

## **294e Rapid Pka Determination of Water-Insoluble Compounds by Multiplexed Capillary Electrophoresis**

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**Purpose.** Acid dissociation constant (pKa) is one of the key physicochemical parameters for early pharmaceutical candidates. Since many pharmaceutical compounds have low solubility in water, estimation of pKa in an aqueous solution is difficult. It is desirable to develop a method for rapid pKa estimation of water-insoluble compounds. **Method.** The experiments were performed using a cePRO 9600 CE system from CombiSep with a PDA detection at 214 nm. The system was equipped with a cartridge containing 96 capillaries. A mixed methanol buffer system was used as the background electrolyte. The apparent pKa value (PsKa) was calculated using the upgraded pKa estimator software. The PsKa values were plotted as a function of % weight methanol (Cosolvent Method) or solution dielectric constants (Yasuda-Shedlovsky Method). The aqueous pKa value was estimated by extrapolation to 0% methanol. **Results.** Numerous compounds with literature pKa values were tested by cePRO 9600 system. A reasonably good correlation was obtained between the tested pKa's and the literature pKa's. **Conclusions.** The method is reliable with good reproducibility. The pKa's of two compounds can be tested per plate.