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Capillary electrophoresis in food analysis

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The application of capillary electrophoresis to food analysis is reviewed. Emphasis is put on quantitative analysis of food samples. The different modes of capillary electrophoresis are presented together with a brief section on basic theory. Points are discussed that have to be considered for the generation of reliable quantitative results. Quantitative applications are reported with information on analyte, sample matrix, a brief summary of the CE method, typical concentrations analysed and validation parameters given.

NOTATION

AAS	atomic absorption spectrometry
AMPD	amino-2-methyl-1,3-propanediol
ANTS	8-aminonaphthalene-1,3,6-trisulfonic acid
BICINE	*N*,*N*-bis(2-hydroxyethyl)glycine
BIS–TRIS	bis(2-hydroxyethyl)amino–tris(hydroxymethyl)methane
Brij®	35 polyethylene glycol dodecyl ether
CAPS	3-(cyclohexylamino)-1-propanesulfonic acid
CDTA	*trans*-1,2-diaminocyclohexane-*N*,*N*,*N*′,*N*′-tetraacetic acid
CE	capillary electrophoresis
CGE	capillary gel electrophoresis
CIA™	capillary ion analysis (Waters/Millipore tradename)
CIE	capillary ion electrophoresis
CIEF	capillary isoelectric focusing
CITP	capillary isotachophoresis
CITP–FSCE	free-solution capillary electrophoresis with capillary isotachophoretic preconcentration
CMP	caseinomacropeptide(s)
CTAB	cetyltrimethylammonium bromide
CTAC	cetyltrimethylammonium chloride
CZE	capillary zone electrophoresis
DMMAPS	3-(*N*,*N*-dimethylmyristylammonio)propanesulfonate
EC	electrochemical (detection)
EDTA	ethylenediaminetetraacetic acid
em.	emission wavelength
EOF	electroosmotic flow
exc.	excitation wavelength
2-FA	2-furaldehyde
FSCE	free-solution capillary electrophoresis
HIBA	α-hydroxyisobutyric acid
5-HMF	5-hydroxymethyl-2-furaldehyde
HPAEC–PAD	high-performance anion-exchange chromatography with pulsed amperometric detection
HPLC	high-performance liquid chromatography
HQS	8-hydroxyquinoline-5-sulfonic acid
IC	ion chromatography
ID	inner diameter
LE	leading electrolyte
MECC	micellar electrokinetic capillary chromatography
MEKC	micellar electrokinetic chromatography
MES	2-(*N*-morpholino)-ethanesulfonic acid
MHEC	methylhydroxyethylcellulose
MS	mass spectrometry
MS–MS	tandem mass spectrometry
m/*z*	mass-to-charge ratio
OFM™Anion–BT	Waters/Millipore proprietary name
PEG	polyethylene glycol
RSD_r	relative standard deviation (repeatability)
RSD_R	relative standard deviation (reproducibility)
Sa	sample
SDS	sodium dodecylsulfate
SDS–PAGE	sodium dodecylsulfate–polyacrylamide gel electrophoresis
SFC	supercritical fluid chromatography
SIM	selected ion monitoring
SRM	selected reaction monitoring
St	standard
TBA	tetrabutylammonium hydrogen sulfate
TBD	*N*,*N*′-tetramethylene-2,2′-bipyridinium dibromide

TE	terminating electrolyte
TRICINE	*N*-[tris(hydroxymethyl)-methyl]-glycine
TRIS	tris(hydroxymethyl)aminomethane
Triton X-100	polyethylene glycol tert-octylphenyl ether
Tropolone	2-hydroxy-2,4,6-cycloheptatrien-1-one
TTAB	tetradecyltrimethylammonium bromide
UHT	ultra-high temperature treated
UV	ultraviolet (absorption detection)
UV-Vis	ultraviolet-visible (absorption)
UV-Cat-1/-2	Waters/Millipore proprietary names

INTRODUCTION

The complexity and diversity of different foodstuffs put great demands on the techniques that are to be used for food analysis. An ideal method for analysis should be robust, highly selective and be applicable to a wide range of food matrices. Different modes of chromatography are often used for the final analysis step which may be preceded by extensive sample clean-up, derivatisation, etc. Method selectivity can be accomplished by means of selective detection or efficient separation. To choose high-performance liquid chromatography (HPLC) with electrochemical detection rather than UV detection may be one way to achieve a high degree of selectivity. Alternatively, the very high resolving power of capillary electrophoresis (CE) can be employed to give an efficient separation. An example where both strategies are used is given in Fig. 1. It can be seen that the poor separation of ascorbic acid (AA) from other components in beetroot with HPLC–UV can cause problems in quantification. Those problems are solved by means of the more selective detection technique in HPLC–EC and alternatively by reaching a separation efficiency with CE–UV ($N = 240000$) that by far surpasses that achieved with the other techniques ($N = 10000$).

The field of capillary electrophoresis has been subject to numerous reviews in the past few years. A recent fundamental review of the field of CE (Monnig & Kennedy, 1994) cites over 100 reviews published in 1992 and 1993 alone. In a recent review (Zeece, 1992) capillary electrophoresis was presented as an attractive technology for the analysis of a variety of compounds found in food systems. The separation principle and different modes of separation were explained but few applications to actual food samples were cited. The use of CE in dairy research has also been reviewed (Olieman, 1993). In addition, CE is frequently mentioned as an attractive alternative technique in reviews and discussions of different areas of food analysis, e.g. pesticide residue analysis (Conaway, 1991), assay of penicillin in food–animal tissues (Boison, 1992), analysis of antibiotic materials in food (Bobbitt & Ng, 1992), fish species identification in sea food products (Sotelo *et al.*, 1993) and wheat protein analysis (Bietz & Simpson, 1992). Thorough comparisons have been made between CE, HPLC and supercritical fluid chromatography (SFC) (Steuer *et al.*, 1990) and between CE and HPLC (Issaq *et al.*, 1991). The strengths of capillary electrophoretic methods are the potential for very efficient separations, low solvent consumption and ease of automation. Drawbacks include high concentration limits of detection. Considerable effort is at present devoted to improving the concentration sensitivity of the technique with new means of detection, modified capillary geometries, etc.

