294g Rapid Pka Determination Using Multiplexed Capillary Electrophoresis
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Purpose. Acid dissociation constant (pKa) is a key physicochemical parameter. The development of combinatorial chemistry has caused a dramatic increase in synthetic production of potential drug candidates. It is desirable to obtain knowledge of pKa values in a high-throughput manner to keep up with the dramatic demand for chemical characterization of new compounds. Methods. The experiments were performed using cePRO 9600 CE system from CombiSep with a PDA detection at 214 nm. The system was equipped with a cartridge containing 96 uncoated fused silica capillaries. Dimethylsulfoxide (DMSO) was employed as a neutral marker. Electropherograms were generated using the MCE2000 software. The pKa value was calculated using the pKa Estimator software. At each pH value, the migration time of the analyte and the EOF marker was entered into the software. The effective mobility of each sample at different pH values was calculated from the difference between the analyte migration time and the EOF marker migration time. Nonlinear regression was performed using the effective mobility versus its pH value. Results. Many compounds with known pKa were tested. Good agreement was observed between the measured pKa and the literature pKa. Conclusions. The method was robust. Over 90% of compounds have pKa values within 0.3 pH unit of the literature pKa value. Acid dissociation constants can be determined for up to eight compounds on one plate.