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Original Research Paper

Application of povacoat as dispersion stabilizer of nanocrystal formulation

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Nanosizing by wet beads milling is one of the methods to improve the solubility of poorly water soluble compounds [1,2]. Hydrophilic polymers, such as Hydroxypropylcellulose-SSL (HPC), Polyvinylalcohol (PVA), and Polyvinylpyrrolidone-K30 (PVP) etc. are used as dispersion stabilizer to prevent aggregation of nanoparticles. However, there are many compounds that cannot be dispersed by ordinary dispersion stabilizers. In this study, we used Povacoat® as a dispersion stabilizer for several poorly water soluble compounds milled to nanoparticles. The influences of aggregation of the nanoparticles on the dissolution behavior and the oral absorption of the compounds were studied using formulations with high and low dispersion characters. In this study, we used various compounds with poorly water solubility such as Griseofulvin (GF), Tolbutamide (TOL), and Hydrochlorothiazide (HYD) etc. The suspension of compound was prepared by milling compound with zirconia beads in polymer aqueous solution by rotation/revolution pulverizer. Then powder formulation of milled compound was prepared by freeze-drying the suspension. We compared the effect of Povacoat on dispersion stability of milled compounds with those of PVA, HPC, and PVP as polymers generally used. The dispersion stability and crystallinity of the milled GF were evaluated by particles size analyzer, scanning electron microscope (SEM), and powder X-ray diffraction (PXRD). We also evaluated the dissolution behavior and the oral absorption of the milled GF with each polymer. We first used GF and compared the dispersion stability of the milled GF with Povacoat to those with the other polymers. GF suspension with Povacoat had higher dispersion stability than the suspensions with the other polymers (Fig. 1). The re-dispersion stability of the GF powder formulation with Povacoat was higher than those with the other polymer. The aggregation of GF nanoparticles was observed by SEM when PVA, HPC, and PVP were used as dispersion stabilizer. The crystallinity of milled GF was found to be maintained by PXRD. Milled GF with Povacoat showed higher dissolution behavior and bioavailability compared with the other polymers. The aggregation of nanoparticles had significant impact on the dissolution behavior and bioavailability of GF (Fig. 2). Povacoat was applied

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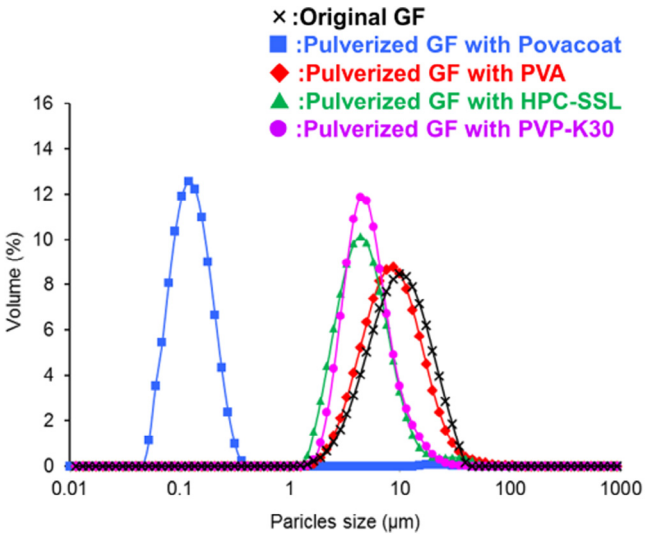

Fig. 1 – Particle size distribution of the Griseofulvin (GF) suspension after re-dispersing the pulverized GF powder with each polymer in water.

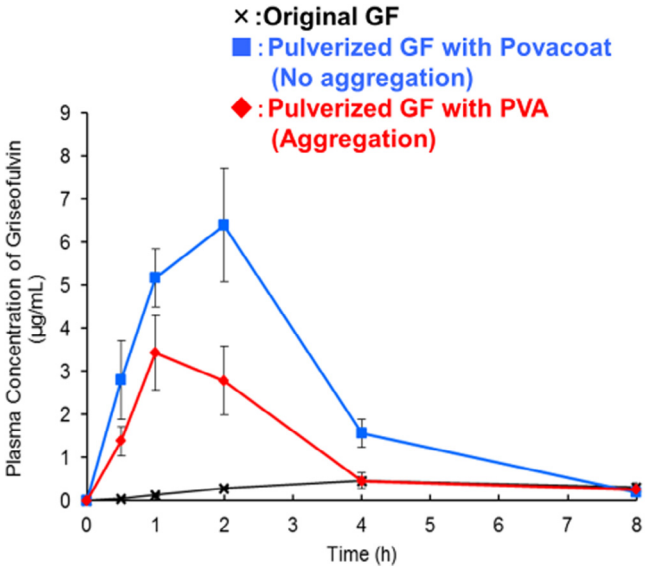

Fig. 2 – Plasma concentrations of Griseofulvin (GF) after oral administration [3].

to TOL and HYD, and the other compounds from the result of GF. In case of both compounds, the formulation with Povacoat had higher dispersion stability than the formulations with the other polymers. It was found that Povacoat could be widely applicable for nanocrystal formulation of poorly water soluble compounds.

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