From having been seen as a technique that would eventually replace other chromatographic and electrophoretic techniques, CE is more and more regarded as a complementary approach for identification and qualitative analysis (Krull & Mazzeo, 1992). With the advent of commercially available equipment and the possibility of automation, an increasing number of quantitative applications have appeared. The ease with which closely related compounds can be separated often facilitates inclusion of internal standards in the analysis (Koh *et al.*, 1993), diminishes the need for extensive sample clean-up (Corradini & Corradini, 1992; Cancalon & Bryan, 1993), and thus often makes method development relatively straightforward. Strategies for method development are covered in a number of textbooks (Li, 1992; Vindevogel & Sandra, 1992; Camilleri, 1993; Weinberger, 1993; Landers, 1994) and overviews (Swartz, 1991; McLaughlin *et al.*, 1992). The quantitative aspects of CE and the problems encountered in such applications have been reviewed (Goodall *et al.*, 1991; Altria, 1993b; Hoyt, 1993; Wätzig & Dette, 1993).

The purpose of this text is to provide an overview of the different modes of capillary electrophoresis, to shed light on the problems encountered in quantitative analysis with CE, and to present the areas of food analysis where capillary electrophoresis has been applied.

MODES OF CAPILLARY ELECTROPHORESIS

The different modes of capillary electrophoresis take advantage of a number of physical phenomena to achieve separation of a diversity of compounds. Several textbooks (Li, 1992; Vindevogel & Sandra, 1992; Camilleri, 1993; Weinberger, 1993; Landers, 1994) and reviews (Issaq *et al.*, 1991) cover the theory of capillary electrophoresis in great detail and the brief theoretical part of this overview is kept on a basic level.

Theory

When an electric field is applied to a solution of charged molecules, these molecules will start to move. The mobility of an ion is dependent on its charge-to-size ratio, the size being determined by molecular weight, three-dimensional structure and degree of solvation. Based on a balance between electromotive and frictional forces, the electrophoretic mobility (μ_{ep}) can be expressed as

$$\mu_{ep} = q/6\pi\eta r \quad (1)$$

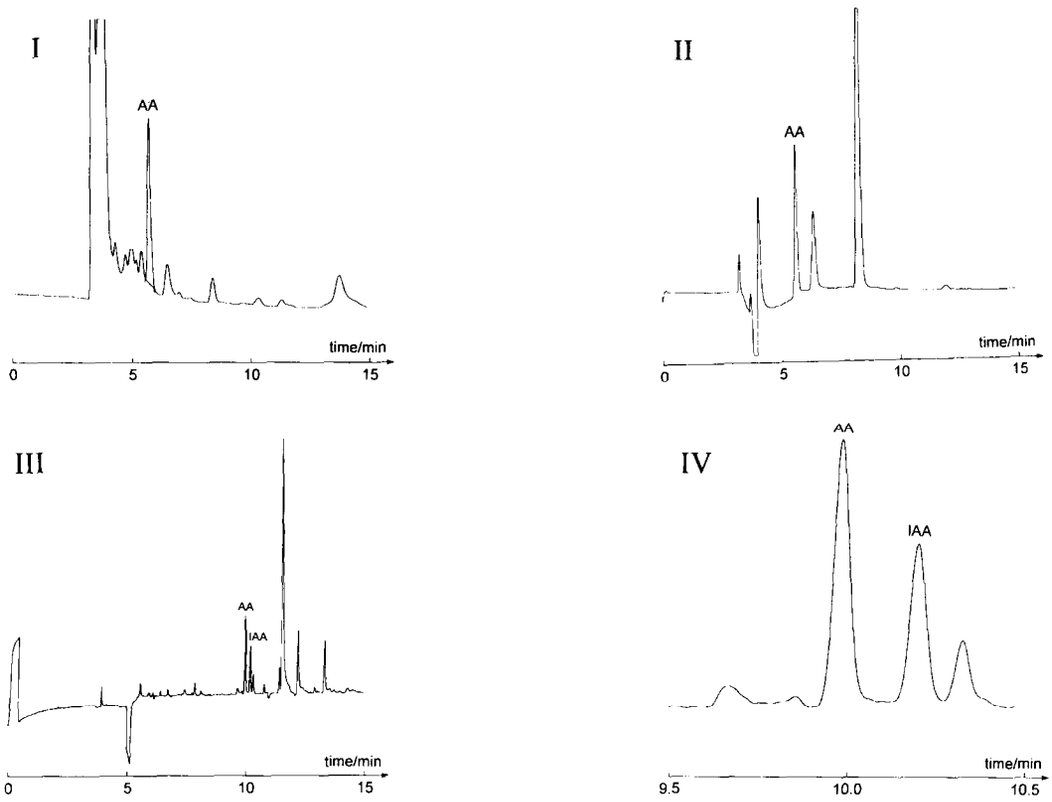

Fig. 1. Determination of ascorbic acid (AA) in beetroot using different strategies: (I), HPLC with UV detection; (II), HPLC with EC detection; (III), CE with UV detection, internal standard: isoascorbic acid (IAA); (IV), as (III), but part of electropherogram enlarged. The sample was homogenised in metaphosphoric acid, filtered and diluted prior to analysis. The separation efficiency expressed as the number of theoretical plates (N) was calculated according to: $N = 8\ln 2(t/w)^2$, where t = migration time and w = peak width at half peak height. HPLC ($N = 10000$): Column, 250 × 4 mm packed with 5 μm LiChrosorb RP-select B (E. Merck, Darmstadt, Germany); Mobile phase, 2% $(NH_4)H_2PO_4$, pH 2.8; Flowrate, 0.5 ml/min; UV, 254 nm; EC, +0.85 V vs. Ag/AgCl. CE ($N = 240\,000$): Capillary, fused silica (57 cm × 75 μm ID, 50 cm to detection window); Electrolyte, 0.1 M BICINE (pH 8.8); Voltage: 20 kV; Resulting current: 85 μA; UV, 254 nm.

where q = net charge, η = viscosity and r = ionic radius. The applied electric field and the difference in electrophoretic mobilities will make anions migrate toward the positive pole and cations migrate toward the negative pole in equal quantities, and make small ions travel faster than large ions of the same charge. Thus charged molecules will be separated in an electric field according to their intrinsic mobility. As for chromatographic separations, the separation efficiency can be expressed as the number of theoretical plates (N) and is in CE (Jorgenson & Lukacs, 1981) related to the applied voltage (V) and to the mobility (μ) and diffusion coefficient (D) of the solute according to:

$$N = \mu V/2D \qquad (2)$$

It can be deduced from (2) that high applied voltages favour efficient separations, but in practice there is a limitation due to the Joule heating that occurs when electric currents pass through the medium. The application of high voltages is only advantageous when the produced heat can be dissipated efficiently, since thermal convection otherwise will lead to mixing of zones that have been separated.

