A Novel Application of Hot Melt Extrusion Technology to Develop a Continuous and Scalable Process for the Production of Fenofibrate Solid Lipid Nanoparticles
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Purpose
The aim of this study was to use Hot Melt Extrusion (HME) Technology to develop a continuous and scalable process to produce Fenofibrate (FBT) solid lipid nanoparticles (SLN), which will provide higher efficiency and improved product quality attributes.

Methods
1. Formulation Development of FBT SLN: Lipid and drug was fed into the co-rotating twin-screw extruder (11 mm Process 11, ThermoFisher Scientific, Karlsruhe, Germany) using a gravimetric feeder. A surfactant aqueous solution was heated to the equivalent of the extrusion temperature and was injected into the extruder barrel through an injection port using a peristaltic pump. Process parameters such as screw speed, barrel zone temperature, zone of addition of surfactant solution were optimized such that the lipid and drug were in a completely molten state when they contacted the surfactant solution and ultimately produced an emulsion. The hot pre-emulsion resulting from hot melt extrusion was passed through an insulated tube connected to the HME die and sample holder of the high-pressure homogenizer (Avestin Emulsiflex C5, Canada) at 85°C/1000 bar for size reduction.
2. Evaluation of FBT SLN: FBT SLNs were characterized for their particle size, polydispersibility index (PDI) and zeta potential.
3. In vivo evaluation of FBT SLN:
Pharmacokinetic studies were performed utilizing a crossover design with Wistar rats and the developed FBT SLN was compared with the marketed FBT micronized formulation. Plasma samples were withdrawn at pre-determined intervals and analyzed by a validated HPLC method.

Results
Processing of SLN at lower screw speeds (160rpm) and modified screw configurations produced SLN with particle sizes below 200 nm and narrow PDI (<0.5). Lipid and surfactant concentration exhibited an important role of SLN particle size. SLN processed with HME and high-pressure homogenization exhibited lower particle sizes of SLN as compared to conventional processes utilized for SLN preparation. In vivo pharmacokinetic studies in Wistar rats showed that the developed FBT SLN formulation demonstrated a prolonged MRT as compared to the conventional FBT formulation.

Conclusion
SLN were successfully prepared by the newly proposed method using HME and high-pressure homogenization technology. Continuous production of SLN can be achieved by this novel method.