FINAL PROGRAM AND EXHIBIT GUIDE

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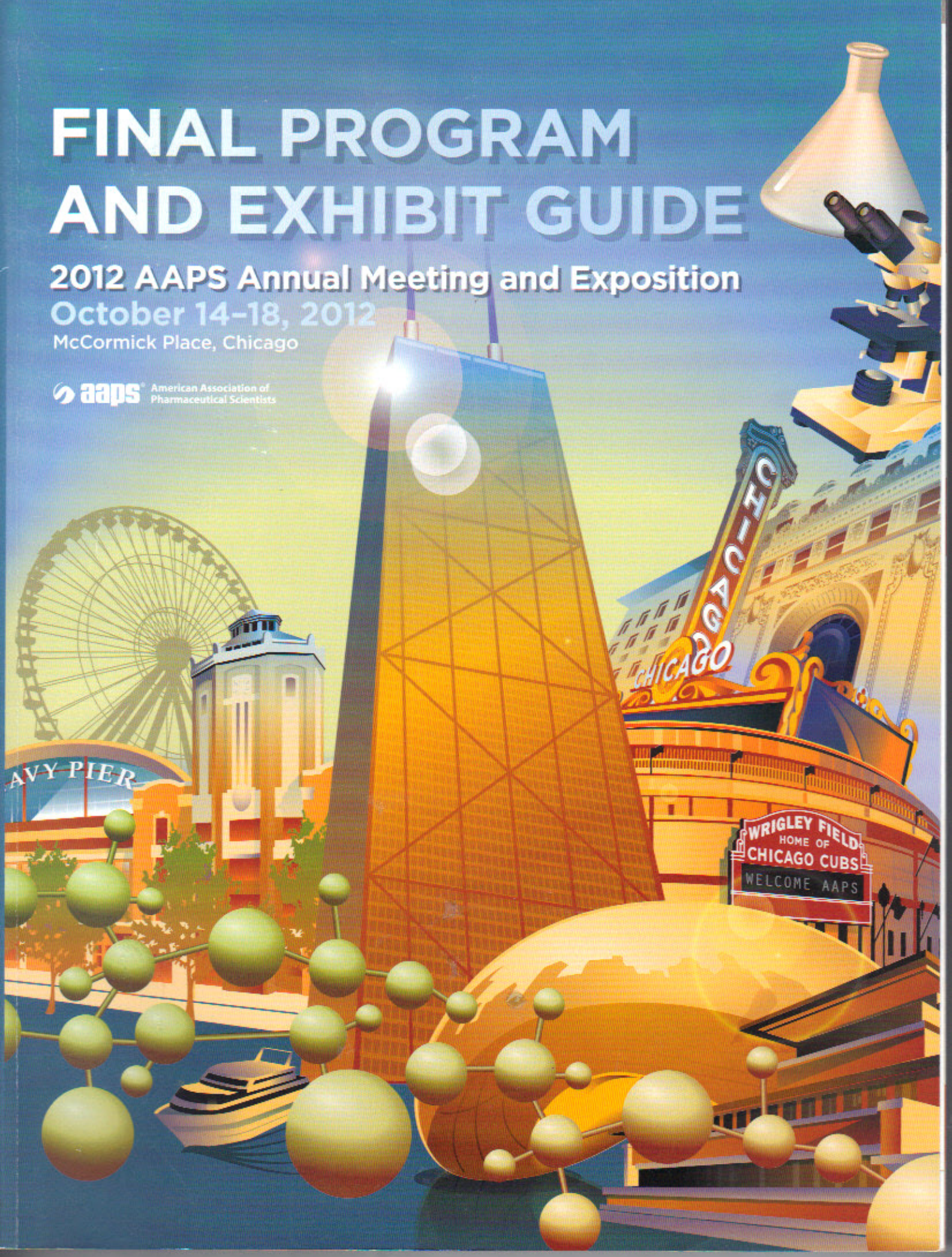

Enhanced Stability and Bioavailability of Clopidogrel Napadisilate Monohydrate by Self-microemulsifying Drug Delivery System(SMEDDS)

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Purpose

To develop a novel clopidogrel napadisilate monohydrate-loaded solid self-microemulsifying drug delivery system (SMEDDS) with enhanced stability and bioavailability

Methods

Liquid SMEDDS composed of oil (Peceol), surfactant (Cremophor RH60) and co-surfactant (Transcutol HP) for oral administration was formulated. Pseudo-ternary phase diagram was used to evaluate the emulsification domain and to confirm formulation. Solid SMEDDS formulations were developed by spray drying liquid SMEDDS along with the solid carriers. The physicochemical characterization was accomplished by particle size determination, scanning electron microscopy (SEM), differental scanning calorimetry (DSC) and powder X-ray diffraction (PXRD). Furthermore, their stability, dissolution and pharmacokinetic study were compared to those of clopidogrel napadisilate monohydrate and clopidogrel bisulfate powder.

Results

The optimized liquid SMEDDS was a system consisting of Peceol, Cremophor RH60 and Transcutol HP at voluminous ratio of 2:3:1. The solid SMEDDS formulation gave a larger emulsion droplet size (200~400 nm) compared to liquid SMEDDS (about 120 nm). The crystal form of solid SMEDDS was found to be converted to amorphous form, which was confirmed by the analysis of DSC and PXRD. The final dissolution rate of solid SMEDDS containing clopidogrel napadisilate monohydrate was 1.2-fold higher than that of pure powder ($p<0.05$). Furthermore, time for complete release of SMEDDS was 4-fold less than that of pure powder. These solid SMEDDS improved stability at the accelerated condition of 50 ¡É/75 % RH for 4 weeks compared to clopidogrel bisulfate, even if it did not improve the stability compared to clopidogrel napadisilate monohydrate. The pharmacokinetic parameters including AUC and Cmax were significantly increased by solid SMEDDS over that of pure clopidogrel napadisilate monohydrate ($p<0.05$).

Conclusion

This solid SMEDDS could be an outstanding candidate for improving the stability and bioavailability of clopidogrel napadisilate monohydrate.