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R17. Solid Crystal Suspensions of Carbamazepine using Hot-melt Extrusion: A Solubility Enhancement Approach

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PURPOSE

Solid crystal suspension (SCS) is an emerging technique for dissolution enhancement, in which the crystalline drug is suspended in crystalline excipient. Development of SCS of carbamazepine (CBM) with carriers mannitol and xylitol via a solvent free Hot-melt extrusion (HME) techniques to improve the dissolution.

OBJECTIVES

The main aim of current research is to investigate the development of solid crystal suspensions (SCS) of carbamazepine (CBM) to improve dissolution by Hot-melt extrusion (HME) techniques. The hydrophilic crystalline carriers xylitol (XYL) and mannitol (MAN) were investigated to assess the formation of SCSs.

METHOD

HME processing

The physical mixtures of CBM with varied drug loads (10% & 20%) and either of the carriers XYL or MAN were prepared by blending for 10 min at 20 rpm in V-blender (GlobePharma, Maxiblend™). The extrusion process was performed using a counter-rotating mini extruder (Haake MiniLab II, Thermo Electron, USA) at a screw speed of 50 rpm and at a processing temperature of 96°C & 170°C for XYL and MAN, respectively. The collected extrudates were cooled at room temperature, milled, sieved and stored in a desiccator until further evaluations. All the prepared formulations (CBM-MAN and CBM-XYL) were characterized by DSC and FTIR.

Differential scanning calorimetry (DSC)

The milled extrudates were characterized using differential scanning calorimetry (TA Instruments) to determine crystalline state of the CBM.

Fourier-transform infrared spectroscopy (FTIR)

FTIR was performed to investigate the solid-state intermolecular interactions between CBM and carrier using Agilent Cary 660 FTIR Spectrometer (Agilent Technologies).

In-vitro dissolution

In-vitro dissolution studies of pure CBM and prepared SCS formulation was performed in 900 mL of 1% SLS in water for 60 min using USP apparatus II (SR8-plus, Hanson) at an agitation speed of 50 RPM and the drug release was evaluated using a UV–Vis spectrophotometer (Genesys 180, Thermoscientific) at a wavelength of 288 nm.

RESULTS

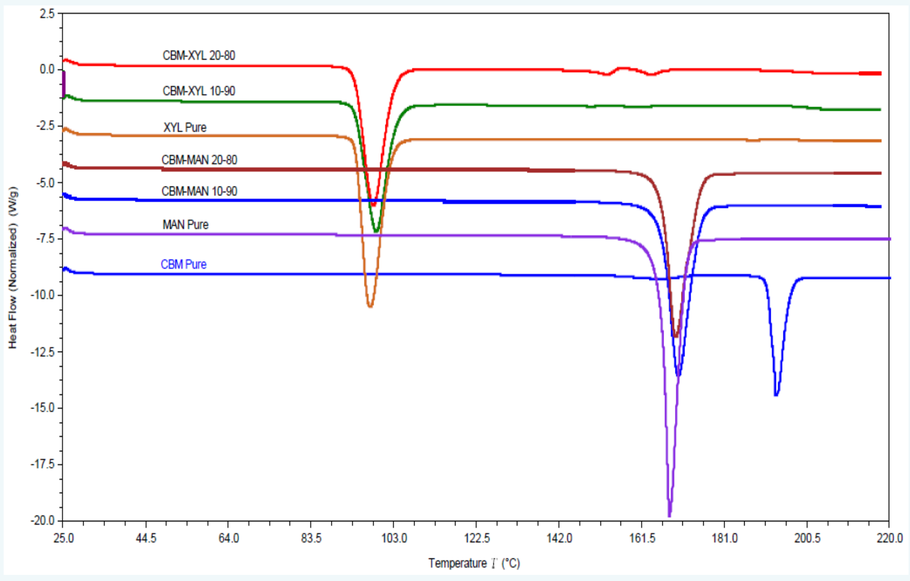

Figure 1. DSC thermograms of CBM, MAN, XYL, and SCS formulations

Formulation	CBM	MAN	XYL
CBM-MAN (10-90)	10	90	-
CBM-MAN (20-80)	20	80	-
CBM-XYL (10-90)	10	-	90
CBM-XYL (20-80)	20	-	80

