S12-3 Drug nanoparticle formation by co-grinding and the effect on intestinal absorption

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Reducing particle size is one of ideas to improve bioavailability of drugs with poor absorption. Our previous studies demonstrated that drug nanoparticles were successfully produced by dry co-grinding of a poorly water-soluble drug with a polymer and a surfactant. The nanosuspension prepared from the ground mixture (GM) dispersed into distilled water exhibited good stability with the mean particle size of ca.100nm or more. The size reduction under 50 nm makes it possible to prepare the transparent solution, which is expected to show enhanced drug absorption. When probucol nanosuspension from probucol/polyvinylpyrrolidone (PVP)/sodium dodecyl sulphate (SDS) ternary GM was administered by oral gavages to rats, ternary GM with PVP K12 demonstrated a superior improvement of probucol absorption compared to the GM with PVP K17. Even when particle size of both formulations was adjusted to ca.40nm, GM suspension with PVP K12 demonstrated higher drug absorption than that with PVPK17. From the results of physicochemical characterization, the observed particles had core-shell structure, i.e. drug nanocrystals were covered with PVP-SDS complex. Structural difference of the complex formed with PVPK12 and PVPK17 seems to affect the difference of dissolution of probucol and the subsequent drug absorption. Thus, physicochemical characterization of drug nanoparticles, especially in the suspended state, is important to optimize the formulation of poorly water-soluble drugs.