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Title:	Multicomponent Pharmaceutical Adducts of α -Eprosartan: Physicochemical Properties and Pharmacokinetic Study
Authors:	Khullar, S. (/jspui/browse?type=author&value=Khullar%2C+S.) Mandal, S.K. (/jspui/browse?type=author&value=Mandal%2C+S.K.)
Keywords:	Solubility Differential scanning calorimetry Mixtures Electron paramagnetic resonance spectroscopy
Issue Date:	2017
Publisher:	ACS Publications
Citation:	Crystal Growth and Design, 17 (4)
Abstract:	Pharmaceutical adducts of α -eprosartan (EPR) with nicotinamide (NIC) and p-hydroxy benzoic acid (PHB) were prepared by a liquid assisted grinding technique. Prior to conducting this study, the single crystal structure of EPR was determined. This study was designed to improve the pH-dependent solubility and dissolution rate of EPR and hence its oral absorption across the gastrointestinal tract. Initially, differential scanning calorimetry and powder X-ray diffractometry were used as a screening tool for rapid cocrystal or eutectic mixture screening. The eutectic mixture of EPR with PHB in a 1:3 stoichiometry ratio shows a better solubility and dissolution rate in all aqueous buffers as compared to EPR/NIC cocrystals and pure EPR. The EPR/NIC cocrystal in a 1:1 stoichiometry ratio shows a better dissolution rate initially as compared to pure EPR but does revert back to EPR within the first 30 min in pH 1.2 and 6.8. Absorption and desorption profile of EPR adducts are reversible, suggesting no solid state transformation under experimental conditions. A significant increase in oral bioavailability in overnight fasted Sprague–Dawley rats is achieved with the EPR/NIC cocrystal (2.4-fold) and EPR/PHB eutectics (6.1-fold), even when the cocrystal transformation is suspected based on in vitro studies.
Description:	Only IISERM authors are available in the record.
URI:	https://pubs.acs.org/doi/abs/10.1021/acs.cgd.6b01588 (https://pubs.acs.org/doi/abs/10.1021/acs.cgd.6b01588) http://hdl.handle.net/123456789/2578 (http://hdl.handle.net/123456789/2578)
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