In classic electrophoretic methods convective mixing has been counteracted with stabilising media like cellulose powder, paper or gels of agar and acrylamide (Vesterberg, 1989). Electrophoresis can also be performed in free solution if only the produced heat can be dissipated efficiently enough. Tubes with small inner diameters have a high surface-to-volume ratio which facilitates heat dissipation, and capillaries are therefore suitable for performing free-solution electrophoresis with relatively high applied voltages. Further control of heat generation is possible with active cooling of the outer wall of the capillary (Knox, 1988). Capillary electrophoresis is almost exclusively performed in fused-silica tubing which has good thermal properties, is transparent to ultraviolet and visible light and can be made with internal diameters smaller than 100 μm. Due to the fragility of naked fused silica, the flexibility of the capillary is improved with a polyimide coating of the outer wall.

Electroosmosis

For a wide range of pH-values, the inner wall of a fused-silica capillary is negatively charged due to ionised

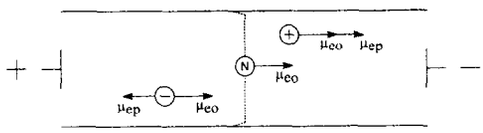

Fig. 2. Free-solution capillary electrophoresis (FSCE). μ_{ep}, Electrophoretic mobility; μ_{eo}, electroosmotic mobility; N, neutral molecule travelling with the electroosmotic flow. Dotted line indicates electroosmotic flow profile. μ_{eo} Is often greater than μ_{ep} for negatively charged molecules, resulting in a net movement of all molecules past the detector at the negative end of the capillary.

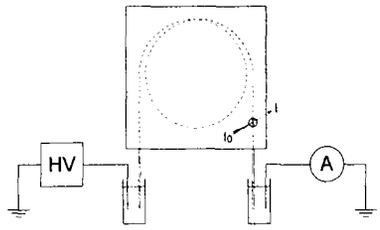

Fig. 3. Typical instrumental set-up for capillary electrophoresis. HV, High-voltage supply; A, amperometer; I_0, intensity of incident light; I, intensity of non-absorbed or emitted light. The capillary is filled with electrolyte and housed in a thermostatted compartment. The electrodes and capillary ends are immersed into the electrolyte, sample is introduced on the high-voltage side, and detection is performed on-capillary.

silanol groups and as a consequence it attracts cationic counterions from the bulk solution. A double layer is formed at the silica–solution interface and when an electric field is applied, the solvated cationic species will migrate toward the negative pole causing bulk solvent molecules to move in the same direction. This electroosmotic flow (EOF) originates at the inner wall of the capillary and the appearance of the flow profile changes from parabolic to flat as the capillary radius becomes greater than seven times the double layer thickness, *d* (Stevens & Cortes, 1983). For an electrolyte with 1 mM potassium chloride in water, *d* is estimated to 10 nm and a flat flow profile can be expected for the commonly used inner diameters in CE (25–100 μm). The result is a minimal broadening of solute zones during CE as opposed to chromatography with pressure-driven pumping and a concomitant parabolic flow profile. The EOF velocity is often greater than the electrophoretic velocity of any molecule present in solution, which results in a net movement of cations, anions and neutral molecules in one direction (Fig. 2).

Free-solution capillary electrophoresis (FSCE)

A typical instrumental set-up for performing capillary electrophoresis is depicted in Fig. 3. The capillary is housed in a thermostatted compartment and the absorbance/fluorescence is measured on-capillary. The capillary is filled with electrolyte and the ends are immersed into vials containing electrolyte or sample solution. If a sample zone is introduced in the positive end of the capillary and detection is performed at the negative end, sample molecules will migrate in the electric field past the detector irrespective of their charge (Fig. 2). Because of differences in intrinsic electrophoretic mobility and the phenomenon of electroosmosis (see above), both cations and anions can be separated in one run. Neutral molecules cannot be resolved since they have no electrophoretic mobility and will travel in one zone with a velocity equal to that of the EOF. The separation method is termed free-solution capillary electrophoresis (FSCE) or capillary zone electrophoresis (CZE). FSCE will be used in this text to avoid ambiguity since some authors have chosen CZE to denote any CE mode where zones migrate independently through the capillary (i.e. FSCE, MEKC and CGE).

Different detection techniques can be utilised in CE. Absorption and fluorescence of ultraviolet or visible light can be recorded on-capillary if the non-transparent polyimide coating is removed from a small section of the fused-silica tubing. By eliminating the use of a separate flow cell, resolution need not be impaired by transfer of the sample zones from capillary to detector cell. UV-Vis absorbance detectors in single wavelength or diode-array mode are frequently found in commercial equipment. It is also possible to buy instruments with lamp and laser-induced fluorescence detectors, and recently a CE instrument equipped with a conductivity detector was introduced on the market. With some instruments it is possible to connect the outlet end of the capillary to a mass spectrometer, thus combining the high separation efficiency of CE with possibilities for structural information with MS. Less common detection principles like potentiometry, amperometry and the measurement of radioactivity have also been utilised with CE, but as yet only with laboratory-built instruments.

Capillary ion electrophoresis (CIE)

FSCE has successfully been applied to the analysis of small inorganic and organic ions in different sample matrices. It is regarded as a technique complementary to ion chromatography and is often termed capillary ion electrophoresis (CIE) or electrophoretic capillary ion analysis (CIA™). Conditions that should be fulfilled for a successful application of CIE have been discussed (Jandik *et al.*, 1992).

In the separation of anions by CIE, the electroosmotic flow is normally reversed in the fused-silica capillary by a dynamic coating of the inner wall with a cationic surfactant added to the electrolyte. The EOF is directed toward the positive pole and since the analytes move in the same direction very fast separations can be achieved. Anions differ enough in individual ionic mobilities to allow the separation of very complex samples despite a short analysis time. For cations it is not necessary to manipulate the EOF, but groups of cations often have similar mobilities and thus do not permit separation without the use of other additives such as

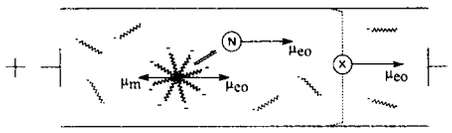

Fig. 4. Micellar electrokinetic chromatography (MEKC) with anionic detergent micelles. μ_m, Electrophoretic mobility of micelle; μ_{eo}, electroosmotic mobility; *N*, neutral molecule partitioning between micelle and electrolyte; *X*, molecule travelling with the electroosmotic flow only. Dotted line indicates electroosmotic flow profile. Neutral molecules will be separated according to degree of partitioning between the liquid and micellar phases.

complexing agents, e.g. EDTA (Kajiwara *et al.*, 1993) or HIBA (Schmitt *et al.*, 1993).

