to effect volatility may cause degradation as well as effecting racemization. However, there may be a limited number of instances in which this technique would be useful, such as for small nonaromatic compounds that simple are not possible to separate by current HPLC and TLC techniques.

6.5. Thin-Layer Chromatography

Thin-layer chromatography (TLC) is a mature chromatographic technique and is still widely used throughout the pharmaceutical industry in research as well as in the control laboratory. It is used throughout the drug development process for determining the purity of the drug substance, reference standards, and intermediates. It possesses many advantages including simplicity, low cost, and a short run time. It is cost effective. Its main disadvantage is variability. Constanzo (8) has proposed a three-point window approach to optimize resolution, and thus to minimize the variability, by controlling the mobile phase composition.

TLC (limit test) is used to complement a non-stability-indicating procedure as indicated in the FDA Guideline for Submitting Samples and Analytical Data for Methods Validation (2).

6.6. Capillary Electrophoresis and Capillary Electrochromatography

As sciences, both capillary electrophoresis (CE) and capillary electrochromatography (CEC) today are probably where HPLC was 10 years ago. CE is a separations technique based on the mobility of ions through a buffer-filled capillary in an electrically charged environment. This would provide a separation of charged species. When CE is coupled with a stationary phase and high pressure, it is known as CEC, in which the separation is based on electrophoretic migration and chromatographic partitioning enabling the separation of neutral species. Both techniques are more applicable to biological systems, in biopharmaceutical and other R&D applications, than in quality assurance/product specification applications. The techniques are very sensitive and well suited for separations of small amounts of expensive biopharmaceuticals. On the other hand, they have less utility as a product release or stability test methodology, especially in product specification applications of small molecular entities where there is an abundance of samples and where sensitivity is not an issue.

The utility of the technique, however, lies in its ability to achieve high sensitivity and resolution through high efficiencies with minimal peak dispersion. Moffatt et al. (9) have reported unusually high efficiencies of up to 2.5 million plates per meter in the capillary electrochromatographic analysis of partially ionized anionic-neutral pyrimidine compounds using a standard C_{18} stationary phase.

The number of manufacturers of CE/CEC equipment are not nearly as many as for HPLC equipment. Major manufacturers include Unimicro Technologies, Thermo Bioanalysis, Beckman Coulter, and Micro-Tech Scientific. The last company's model Ultra-Plus II has an integrated, gradient capillary HPLC/CE/CEC system. This combination of gradient elution and electrophoretic migration provides a rapid analysis with high resolution (10).