Table 1. SCS formulations composition

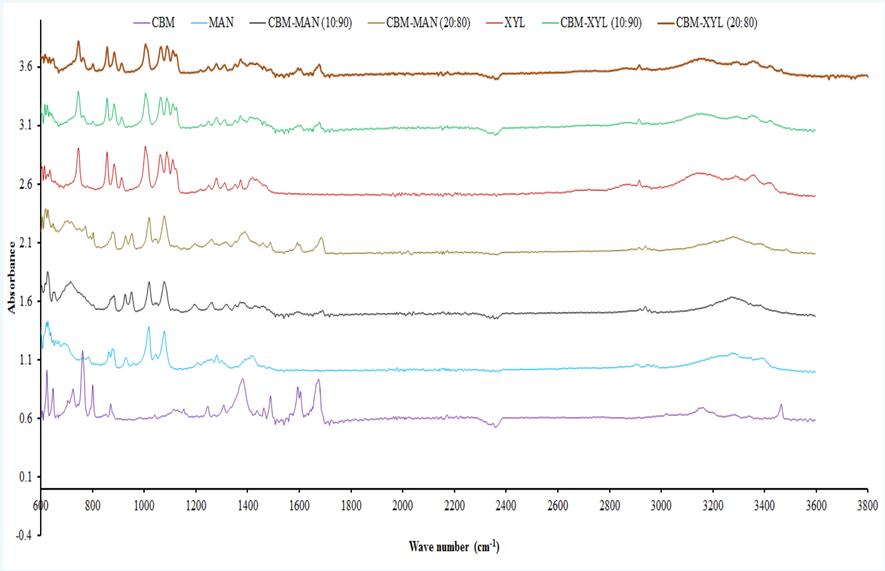

Figure 2. FTIR spectra of CBM, MAN, XYL, and SCS formulations

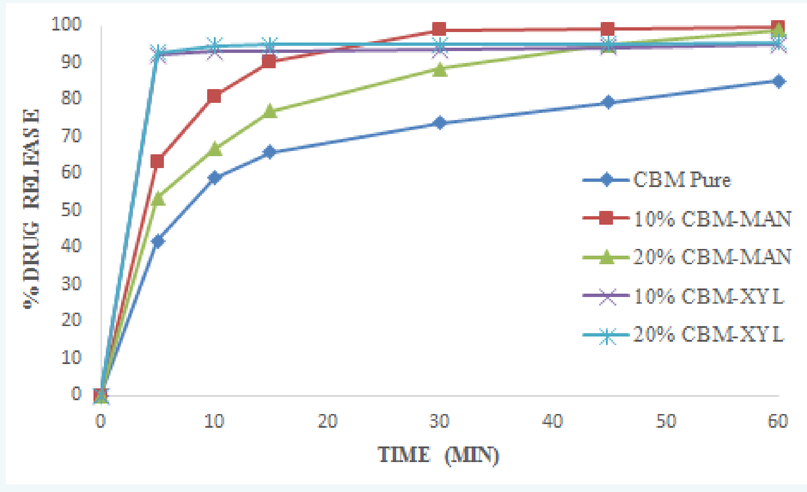

Figure 3. Dissolution of CBM, MAN, XYL, and SCS formulations in 1% SLS in water

CONCLUSION

CBM-MAN and CBM-XYL solid crystal suspensions were successfully prepared by hydrophilic carriers using HME. Studies revealed existence of formulations in crystalline form with no interactions. Furthermore, SCS was identified as a promising approach for enhancing solubility and dissolution of poorly soluble drugs.

ACKNOWLEDGEMENTS

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