Some ions can be detected in a straightforward way with a UV-detector, e.g. bromide, nitrite and nitrate (Jones & Jandik, 1992) and benzoic acid (Ng *et al.*, 1992), but most ions lack strong chromophores and a UV-absorbing co-ion is usually included in the electrolyte. The co-ion should absorb light in a region different from the analyte(s). In addition, symmetrical peaks are produced in CIE only when the mobility of the co-ion is closely matched with that of the analyte ions. This means that electrolyte composition has to be carefully selected unless sensitivity and separation efficiency be impaired. Frequently used UV-absorbing co-ions include chromate, benzoate, phthalate, imidazole and proprietary products like UV-Cat-1 and -2 (Waters/Millipore).

Micellar electrokinetic chromatography (MEKC)

The separation and analysis of neutral molecules is made possible with the inclusion of micelle-forming detergents in the electrophoretic medium (Terabe *et al.*, 1984). Molecules will be distributed between the aqueous and micellar phases to different degrees according to their polarity. This pseudo-chromatographic mode of CE is called micellar electrokinetic capillary chromatography (MECC) or micellar electrokinetic chromatography (MEKC). The most commonly used detergents are alkyl sulfates like sodium dodecylsulfate, bile salts like sodium cholate and hydrophobic-chain ammonium salts like tetradecyltrimethylammonium bromide. Charged micelles provide possibilities for ionic interaction with analytes in addition to partitioning into the interior of the micelle. Neutral detergents (e.g. Triton X-100 or Brij 35) can be incorporated into charged micelles to modify the micelle properties. Fig. 4 shows a schematic view of MEKC using anionic detergent micelles.

The degree of distribution between aqueous and micellar phase can be manipulated by carefully choosing detergents (cationic, anionic or neutral), by changing the pH of the buffer or by including an organic modifier in the electrolyte. The addition of cyclodextrins to the aqueous phase also alters the distribution and can make possible the analysis of highly hydrophobic compounds. A thorough introduction to the field of MEKC has been published (Vindevogel & Sandra, 1992).

Capillary gel electrophoresis (CGE)

Although not necessary for anti-convection purposes, gels can be used in CE to introduce a molecule-sieving mechanism. It is especially useful for the separation of molecules with a similar charge-to-size ratio, e.g. oligo- and polynucleotides (Schwartz *et al.*, 1991) and denatured proteins in the equivalent of SDS–PAGE (Ganzler *et al.*, 1992). Common gel materials include polyacrylamide and agarose, while methylcelluloses, dextrans and polyethylene glycol have been used to form polymer networks. Extremely efficient separations have been achieved in this mode of CE (Schwartz *et al.*, 1991).

Capillary isoelectric focusing (CIEF)

In isoelectric focusing, charged solutes migrate through a pH gradient in an electric field. When a solute reaches the point in the pH gradient where it becomes neutral, it will cease to migrate. Conventional isoelectric focusing is performed in a slab-gel to minimise convection, but CIEF can be performed in free solution. Carrier ampholytes, series of polyamino, polycarboxylic (or polysulfonic) acids, are used to generate the pH gradient. The capillary is filled with the ampholytes together with the analytes (usually proteins) and all components are allowed to migrate electrophoretically, usually with phosphoric acid as the anodic buffer and with sodium hydroxide at the cathodic end. The electroosmotic flow is kept to a minimum by the use of coated capillaries, and when the analytes and carrier ampholytes have been focused the current drops to near zero. The content of the capillary is then mobilised electrophoretically by the addition of salt to the anodic or cathodic reservoir, which makes the ampholytes and analytes travel past the detector. Alternatively, mobilisation can be accomplished hydrodynamically or by keeping the electroosmotic flow low but at a sufficient level to transport the capillary content past the detector.

Capillary isotachophoresis (CITP)

Isotachophoresis has been performed in capillaries for decades (Bocek *et al.*, 1985) and instruments for CITP have been commercially available since 1974. Most reported applications have been developed for relatively wide (> 500 μm ID) Teflon capillaries with conductivity detection of the analytes, but it is also possible to perform CITP with modern CE instruments using more narrow (50–75 μm ID) fused-silica tubing and on-capillary UV detection.

In isotachophoresis, the sample zone is sandwiched between a leading and a terminating electrolyte in the capillary. The leading electrolyte is chosen so that it has a higher mobility than any other compound in the capillary, and in the same manner the terminating

electrolyte is selected to have the lowest mobility. Solutes in the sample zone will migrate according to their intrinsic mobilities, and as individual solute zones are formed discontinuities in electric field strength will appear in the zone between the electrolytes. When equilibrium is reached, discrete bands of leading electrolyte (LE), sample solutes and terminating electrolyte (TE) have been formed and they will travel with the same speed through the capillary according to:

$$v_{ITP} = \mu_{LE}E_{LE} = \mu_A E_A = \mu_B E_B = \mu_{TE}E_{TE} \quad (3)$$

where v_{ITP} = velocity of the zones at isotachophoretic equilibrium and indices A and B correspond to sample solutes A and B. Each zone will have its own electric field strength (E) that matches its mobility (μ), the lowest field strength being in the leading electrolyte. Should a solute diffuse into an adjacent zone it will experience a different electric field strength and either accelerate or slow down so that the zone is sharpened again. This focusing phenomenon can be utilised to concentrate large zones of dilute sample and is sometimes used in a transient mode as an on-capillary zone-sharpening step prior to FSCE (see below). Cationic and anionic analytes have to be determined in different runs, because the electrolyte compositions will have to be different, and neutral compounds cannot be separated.

Capillary electrochromatography (CEC)

In CEC the fused-silica tubing is either packed with a spherical stationary phase (packed CEC) or its inner surface is coated with some type of adsorbent (open-tubular CEC). Electroosmotic flow sweeps eluent and sample through the capillary and separation occurs because of partitioning of the analytes between mobile and stationary phase in addition to possible differences in electrophoretic mobility. The main advantage of this technique as compared to conventional capillary chromatography is the easily produced low flow rates that are necessary for narrow bores. The flow is pulse-free and the negligible back-pressure makes high linear velocities possible even for small-diameter packing materials (Knox & Grant, 1991; Yamamoto *et al.*, 1992). A flatter flow profile (Stevens & Cortes, 1983) contributes to improved separation efficiency for electroosmotically driven chromatography as opposed to pressure-driven chromatography, but the effect is dramatic only for very low capacity factors (Weinberger, 1993). Bubble formation frequently occurs in the packed capillary even at low currents and poor reproducibility of electroosmotic flow and capacity factors between capillaries also limits the use of CEC (Yamamoto *et al.*, 1992).

