Amorphous Solid Dispersion of Felodipine with Zein Protein as the Excipient by Spray Drying

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Poorly-water soluble bioactive compounds (BCS II or IV) account for a significant percentage in the global market, which limit their bioaccessibility in the oral solid dosage form. Thus solubilization is still one major target to enhance the oral bioaccessibility of Biopharmaceutical Classification System II or IV entities. The amorphous solid dispersions is an effective strategy, in which fully synthetic or semi-synthetic polymers are used as common excipients up to now. In this work Felodipine with very poor solubility was chosen as the model compound from BCS II, Limiting the therapeutic application and efficacy for treatment of chronic hypertension. Regarding the excipient, zein protein as the food-grade polymer in food science area was used for spray drying. As a food-grade prolamin extracted from corn, the unique characteristics (biocompatibility, biodegradability, ease fabrication of particles, etc.) of zein protein make it a promising material in placement of synthetic or semi-synthetic ones for biomedical application like drug delivery and tissue engineering.

In the present work, we successfully prepared amorphous solid dispersions (ASD) of Felodipine with 30% of initial loading using zein protein as the excipient. Another two batches with same loading were also prepared using semi-synthetic polymer HPMC-AS and synthetic polymer PVP-VA as the controls. The prepared ASD batch Felodipine/Zein was characterized by XRPD (X-ray Powder Diffraction), PLM (Polarized Light Microscopy) and mDSC (Modulated Differential Scanning Calorimetry). The results showed non-birefringent spherical particles at the size of ~1um were formed, with one possible glass transition (Tg) at 128.6 °C observed from reversible heat flow curve of mDSC, indicating the amorphous material was successfully prepared. In the dissolution study, solubility of Felodipine from ASD batch using zein as polymer increased by more than 100 times in simulated intestinal fluid (SIF) when compared to crystalline Felodipine, and relatively prolonged high exposure was maintained within 6h as similar as the commercial common used polymers HPMC-AS and PVP-VA.