Gakuin University. He received his doctoral degree in 1970 in pharmaceutical engineering at Kyoto University. Professor Yoshiaki Kawashima is the pioneer and a world-leading pharmaceutical scientist to develop a new platform for particulate design engineering. The most unique particle engineering process developed by him is "spherical crystallization technique." This built up design system was evaluated as the receipts of many honors and awards, including the Pharm. Sci. World Congress Award, Colorcon Intnl. (FIP) Award and KONA Award. He has coauthored more than 400 scientific papers, 120 review papers, 50 books/chapters, and 70 patents. He is an International Fellow of AAPS, SGPhW and JAPST.