QUANTITATIVE ANALYSIS

The majority of capillary electrophoretic applications have been related to the separation of model mixtures or to the qualitative characterisation of samples of a varying degree of complexity. Applications concerning quantitative analysis have been relatively rare, in particular those for more complicated matrices. Quantitative analysis of pharmaceuticals and drug related impurities by CE has been reviewed (Altria, 1993b), as have quantitative aspects of CE in general (Moring *et al.*, 1990; Goodall *et al.*, 1991; Hoyt, 1993; Wätzig & Dette, 1993). Care has to be taken in order to achieve reliable quantitative results and some important points that have to be considered are discussed below. Since most reported applications for food analysis involve either FSCE or MEKC, the discussion below is centred around these CE modes.

Introducing well-defined sample volumes

Several types of sample introduction are used in commercially available CE instruments. Samples can be hydrodynamically introduced by applying positive pressure to the inlet end of the capillary or negative pressure to the outlet, for a specified period of time. A less common procedure is to raise the inlet end to a height above that of the outlet end, thereby creating a temporary flow of sample solution into the capillary. Alternatively, electrokinetic introduction is used where the electroosmotic flow is allowed to transport a sample aliquot into the capillary. In some instances, e.g. with gel-filled capillaries electrokinetic introduction is the only choice. For all methods, it is important to keep the temperature under control. The hydrodynamically introduced volume per time unit is inversely proportional to the viscosity of the solution, which for water is 20% lower at 30°C than at 20°C (Sengers & Watson, 1986). The electroosmotic mobility and the mobility of sample ions are dependent on the viscosity of the solution and temperature control is thus necessary also for reproducible electrokinetic sample introduction (Knox, 1988). Inadvertent hydrodynamic flow due to different liquid levels in inlet and outlet reservoirs, and diffusion because of concentration gradients can also modify effective introduced volumes (Moring *et al.*, 1990; Dose & Guiochon, 1992). Loss of sample can also be induced by thermal expansion of the liquid in the capillary during sample introduction. Voltage ramping is recommended to avoid this problem (Knox & McCormack, 1994).

It should be noted that electrokinetic introductions of sample are biased in that sample molecules with high mobilities will be overrepresented in the introduced sample plug (Huang *et al.*, 1988). This can be compensated for if internal standards are used to calculate the amounts that are actually introduced (Dose & Guiochon, 1991). The use of internal standard(s) with either introduction technique also makes correction possible for variations in introduced volume and for losses during sample clean-up. Alternatively, differences in sample conductivities can be corrected by integration of the current during electrokinetic introduction (Lee & Yeung, 1992). The actual amount of sample introduced

into the capillary by hydrodynamic means has been reported to differ systematically from the theoretical value (Ermakov *et al.*, 1994).

The small sample volumes that are used for CE can present problems with solvent evaporation (Moring *et al.*, 1990), with pH shifts and with the formation of electrochemical reaction products during electrokinetic introduction (Rose & Jorgenson, 1988a). These problems can be circumvented by using capped sample vials, by cooling the sample compartment, by keeping the sample vial in a humid atmosphere or by using hydrodynamic means for sample introduction.

Keeping migration times constant

Migration times are dependent on the electroosmotic mobility and electrophoretic mobilities of the analytes. The analyte mobility is influenced by the temperature and pH of the electrolyte (Roberts *et al.*, 1989). In addition to that, electroosmosis is influenced by the status of the capillary inner surface (Lambert & Middleton, 1990). It is therefore important not only to keep the temperature under control as argued above, but also to ascertain that the electrolyte pH is the same throughout the experiment. This can be accomplished by choosing a buffer with good buffering capacity at the relevant pH and by replenishing or frequently changing the inlet and outlet electrolyte reservoirs (McLaughlin *et al.*, 1992). Rinsing of the capillary between runs using sodium hydroxide, water, buffer, detergents, etc., helps recondition the inner surface to a standardised state. Another approach is to calculate the migration time relative to an internal standard. The precision that can be achieved is dependent on how close the analyte and internal standard travel, but relative migration times can be achieved that are consistent enough to validate method transfer between laboratories (Altria *et al.*, 1994). The CGE and CIEF modes often demand the use of an internal standard to correct for variations in migration time.

Measuring peaks

A high data sampling rate is required to make calculations possible for the sharp peaks that often are produced in CE. Peak areas have been reported to give a higher linear dynamic range than peak heights (Moring *et al.*, 1990). As opposed to what happens with chromatographic techniques, analytes that are separated by CE do not pass the detector at the same speed. Differencies in migration velocities are the basis for separation, and as the analytes travel past the detector fast zones will produce sharper peaks with a smaller area as compared to slow zones, even though they have the same concentration and extinction coefficients (for UV detection) (Hjertén *et al.*, 1987; Huang *et al.*, 1989a). Normalised peak areas (peak area divided by migration time) have to be used for quantification relative to internal standards, if area percentage is to be calculated (Altria, 1993a), or if peak areas are to be compared between runs with varying migration times. Normalised peak areas were used to achieve relative standard deviations below 1% between laboratories in an inter-company cross-validation exercise (Altria *et al.*, 1994). Normalised areas have not been used for quantification in several of the publications presented in Table 1.

Peaks can be quantified against internal or external standards. As argued above, internal standards are preferred since they also correct for analyte losses during sample clean-up, compensate for irreproducible introduction volumes and allow for the calculation of relative migration times. Care should be taken to avoid non-linear response when using high standard concentrations to generate calibration data (Weinberger & Albin, 1991).

Identifying peaks

Some commercial CE instruments are equipped with diode-array UV-detectors or UV-detectors with possibilities to perform fast scanning of the wavelength spectrum. The registration of peak spectra facilitates peak identification (Vindevogel *et al.*, 1990; Beck *et al.*, 1993; Heiger *et al.*, 1994). Subtraction of the electroosmotic mobility from the electrophoretic mobility of the sample and comparison of the resulting effective mobility of an analyte peak with that of a standard peak, has been suggested for peak identification and screening purposes (Beckers *et al.*, 1991). Mass spectrometric detection offers structural information of separated compounds, but the most straightforward way to establish peak identity may be to run the sample with and without standard addition.

