Title:	Amorphous Salts Solid Dispersions of Celecoxib: Enhanced Biopharmaceutical Performance and Physical Stability
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Keywords:	celecoxib amorphous salts solid dispersions aqueous solubility dissolution rate
Issue Date:	2021
Publisher:	ACS Publications
Citation:	Molecular Pharmaceutics, 18(6), 2334–2348.
Abstract:	Numerous amorphous solid dispersion (ASD) formulations of celecoxib (CEL) have been attempted for enhancing the solubility, dissolution rate, and in vivo pharmacokinetics via high drug loading, polymer combination, or by surfactant addition. However, physical stability for long-term shelf life and desired in vivo pharmacokinetics remains elusive. Therefore, newer formulation strategies are always warranted to address poor aqueous solubility and oral bioavailability with extended shelf life. The present investigation elaborates a combined strategy of amorphization and salt formation for CEL, providing the benefits of enhanced solubility, dissolution rate, in vivo pharmacokinetics, and physical stability. We generated amorphous salts solid dispersion (ASSD) formulations of CEL via an in situ acid–base reaction involving counterions (Na+ and K+) and a polymer (Soluplus) using the spray-drying technique. The generated CEL-Na and CEL-K salts were homogeneously and molecularly dispersed in the matrix of Soluplus polymer. The characterization of generated ASSDs by differential scanning calorimetry revealed a much higher glass-transition temperature (Tg) than the pure amorphous CEL, confirming the salt formation of CEL in solid dispersions. The micro-Raman and proton nuclear magnetic resonance spectroscopy further confirmed the formation of salt at the −S═O position in the CEL molecules. CEL-Na-Soluplus ASSD exhibited a synergistic enhancement in the aqueous solubility (332.82-fold) and in vivo pharmacokinetics (9.83-fold enhancement in the blood plasma concentration) than the crystalline CEL. Furthermore, ASSD formulations were physically stable for nearly 1 year (352 days) in long-term stability studies at ambient conditions. Hence, we concluded that the ASSD is a promising strategy for CEL in improving the physicochemical properties and biopharmaceutical performance.
Description:	Only IISERM authors are available in the record.
URI:	https://doi.org/10.1021/acs.molpharmaceut.1c00144 (https://doi.org/10.1021/acs.molpharmaceut.1c00144) http://hdl.handle.net/123456789/4941 (http://hdl.handle.net/123456789/4941)
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