Investigation of the solubility enhancement potential of Kollicoat® Smartseal 100P using Hot Melt Extrusion techniques

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PURPOSE

Solubility is an essential characteristic of active pharmaceutical ingredients (APIs), with profound effects on process and clinical development, formulation, and commercialization. For a drug to dissolve completely and get absorbed, it must be highly soluble in water. However, most of the newly discovered drugs are poorly soluble in water, leading to low bioavailability and high variability. Therefore, overcoming poor solubility is highly essential. Among the various methods available to improve solubility like complexation, use of surfactants, micronization and solid dispersions, the most common method used is by forming a solid dispersion of drug in the carrier polymer. Hot melt extrusion is the promising technology for enhancing the solubility by dissolving and distributing the drug in the polymer matrix because of its unique advantages like continuous processing and elimination of solvents.

OBJECTIVE

The objective of this study was to investigate the potential of Kollicoat® Smartseal 100P polymer to enhance solubility of poorly soluble Efavirenz (EFV) via hot melt extrusion (HME) technology.

METHODS

Extrusion:

- Kollicoat® Smartseal 100P, Polyethylene Glycol (PEG) 1500 and Efavirenz were tumble-mixed on a Maxiblend™ (GlobePharma, New Brunswick, NJ, USA) at 25 rpm for 15 minutes.
- The resulting blend was fed into a 11mm co-rotating twin screw extruder (Thermo Fisher Scientific, Waltham, MA, USA) and processed at 100 RPM at temperature varied from 120°C to 130°C according to the processability. PEG 1500 was used as plasticizer to lower the extrusion temperature and improve processability.
- The extrudates obtained were milled and sifted through ASTM #30 and the sieved powder was used for further studies.

Characterization:

- Differential Scanning Calorimetry (DSC) and X-Ray Diffraction (XRD) studies were done to investigate the nature and miscibility of drug with the excipients.
- FTIR spectroscopy was performed to check the interactions between the excipients and drug.
- In vitro dissolution studies were performed in simulated gastric fluid (SGF) without enzymes for 2 hours using USP apparatus II (SR8-plus, Hanson) at an agitation speed of 50 RPM and compared with that of pure EFV.
- Dissolution parameters like Dissolution Efficiency(DE), t50, Initial dissolution rate in 15minutes (IDR50) were evaluated.

RESULTS

- DSC results demonstrated that the polymer, PEG and drug were miscible, and the drug converted to an amorphous form after hot melt extrusion, as the sharp melting peak of Efavirenz at 140°C disappeared in the DSC thermograms of the extrudates (Fig. 1).
- The FTIR results showed that there is no significant chemical interactions between the drug and polymer but there might be weaker interactions like hydrogen bonding due to slight shifting of peaks as compared to pure EFV
- The release studies showed that the percentage of drug release from formulations (F1-F3) were 100%, 92% and 32% for 10%, 20%, and 30% drug loads, respectively in 2 hours, whereas only 16% of free efavirenz dissolved in 2 hours. The formulations (F4-F6) showed 100%, 60% and 32% drug release in 2 hours for 10%, 20%, and 30% drug load, respectively.
- These results suggested increased dissolution rates in formulations with high Kollicoat® Smartseal 100P content. All the extruded formulations demonstrated higher drug release as compared to the free drug.
- The dissolution parameters in Table 1 also suggest that the dissolution profile of EFV was improved by Kollicoat® Smartseal 100P polymer at all drug concentrations. Among all, formulations with 10% drug load showed the highest DE % of more than 92%, maximum IDR of around 5.5 and least t50 of 4 minutes.
- Therefore, maximum solubility enhancement was achieved with 10% drug load.

S.no	Efavirenz (%)	Kollicoat® Smartseal 100P (%)	Temperature (°C)	DE (%)	t_{50} (minutes)	IDR_{15}
F1*	10	80	130	91.86	4.5	5.89
F2*	20	70	125	68.33	25	3.07
F3*	30	60	120	21.12	>120	0.74
F4**	10	70	130	93.59	4.1	5.54
F5**	20	60	130	40.93	80	1.39
F6**	30	50	120	21.51	>120	0.73
Free EFV	100	___	___	12.54	>120	0.55

*10% PEG 1500; **20% PEG 1500

Table 1. Extrusion parameters and dissolution parameters

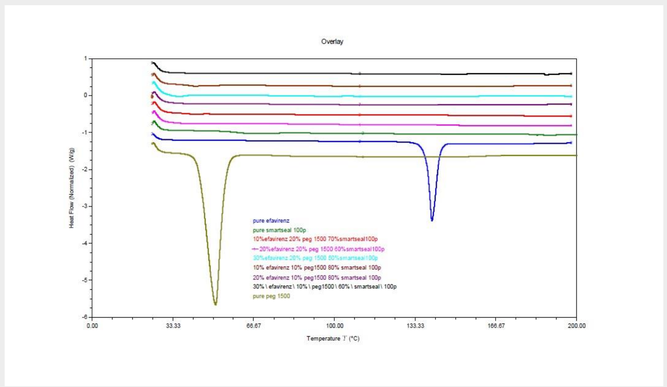

Fig 1. Overlay of DSC thermograms of pure EFV, Kollicoat® Smartseal 100P and formulations

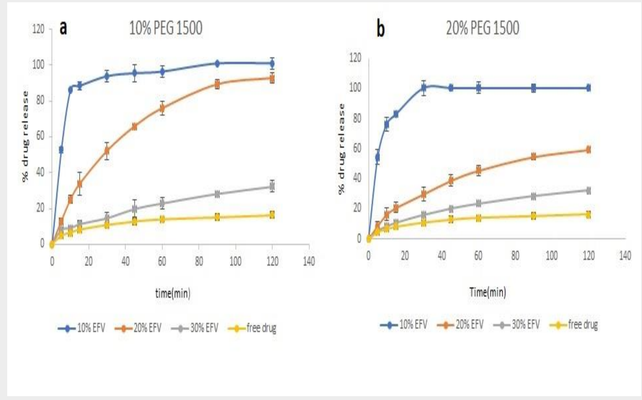

Fig 2. Dissolution studies of formulations containing 10% PEG 1500 and 20% PEG 1500 in Simulated Gastric Fluid without enzymes

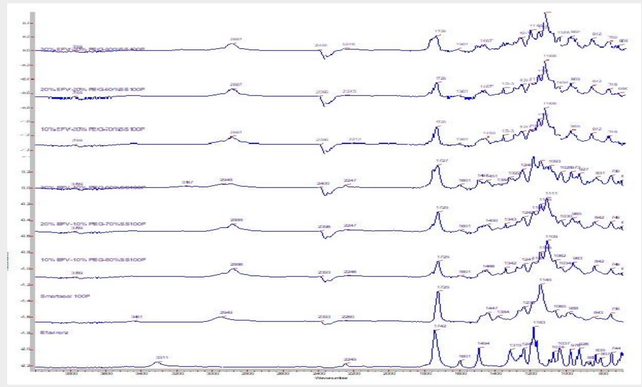

Fig 3. Overlay of FTIR spectra of pure EFV, Kollicoat® Smartseal 100P and formulations

CONCLUSIONS

- The solubility of Efavirenz was improved by the polymer, Kollicoat® Smartseal 100P using hot melt extrusion.
- The solubilization effect is dependent on the amount of polymer in the extrudates.
- As the polymer concentration is increased, the solubility enhancement was increased.
- Thus, Kollicoat® Smartseal 100P is a potential polymer to improve the dissolution of poorly soluble drugs using hot melt extrusion techniques.

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