Improving detectability

The main disadvantage of using CE for quantitative analysis may be the high concentration limits of detection that arise from the short optical pathlengths and small introduction volumes inherent to the technique. This drawback is partly compensated for by the fact that the sharp peaks produced make integration easier. Attempts have been made to modify capillary geometries in order to achieve longer pathlengths (Heiger *et al.*, 1994), but it should also be noted that the short optical pathlength that is the main reason for impaired detectability makes possible the use of low wavelengths for detection (down to 185 nm) even for relatively high electrolyte concentrations (Jones & Jandik, 1992).

Several methods exist to preconcentrate analytes during or immediately after injection. Sample stacking allows for larger injection volumes and takes advantage of a higher field strength in the sample zone (Chien & Burgi, 1992). Sample ions migrate very rapidly until they experience the lower field strength of the electrolyte and thus stack at the sample–electrolyte boundary. The discontinuity in electric field strength is produced by a lower ionic strength in the injected sample than in the

Table 1. CE applied to the quantitative analysis of food samples

Analyte	Sample matrix	Typical concentration	CE mode	Validation[a–c]	Internal standard	References
Inorganic compounds						
Potassium, sodium, calcium, magnesium	Mineral water, apple vinegar	0.6–200 μg/ml	FSCE, indirect UV (imidazole, 214 nm), imidazole/sulfuric acid (pH 4.5)	Linearity; RSD_r (2%); comparison with HPLC		Beck & Engelhardt (1992)
Potassium, sodium, calcium, magnesium	Apple juice, orange juice	0.5–3 μg/ml, 20–40 μg/ml (K)	FSCE, indirect UV (imidazole, 214 nm), imidazole/sulfuric acid (pH 4.5)	Linearity; detection limit (0.1 μg/ml, 0.05 μg/ml (Mg)); RSD_r (0.7–4%); RSD_R (1–6%); comparison with AAS		Yang *et al.* (1994)
Potassium, sodium, calcium, magnesium	Pretzels, bread crumbs, peanut butter, parsley, Parmesan cheese	0.2–50 mg/g	FSCE, indirect UV (UV-Cat-2, 185 nm), UV-Cat-2/Tropolone (pH not given)	Comparison with IC and AAS		Morawski *et al.* (1993)
Sodium, calcium, magnesium	Milk	0.4 mg/ml (Ca)	FSCE, indirect UV (UV-Cat-1, 214 nm), UV-Cat-1/HIBA (pH 4.4)	RSD_r (5–7%); comparison with AAS (Ca)		Schmitt *et al.* (1993)
Calcium, magnesium	Wheat flour	0.07 mg/g (Ca), 0.15 mg/g (Mg)	FSCE, UV (200 nm), ethylene glycol and EDTA in borate (pH 9.2)	RSD_r (2–4%); comparison with AAS	Cobalt sulfate	Kajiwara *et al.* (1993)
Chloride, citrate, phosphate	Milk	0.7 mg/ml (phosphate)	FSCE, indirect UV (chromate, 254 nm), OFM Anion–BT/ chromate (pH not given)	RSD_r (3–6%))		Schmitt *et al.* (1993)
Phosphate	Cola drink	1 mg/ml	FSCE, indirect UV (chromate, 254 nm), CTAB in chromate (pH 8.5)	Detection limit (0.1 μg/ml); RSD_r (6%)		Li & Li (1994)
Nitrate, chloride, sulfate	Orange juice, orange pulpwash, processing plant water	50 μg/ml, 0.2–10 μg/ml (nitrate)	FSCE, indirect UV (chromate, 254 nm), OFM Anion–BT/chromate/lactate (pH 8.0); Nitrate: UV (214 nm), OFM Anion–OH/ NaCl/NaOH (pH 8.0)	Linearity; detection limit (0.2 μg/ml); comparison with IC		Swallow & Low (1994)

Table 1. — *continued*

Analyte	Sample matrix	Typical concentration	CE mode	Validation[a–c]	Internal standard	References
Chloride, sulfate, nitrate	Drinking water	20–60 μg/ml	FSCE, potential gradient detection, cadmium acetate (pH not given)	Linearity; RSD_r (2% (nitrate))		Gebauer *et al.* (1983)
Chloride, sulfate, nitrate, fluoride	Drinking water	3–40 μg/ml, 0.06 μg/ml (fluoride)	FSCE, indirect UV (chromate, 254 nm), OFM Anion-BT/ chromate (pH 8.1)	Linearity; RSD_r (1%); comparison with IC		Romano & Krol (1993)
Chloride, sulfate, nitrate, fluoride	Tap water	4–50 μg/ml	FSCE, indirect UV (pyromellitic acid, 250 nm), hexamethonium hydroxide/triethanol amine (pH 7.7)	Linearity; detection limit (1–2 μg/ml); RSD_r (7–11%, 67% (fluoride)); RSD_R (10–15%, 53% (fluoride))		Rhemrev-Boom (1994)
Chloride, sulfate, nitrate, carbonate	Tap water, mineral water	0.1–30 μg/ml, 3–400 μg/ml (carbonate)	FSCE, indirect UV (chromate, 254 nm), CTAB in chromate (pH 8.5)	Detection limit (0.2–0.3 μg/ml); RSD_r (2–6%)		Li & Li (1994)
Nitrate, nitrite	Water	7 μg/ml (nitrate)	FSCE, UV (214 nm), coated capillary, DMMAPS and Brij 35 in phosphate (pH 3)	Linearity; RSD_r (1–10%); quantification limit (0.5 μg/ml)		Janini *et al.* (1994)
Free sulfur oxide	Wine, grape juice	Not given	FSCE, UV (210–216 nm), coated or uncoated capillary, phosphate (pH 2.3–2.8)	Linearity; detection limit (1–2 μg/ml)		Collins *et al.* (1993)
Organic acids						
Malate, citrate, pyruvate, succinate, acetate, lactate	Beer	0.4–2 μg/ml	FSCE, indirect UV (phthalate, 254 nm), TTAB in phthalate (pH 5.5)	Linearity; RSD_r (1–4%); RSD_R (0.6–4%)		DeVries (1993)
Malate, acetate, lactate	Apple juice	4 mg/ml (malate), 0.05 mg/ml (acetate), 0.3 mg/ml (lactate)	FSCE, indirect UV (phthalate, 254 nm), OFM Anion-BT/ phthalate (pH 7.0)	Linearity; detection limit (1 μg/ml)	Butyrate	Kenney (1991)
Lactate	Yogurt	Not given	FSCE, conductivity, TTAB in MES/histidine (pH 6)		Butanoate	Huang *et al.* (1989b)

