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# Preparation of a Crystalline Salt of Indomethacin and Tromethamine by Hot Melt Extrusion Technology

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## Abstract

Although salt formation is the most ubiquitous and effective method of increasing the solubility and dissolution rates of acidic and basic drugs, it consumes large quantities of organic solvents and is a batch process. Herein, we show that the dissolution rate of indomethacin (a poorly water-soluble drug) can be increased by using hot melt extrusion of a 1:1 (mol/mol) indomethacin:tromethamine mixture to form a highly crystalline salt, the physicochemical properties of which are investigated in detail. Specifically, pH–solubility studies demonstrated that this salt exhibited a maximal solubility of 19.34 mg/mL (>1000 times that of pure indomethacin) at pH 8.19. A solvent evaporation technique was also used for salt formation. Spectroscopic analyses (infrared, nuclear magnetic resonance) of both; demonstrated, in situ salt formation with