

Title	Mitigation of the Pharmaceutical Food Effect: Investigation of Nanocrystals and Lipids
Keywords (up to 5)	Nanocrystal, Lipid, Silica, Oral Delivery
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Abstract	<p>Lipid-based formulations (LBFs) are well known to mimic the natural food effect by presenting the drug in its molecularly dispersed state, thus facilitating solubilisation in the gastrointestinal environment. An alternative approach to reduce fed/fasted state variation is the utilisation of drug nanocrystals which have the ability to undergo rapid dissolution irrespective of the presence or absence of food.</p> <p>This project explores the individual and synergistic effect of drug nanosizing and silica-lipid hybrid (SLH) microparticles as a solid-state LBF to enhance fasted-state drug solubilisation in the gastrointestinal tract. Lurasidone (LUR) is an antipsychotic drug which can benefit from such a formulation approach due to exhibiting poor aqueous solubility and a clinically significant pharmaceutical food effect.</p> <p>A nanosuspension containing LUR and HPMC E50 was fabricated using high-pressure homogenization, achieving a mean particle size of 434 ± 15 nm. During <i>in vitro</i> dissolution studies in simulated intestinal media, this formulation displayed an 11-fold increase in the rate and 1.7-fold increase in the extent of dissolution compared to pure, unmodified drug.</p> <p>Novel LUR nanocrystal-SLH microparticles were prepared by spray-drying a LUR and Capmul MCM emulsion with an aqueous dispersion of silica nanoparticles. Formulations were characterised for particle size, morphology and crystal state. The ability of the material to optimize LUR solubilisation was investigated during <i>in vitro</i> dissolution in fed and fasted media under digesting conditions. Studies revealed the novel formulation to significantly enhance fasted-state solubilisation levels compared to pure drug (> 24-fold increase), whilst significantly reducing fed/fasted state variability.</p> <p>The results illustrate the potential of a novel formulation combining the advantages of lipids and drug nanosizing to improve the oral delivery of LUR.</p>
References	<ol style="list-style-type: none"> 1. Denning T. <i>et al. European Journal of Pharmaceutics and Biopharmaceutics</i>. 2016 (101) 36-42. 2. Tan A. <i>et al. Journal of Controlled Release</i>. 2009 (134) 62- 70.