Table 1. — ***continued***

Analyte	Sample matrix	Typical concentration	CE mode	Validation[a–c]	Internal standard	References
Citrate, malate, acetate, lactate	Tomato juice	4 mg/ml (citrate), 0.4 mg/ml (malate), 0.1 mg/ml (acetate), 0.07 mg/ml (lactate)	FSCE, indirect UV (phthalate, 254 nm), OFM Anion–BT/ phthalate (pH 7.0)	Linearity; detection limit (1 μg/ml)	Butyrate	Kenney (1991)
Citrate, tartrate, malate, succinate, acetate, lactate	Dark grape juice, Chablis wine	0.1 mg/ml (citrate), 3–4 mg/ml (tartrate, malate), 0.3 mg/ml (succinate, acetate, lactate)	FSCE, indirect UV (phthalate, 254 nm), OFM Anion–BT/ phthalate (pH 7.0)	Recovery (100%); linearity; detection limit (1 μg/ml); RSD_r (1–14%)	Butyrate	Kenney (1991)
Citrate, isocitrate	Orange juice	9 mg/g (citrate), 1 mg/g (isocitrate)	FSCE, indirect UV (phthalate, 254 nm), CTAB and methanol in phthalate (pH 7.0)	Recovery (94%); linearity; detection limit (0.06 mg/g);		López Martínez & Rodrigues Roldán (1993)
Formate, tartrate, malate, succinate, glycolate	Chicory root juices	0.03–0.8 mg/g, 0.6–6 mg/g (malate)	FSCE, indirect UV (phthalate, 254 nm), calcium chloride in OFM Anion–BT/ phthalate (pH 5.6)	Linearity; RSD_r (0.2–10%)		Lalljie *et al.* (1993)
Formate	Beet sugar juices	0.004–2 mg/g	FSCE, indirect UV (phthalate, 254 nm), calcium chloride in OFM Anion–BT/ phthalate (pH 5.6)	RSD_r (0.4–10%)		Lalljie *et al.* (1993)
Propionate	Bread	1 mg/g	FSCE, indirect UV (benzoic acid, 214 nm), TRIS/benzoic acid (pH 4.6)	Recovery (95%); effective mobility checked; llinearity; detection limit (0.1 mg/g)		Ackermans *et al.* (1992a)
Ascorbic acid, total vitamin C	Orange juice	0.5 mg/ml	FSCE, UV (254 nm), coated capillary, phosphate (pH 7.0)	Recovery ('complete'); linearity; RSD_r (3%); comparison with HPLC	Phthalic acid	Chiari *et al.* (1993)
Ascorbic acid	Orange, apple, grapefruit and vegetable juice	0.1–0.4 mg/ml	FSCE, UV (254 nm), TRICINE (pH 8.8)	Linearity; detection limit (2 μg/ml)	Isoascorbic acid	Koh *et al.* (1993)

Table 1. — *continued*

Analyte	Sample matrix	Typical concentration	CE mode	Validation[a–c]	Internal standard	References
Ascorbic acid	Lemon juice, orange juice	0.4 mg/ml	FSCE, UV (265 nm), phosphate (pH 5.0)	Recovery (99%); linearity; detection limit (0.5 μg/ml); RSD_r (< 5%)		Lin Ling *et al.* (1992)
Sorbic acid	Fruit juice concentrates, soft drinks, wine, marmalade, margarine	0.6–8 μg/ml	FSCE, UV (254 nm), PEG in MES/BIS–TRIS (pH 5.2)	Recovery (98–102%); linearity; detection limit (0.06 μg/ml); RSD_r (0.9–4%)		Kaniansky *et al.* (1994b)
Hippuric acid, orotic acid	Whey	0.02–0.07 mg/g	FSCE, UV (254 nm, 280 nm (orotic acid)), AMPD/BICINE (pH 8.8)	Linearity; RSD_r (0.9–2%); comparison with HPLC	Sorbic acid	Tienstra *et al.* (1992a)
Benzoic acid	Oyster sauce	0.5 mg/g	FSCE, UV (190 nm), TBA in phosphate/ borate (pH 7.0)	Recovery (99%); linearity; RSD_r (0.4%)		Ng *et al.* (1992)
Other organic compounds						
Caffeine, aspartame, benzoic acid	Diet cola drink	0.1–0.5 mg/ml	FSCE, UV (214 nm), phosphate (pH 11)	Linearity; detection limit (2–5 μg/ml); RSD_r (1–3%); RSD_R (14–15%); accuracy; comparison with HPLC		Jimidar *et al.* (1993)
Aspartame	Artificial sweetening powders	40 μg/ml (one packet in 1000 ml)	FSCE, UV (214 nm), phosphate (pH 11)	Linearity; detection limit (5 μg/ml); RSD_r (1–2%); RSD_R (14%); accuracy; comparison with HPLC		Jimidar *et al.* (1993)
Caffeine	Coffee, tea, cola drink, cocoa mix	0.6 mg/ml (coffee), 0.2 mg/ml (tea), 0.08 mg/ml (cola), 0.02 mg/ml (cocoa)	FSCE, UV (280 nm), borate (pH 9.6)	Linearity; RSD_r (2%); comparison with HPLC		Hurst & Martin (1993)
Caffeine	Coffee	1 mg/g (decaffeinated), 20 mg/g (regular), 40 mg/g (instant)	MEKC, UV (214 nm), CTAC in phosphate (pH 10.4)	RSD_r (1%); comparison with HPLC		Burton *et al.* (1994)

