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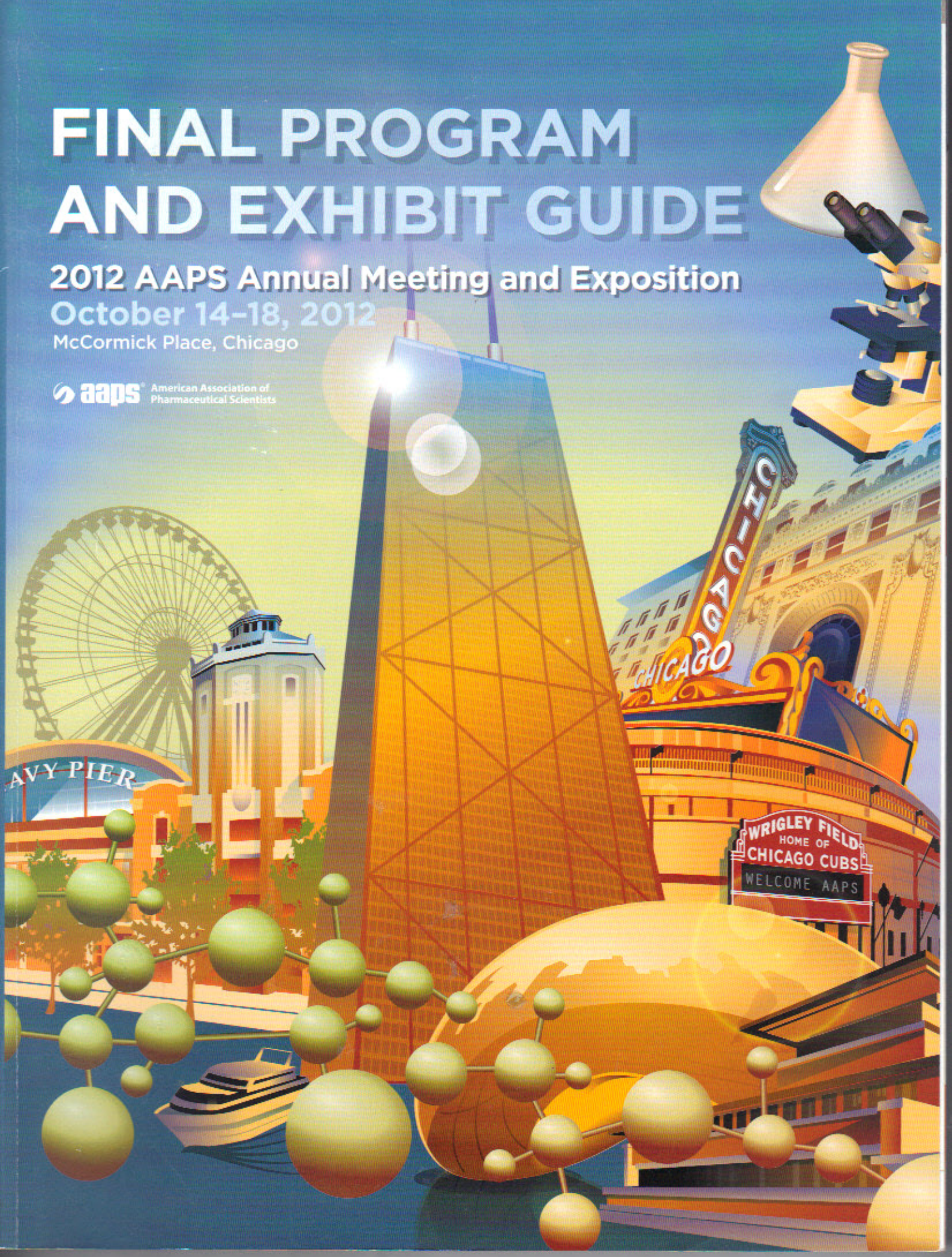

Physicochemical Characterization and In Vivo Evaluation of Fenofibrate-loaded Solid Dispersions Prepared by Various Methods using Spray Drying Technique

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Purpose

To compare the crystalline property, solubility, dissolution and bioavailability of fenofibrate in the solid dispersions prepared by different methods.

Methods

Various fenofibrate-loaded solid dispersions were prepared with water, polyvinylpyrrolidone (PVP) and sodium lauryl sulfate (SLS) using spray drying technique via the surface-attached method. The constituent's ratio with the highest solubility and dissolution was used to prepare solid dispersions by the same technique via the solvent-evaporation method and solvent-wetting method with 95% ethanol and acetone, respectively. The physicochemical properties were investigated by SEM, DSC and PXRD. The solubility, dissolution and pharmacokinetic studies were performed in comparison with fenofibrate powder.

Results

In the surface attached method, the solid dispersion with fenofibrate/PVP/SLS at the weight ratio of 5/3/2 showed the highest solubility and dissolution. The results of XRD, DSC and SEM confirmed that the solid dispersions obtained by the surface attached method and the solvent wetting method appeared as heterogeneous systems (solid suspensions) with crystalline drug and carriers suspended, respectively. Conversely, the system was homogeneous (solid solution) in case of solid dispersion prepared via the solvent evaporation method. The crystalline fenofibrate was not changed to amorphous in case of the surface attached method. However, the drug was converted to amorphous in the solid dispersions prepared by solvent evaporation and solvent wetting methods. The solubility, dissolution and bioavailability (AUC and Cmax) of fenofibrate were improved in order of the solid dispersions possessing: homogeneous amorphous system > heterogeneous amorphous system > heterogeneous crystalline system. In comparison with water-insoluble fenofibrate powder, the solubility of the drug was improved up to 145 μg/mL in the solid dispersions prepared via the surface attached method. In case of the solvent wetting and solvent evaporation methods, solubility was found 2 times and 3 times that of solid dispersion with no crystalline change, respectively.

Conclusion

The amorphous form of fenofibrate and the extent of molecular level intermingling of the drug with PVP and SLS play their significant part in improving the dissolution, solubility and oral bioavailability of the drug.