Utilizing the Drug-Polymer Interaction to Improve Chemical Stability of Hot-Melt Extruded Solid Dispersions
Z. Guo, M. Lu, Y. Li, H. Pang, C. Wu
Sun Yat-Sen University

Purpose
Hot melt extrusion (HME) is a novel technique for the preparation of amorphous solid dispersion, with many advantages such as low-cost and solvent-free. However, thermal degradation of heat-sensitive drugs at high processing temperature seriously limits the commercial application of HME. The present study was aimed to investigate whether or not the application of drug-polymer interaction was a potential method for preparing chemically stable amorphous solid dispersions of heat sensitive drugs by HME.

Methods
Diflunisal, which is degraded upon melting, was selected as a model drug. Four potential polymeric carriers (PVP K30, PVP VA64, HPMC and Soluplus) were selected for their hydrogen bonds donor/acceptor groups. Interactions between diflunisal and polymers were investigated by differential scanning calorimetry (DSC) and Fourier-transform infrared spectroscopy (FTIR). The phase transformation of diflunisal in polymer melts was studied by using hot stage polar microscopy (HSPM). The solid dispersions of Diflunisal were hot-melt extruded based on the above studies. Physical state, chemical degradation and dissolution behavior of the extrudates were studied by using powder X-ray diffraction (XRD) and high performance liquid chromatography (HPLC).

Results
Strong hydrogen bonds between diflunisal and those polymeric carriers were confirmed by the peak shift in FTIR patterns, the melting point depression in DSC curves and the negative interaction parameters. The results of HSPM indicate that diflunisal was dissolved in molten polymers at 160 °C, much lower than its melting point (215 °C). At this temperature, amorphous solid dispersions were successfully produced by HME, as confirmed by the XRD results. The related impurities in solid dispersions were lower than 0.3%, indicating that thermal degradation was effectively minimized. The dissolution of diflunisal from amorphous solid dispersions was significantly enhanced as compared with the crystalline pure drug.

Conclusion
Drug-polymer interaction was successfully utilized to depress processing temperature and prevent the thermal degradation of heat-sensitive drugs. This technique provides an attractive opportunity for the development of heat-sensitive drugs by HME.