Ultra-Low Level Impurity Analysis by Capillary Zone Electrophoresis

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Pharmaceutical/ chemical

Abstract

Capillary zone electrophoresis (CZE) is an inherently high efficiency liquid phase separation technique. This makes it very suitable for the separation of closely related compounds and can be of particular use in the analysis of drug impurities. Regulatory requirements demand the demonstration of the purity of any drug substance and the acceptable criteria for presence of impurities are around 0.1 %. This means that the analysis not only has to have an adequate sensitivity, but also that the linear range is such that the minor component may be quantitatively reported as a corrected (area/area) percent of the main component. By using the Agilent CE high sensitivity detection cell, sensitivity can be increased by an order of magnitude, with linearity increased over 3-fold compared to conventional capillaries. This enables the determination of impurities in drug substances below the 0.1 % area/area level. Figure 1 shows the linear range achievable using the high-sensitivity cell, illustrating its linearity over 2.2 AU.

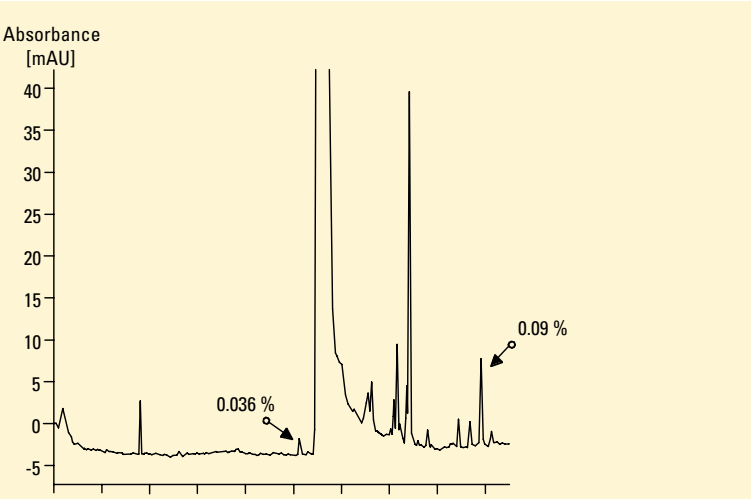

Figure 1
Linear range of high sensitivity cell

Experimental

All experiments were performed on the Agilent Capillary Electrophoresis system which is computer controlled via Agilent ChemStation software. High sensitivity detection was achieved using the Agilent CE high-sensitivity detection cell (order number G1600-68713) and capillaries.

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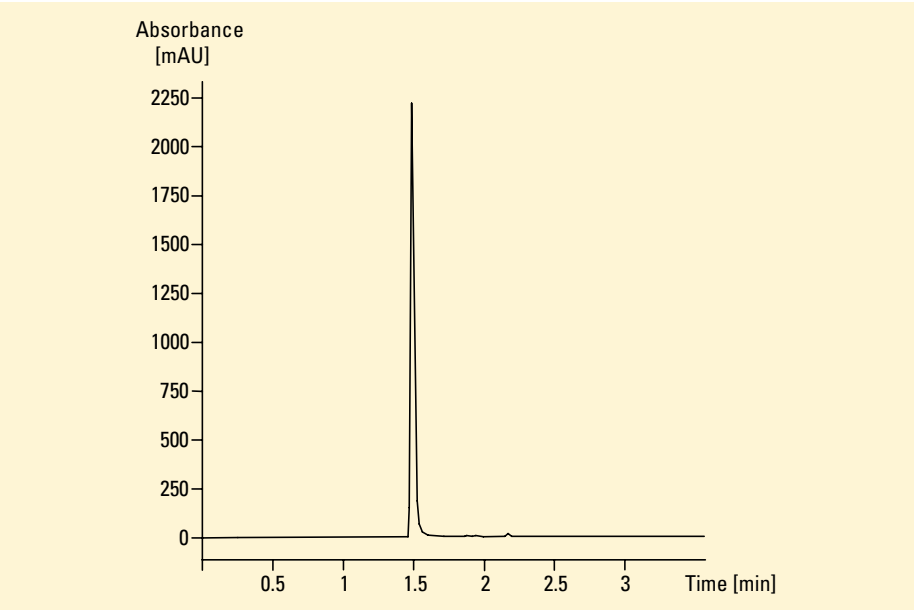

Figure 2
CZE analysis of ranitidine

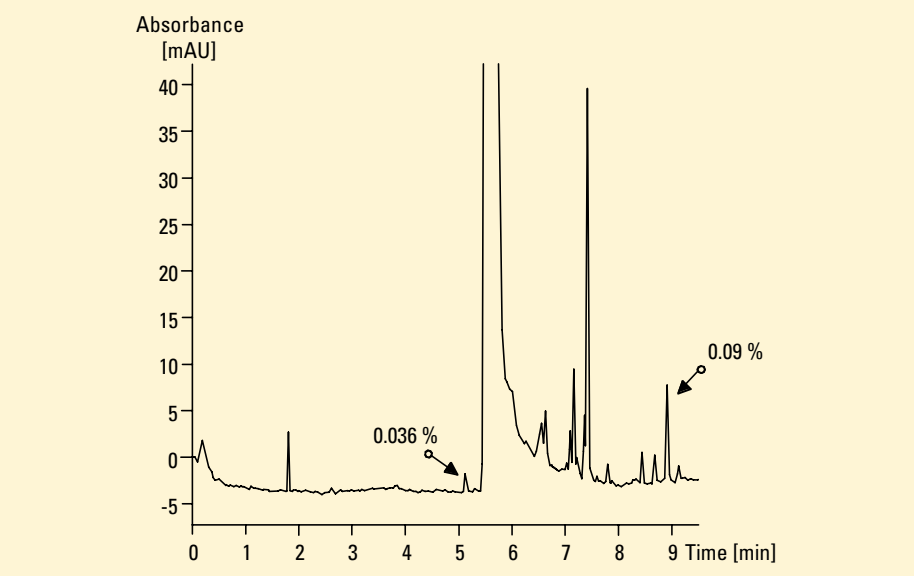

Figure 3
Low level determination of ranitidine impurities

During a shelf life study of ranitidine, the anti-ulcer drug was analyzed for the presence of impurities after 12 months exposure to light and room temperature. Figure 2 shows the analysis of the main peak indicating that this is at the upper levels of the linear range of detection. An expanded view of the base of the peak shows the number of impurities present at very low levels. Given the linear range of the detection cell, it is possible to calculate the impurity level of these peaks at less than 0.1 % area/area of the main peak.

Conditions (figures 2, 3)

Buffer 20 mM borate pH 9.3
Capillary
56 cm eff (64.5) × 75 µm i.d.
Injection 200 mbars
Run 20 °C, 30 kV
Detection
225/20 nm (high sensitivity cell)

Conclusions

CZE in conjunction with the high-sensitivity detection cell, may be used to determine impurity levels in drugs at less than 0.1 % area/area. This level is appropriate to that required for regulatory submissions.

Equipment

- Agilent Capillary Electrophoresis system
- Agilent CE high-sensitivity detection cell
- Agilent ChemStation + software

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