Development of Novel Solid Dispersion of Tranilast Using Amphiphilic Block Copolymer for Improved Oral Bioavailability

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Purpose
Several types of strategy have been proposed to improve the aqueous solubility of BCS class II/IV drugs: in particular, solid dispersion (SD) approach can achieve dissolution and solubility enhancement by dispersing the poorly soluble drug in a solid carrier matrix. The present study aimed to develop novel SD formulation of tranilast (TL), a typical BCS class II drug, using amphiphilic block copolymer, poly[MPC-co-BMA] (pMB), to improve the dissolution and pharmacokinetic behavior of TL.

Methods
pMB-based SD of TL (pMB-SD/TL) with drug loading of 50% (w/w) was prepared by wet-mill technology, and the physicochemical properties were characterized in terms of morphology by electron microscope, crystallinity by powder X-ray diffraction (PXRD) and polarized light microscope (PLM), dissolution, and hygroscopicity by dynamic vapor sorption. Pharmacokinetic behaviors of orally dosed TL formulations were evaluated in rats using UPLC/ESI-MS.

Results
PXRD and PLM experiments demonstrated high crystallinity of TL in pMB-SD/TL. The pMB-SD/TL exhibited immediate micellization when introduced to aqueous media, forming fine droplets with a mean diameter of ca. 122 nm. Under acidic conditions, there was marked improvement in the dissolution behavior for the pMB-SD/TL compared with crystalline TL and nanocrystalline solid dispersion of TL (CSD/TL), although the supersaturated TL concentration gradually decreased (Fig. 1). NMR analyses demonstrated interaction between TL and pMB, as evidenced by the chemical shift drifting and line broadening (Fig. 2). After oral administration of pMB-SD/TL (10 mg TL/kg) in rats, enhanced TL exposure was observed with increases of Cmax and AUC by 208- and 53-fold, respectively, compared with those of crystalline TL (Fig. 3).

Conclusion
From these findings, the newly developed pMB-SD formulation might be an efficacious dosage option for TL and other poorly water-soluble drugs to achieve improvements in dissolution and oral absorption.