508a CO2-Induced Plasticization and Viscosity Reduction in Pharmaceutical Polymers

Dehua Liu, Hongbo Li, David Tomasko, Geert Verreck, Albertina Arien, Peeters Jef, and Brewster Marcus

Solid dispersion of an active component in a polymer carrier is a major delivery vehicle for pharmaceuticals. Currently available processing techniques include organic solvent-based methods and melt extrusion. In general, dispersion at the molecular level, retaining activity of the ingredient, and minimization of toxicity are important aspects for developing a suitable processing technique. Unfortunately, organic solvents pose the problem of removing the toxic solvent from the dispersion, and the melt extrusion requires the thermal stability of ingredients and acceptable rheological properties of polymer carrier. CO2 has emerged as a powerful alternative and been extensively studied in processing bio-related polymers. In this work, we studied the effects of CO2 on the glass transition temperature and viscosity of two pharmaceutical polymers (Eudragit E100 and PVP) using high pressure DSC and slit die rheometer, and performed extrusion of the pure polymer and polymer blend with the help of CO2. The results clearly show that viscosities of both PVP and Eudragit are reduced by a factor of up to 5 with CO2 compared with the conditions without CO2, which indicate that at lower temperatures, the extrusion of both polymers becomes feasible or easier than at their normal processing temperature with the addition of CO2. The high pressure DSC investigation also demonstrates a nearly 30oC decrease in Tg across the CO2 pressure range of 1 to 65 bar for polymer PVP, which strongly verifies the interaction between the PVP and CO2 and an improved polymer chain mobility upon CO2 sorption. Extrusion experiments validated the conclusions from Tg and viscosity characterization, such that CO2 could reduce the processing extrusion temperature by 20oC or higher. DSC analysis for the PVP/Eudragit blends extrudated at 95oC with the aid of CO2 confirms the presence of both polymer phases. The solid dispersion of drug in polymer matrix were prepared correspondingly at a lower temperature that won't induce the thermal degradation of drug molecules. The DSC analysis on extruded products shows that CO2 is also beneficial for improving the molecular level dispersion of drug molecules in polymer.