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Title:	Characterization and Evaluation of Multi-Component Crystals of Hydrochlorothiazide
Authors:	Khullar, S. (/jspui/browse?type=author&value=Khullar%2C+S.) Mandal, S.K. (/jspui/browse?type=author&value=Mandal%2C+S.K.)
Keywords:	Acute toxicity Antihypertensive activity Multi-component crystals Poorly water soluble drugs Solubility
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Citation:	Pharmaceutical Research,31(9), pp.2479–2489.
Abstract:	<p>Results: Both 1 and 2 crystallized in the orthorhombic space group P212121 and formation of salts were confirmed. The solubility profiles of 1 and 2 in basic media showed a maximum release of 2.5 mg/ml and 1.9 mg/ml, respectively, in comparison to the drug (0.82 mg/ml). The in-vivo antihypertensive activity of 1 in deoxycorticosterone acetate salt induced hypertensive rats showed 1.5 fold improvement. No increase in the signs of toxicity were revealed in rats during the acute toxicity studies even at doses of 2,000 mg/kg by body weight in comparison to the free drug. Histopathological findings supported the safety of these multi-component crystals.</p> <p>Conclusions: The new solid phases exhibit potential to be explored for the oral drug delivery of HCT with improved solubility and therapeutic outcome. Purpose: The present work aims at improving the physicochemical properties of hydrochlorothiazide, a poorly water soluble antihypertensive drug by preparing its multi-component crystals with nicotinic acid (HCT-NA) and 2-picolinic acid (HCT-PIC). Methods: The crystals prepared by solution crystallization were investigated by thermoanalytical techniques. The crystal structures of HCT-NA (1) and HCT-PIC (2) were determined by the single crystal X-ray diffraction and were assessed for their aqueous solubility, antihypertensive activity and acute toxicity in rats.</p>
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