Supporting Information

Phase behavior and FTIR study of the interaction between fenofibrate (FNB) and PEG

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Phase diagram of FNB/PEG systems

The phase diagram of FNB/PEG (MW of PEG is 3350) was constructed by optical microscopic determination of melting points and differential scanning calorimetry (DSC) measurements. [1, 2]

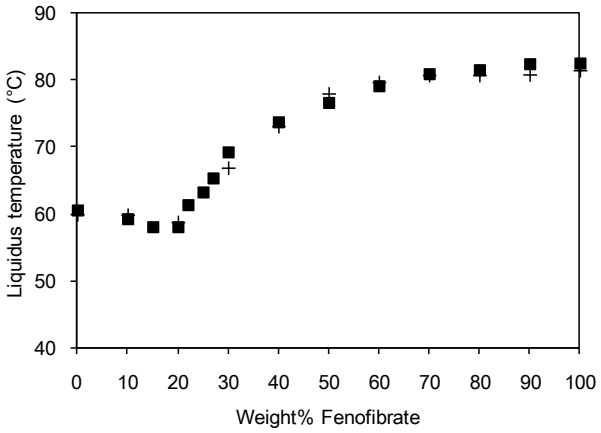

Figure S1. Phase diagram of FNB/PEG systems

(■: based on cross-polarized optical microscopy observation; +: based on DSC method)

FNB and PEG were physically mixed, heated to the melting point of the API, followed by cooling to allow solidification. After storage for about 1 week at low relative humidity, the FNB/PEG solid dispersions were ground using a mortar and pestle. The resultant powder was evaluated using a Nikon Eclipse E600 polarized light microscope (Nikon Inc., Melville, NY) equipped with a Linkam THMS 600 hot-stage (Linkam Scientific Instruments Ltd., Surrey, UK). The samples were heated at 1 °C/min until completely melted. The temperature where the last crystal melted was recorded, and was used to construct the phase diagram (Figure S1).

Samples were also analyzed using a TA Instruments Q2000 differential scanning calorimeter (TA instruments, New Castle, DE, USA) with a nitrogen purge of 50ml/min. The instrument was calibrated for temperature and enthalpy/cell constant by using indium (TA instruments, New Castle, DE, USA). Samples were analyzed in sealed aluminum pans and were first equilibrated at 25 °C, followed by heating to above the melting point of the pure FNB at a rate of 1 °C/min. The offset melting temperature was recorded (shown in Figure S1). From Figure S1, it can be clearly seen that FNB/PEG showed eutectic formation.

FTIR study of the interaction between FNB and PEG

The infrared spectra for pure FNB, PEG (MW 3350) and FNB/PEG (20/80% w/w) mixture in the molten state were collected using a Bio-Rad FTS-6000 (Bio-Rad, Cambridge, MA, USA) equipped with an attenuated total reflectance (ATR) accessory (diamond crystal, Golden Gate, Graseby Specac, Inc., Cranston, RI, USA). The sample (~20 mg) was scanned between 500 and 4000 cm^{-1} wavenumber, resolution of 4 cm^{-1}, and 128 scans. The system was purged with dry, CO_2-free air.

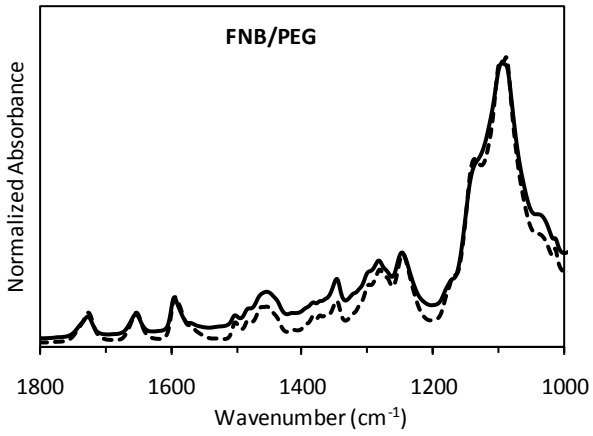

Figure S2. Infrared spectra of FNB/PEG (20/80) mixture at molten state. Solid (-) and dashed (--) lines represent the experimentally measured and calculated spectra of FNB/PEG (20/80) mixture respectively. The calculated spectrum for FNB/PEG is based on reference peaks at 1655 cm^{-1} (FNB) and 1094 cm^{-1} (PEG) of the pure materials.

Figure S2 shows a comparison between the calculated spectrum of a physical mixture and the experimental spectrum of the FNB-PEG mixture at molten state. If no FNB-PEG interactions are present, the calculated spectrum should be very similar to the experimental spectrum, which is the case for FNB-PEG mixture.

References

1. Baird, J. A.; Taylor, L. S. Evaluation and modeling of the eutectic composition of various drug-polyethylene glycol solid dispersions. *Pharm. Dev. Technol*. **2011**, *16(3),* 201-211.

2. Zhu, Q.; Harris, M. T.; Taylor, L. S. Time-resolved SAXS/WAXS study of the phase behavior and microstructural evolution of drug/PEG solid dispersions. *Mol. Pharmaceutics* **2011**, *8*, 932-939