Influence of Supercritical Carbon Dioxide on Ketoprofen-Incorporated Hot-Melt Extruded Low Molecular Weight Hydroxypropylcellulose Matrices
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Purpose
The aim of the current research was to investigate the effect of supercritical carbon dioxide (SC-CO2) on the physico-mechanical properties of Ketoprofen and hydroxypropylcellulose (HPC) matrices produced using hot-melt extrusion techniques.

Methods
Ketoprofen 15–30% w/w with Klucel™ ELF/EF/LF HPC were subjected to thermal gravimetric analysis (TGA) to determine their stability at extrusion temperatures. Ketoprofen and polymer were sieved using ASTM #30 mesh and mixed using a V-shell blender. The resulting blends were extruded with or without SC-CO2 injection using a twin-screw extruder (16 mm Prism EuroLab, ThermoFisher Scientific) at screw speeds of 100 rpm (temperature range 90–140°C). SC-CO2 was injected into the extruder using a high-pressure regulator connected with flexible stainless steel armor-cased hosing. The other end of the hose was connected to the injection port seating on segment 6 of the extruder barrel. All of the extrudates were milled and sieved through ASTM #40 mesh. Bulk density, tap density, surface area and pore volume as well as drug release profiles of the milled extrudates were evaluated to understand the effect of SC-CO2 injection on the physico-mechanical properties. API physical form in the extrudates (initial and on stability) was determined by differential scanning calorimetry and confirmed using PXRD.

Results
TGA studies indicated stability of Ketoprofen and HPC at the employed extrusion processing temperatures for all formulations. Hot-melt extrusion assisted with SC-CO2 altered the morphology of the extrudates to foam-like structures and enhanced milling efficiency with minimal uptake of moisture. Milled extrudates exhibited lower bulk density, higher surface area and porosity and also demonstrated enhanced drug release compared to the extrudates processed without SC-CO2. The amorphous form of API was maintained in the extrudate during stability studies.

Conclusion
Hot-melt extrusion processing assisted with supercritical carbon dioxide increased porosity and enhanced the milling efficiency of extrudates and drug-release profiles. These processed properties of materials would provide numerous benefits during manufacturing of various solid dosage forms.

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