Table 1. — ***continued***

Analyte	Sample matrix	Typical concentration	CE mode	Validation[a–c]	Internal standard	References
Histamine	Red wine	3 μg/ml	FSCE, fluorescence (post-capillary derivatization, exc. 312 nm, em. 400 nm), KCl in borate (pH 9.5)			Rose & Jorgenson (1988b)
Histamine	Fish	0.005–5 mg/g	FSCE, UV (210 nm), citrate (pH 2.5)	Recovery (94–110%); linearity; RSD_r (< 3%, St); comparison with fluorometry		Mopper & Sciacchitano (1994)
5-Hydroxymethyl-2-furaldehyde , 2-furaldehyde	Grapefruit juice	15 μg/ml (5-HMF), 0.6 μg/ml (2-FA)	MEKC, UV (280 nm), SDS in phosphate (pH 7.5)	Linearity; RSD_r (1–2%)	2-Furylmethylketone	Corradini & Corradini (1992)
5-Hydroxymethyl-2-furaldehyde	Honey	30 μg/g	MEKC, UV (280 nm), SDS in phosphate (pH 7.5)	Linearity; RSD_r (1–3%)	2-Furylmethylketone	Corradini & Corradini (1994)
Herbicides (metsulfuron, chlorsulfuron)	Tap water	0.1–5 ng/ml	FSCE, UV (214 nm), borate (pH 9.0)	Recovery (94%); linearity; quantification limit (0.1 ng/ml before concentration); comparison with bioassay		Dinelli *et al.* (1993)
Herbicides (linuron, metolachlor, atrazine, metsulfuron)	Spiked drinking water	1–50 ng/ml	MEKC, UV (214 nm), methanol and SDS in borate (pH 8.0)	Recovery (80–92%); linearity; detection limit (0.5 ng/ml)		Dinelli *et al.* (1994)
Herbicides (paraquat, diquat)	Spiked drinking water	0.7–30 ng/ml	CITP–FSCE, UV (310 nm), MHEC in potassium/citrate (pH 6.08) (LE), TRIS/citrate (pH 7.80) (TE), PEG in TRIS/citrate (pH 6.08)	Detection limit (0.2 ng/ml); RSD_r (5–7%)		Kaniansky *et al.* (1994a)
Herbicides (paraquat, diquat)	Potato	0.05–1 μg/g	FSCE, UV (200 nm), coated capillary, phosphate (pH 2.5)	Recovery (70%); linearity; detection limit (0.01 μg/g); RSD_r (10%)	TBD	Wigfield *et al.* (1993)
Iso-α-acids	Beer	0.8–9 μg/ml	MEKC, UV (254 nm); SDS in phosphate (pH 7.6)	Recovery (91–102%); linearity; detection limit (0.09–0.4 μg/ml); RSD_r (2–8%)		Szücs *et al.* (1993)

Table 1. — ***continued***

Analyte	Sample matrix	Typical concentration	CE mode	Validation[a–c]	Internal standard	References
Phytate	Soy-beans	10–20 mg/g	FSCE, indirect UV (benzoate, 254 nm), benzoate/histidine (pH 6.2)	Recovery (93%); linearity; detection limit (40 μg/g); RSD_r (0.6%)	Aspartic acid	Nardi *et al.* (1992)
Inosine-5′-mono-phosphate, inosine, hypoxanthine	Fish	0.3 mg/ml extract	FSCE, UV (250 nm), CAPS (pH 11)	Comparison with enzymatic method		Luong *et al.* (1992); Nguyen *et al.* (1990b)
Sulfonamides	Pork meat	0.01 mg/ml extract	FSCE, UV (254 nm), phosphate–borate (pH 7.0)	Effective mobility checked; linearity; detection limit (2–9 μg/g)		Ackermans *et al.* (1992b)
Sulfadimethoxine	Oyster	1 μg/g extract	FSCE, MS (SIM–m/z 311) or MS–MS (SRM–m/z 311 > 156), TRIS (pH 7.2)			Pleasance *et al.* (1992)
Saxitoxin	Scallop	1 μg/g	CITP–FSCE, UV (200 nm), coated capillary, formic acid (TE), morpholine (pH 5)			Locke & Thibault (1994)
Saxitoxin, neosaxitoxin, gonyautoxins	Scallop	0.1–1 μg/g	CITP–FSCE, MS (SIM –m/z 300, 316, 396), coated capillary, formic acid (TE), morpholine (pH 5)	Detection limit (10 ng/g)		Locke & Thibault (1994)
Saxitoxin	Clam, oyster, scallop	0.01–0.5 μg/g	FSCE, UV (208 nm), borate (pH 9.2)	Recovery (96–100%); linearity; RSD_r (3%)		Sciacchitano & Mopper (1993)
Domoic acid	Mussels		FSCE, UV (242 nm), CAPS (pH 10.3)	Linearity; detection limit (10 μg/g)		Nguyen *et al.* (1990a)
Glucose, fructose, sucrose	Apple, orange and grape juices	20–80 mg/ml	FSCE, UV (395 nm), methanol in borate (pH 9.5)	Linearity; detection limit (0.04–0.1 mg/ml (St)); RSD_r (2% (St), 0.5–6% (Sa)); RSD_R (10–18% St)); comparison with HPAEC–PAD	Glucuronic acid	Klockow *et al.* (1994a)

Table 1. — *continued*

Analyte	Sample matrix	Typical concentration	CE mode	Validation[a–c]	Internal standard	References
Flavonoids (swertiajaponin, schaftoside, isoschaftoside, orientin)	Sugarcane	0.02–0.2 mg/g	FSCE, UV (395 nm), methanol in borate (pH 9.5)	Linearity; detection limit (8 μg/g); RSD_r (2–8%)	Apigenin	McGhie (1993)
Isoflavones (daidzin, daidzein, genistin, genistein, biochanin A)	Soy-bean products	0.04–0.7 mg/g	FSCE, UV (254/214 nm), borate (pH 8.6)	Linearity; detection limit (0.03 mg/g, genistein); RSD_r (1–4%, peak height); comparison with HPLC	3-Methyl-1-isobutylxanthine	Shihabi *et al.* (1994)
Proteins						
α-Lactalbumin, β-Lactoglobulin	Whey from raw and UHT milk	0.04–4 mg/ml	CGE (?), UV (214 nm), PEG and SDS in TRIS/borate (pH 8.6)	Detection limit (0.02–0.03 mg/ml); RSD_r (3–6%); RSD_R (3–11%); comparison with HPLC		Cifuentes *et al.* (1993)
α-Lactalbumin, β-Lactoglobulin	Acid and rennet whey	1–4 mg/ml	FSCE, UV (214 nm), phosphate (pH 2.5)	Recovery (94–110%); linearity; detection limit (6–10 μg/ml); RSD_r (0.7–1%)		Otte *et al.* (1994a)

[a]Repeatability (r) and reproducibility (R) are expressed as relative standard deviations (RSD_r and RSD_R) and relate to area unless otherwise indicated. Unless further specified, reproducibility data are taken as within-day variation (r).
[b]Values are for analytes in unaugmented samples unless otherwise indicated.
[c]Accuracy is comparison between standard addition and external calibration curve.

background electrolyte (Moring *et al.*, 1990) or by producing a transient isotachophoretic steady state in the sample zone (Jandik & Jones, 1991). Optimised conditions for sample stacking have been determined (Burgi & Chien, 1991). A similar stacking effect can be created for zwitterions by using a sample solvent with a different pH than the background electrolyte (Aebersold & Morrison, 1990). A short plug of packed material at the inlet end of the capillary can be used to concentrate samples prior to electrophoretic separation in a manner analogous to solid-phase extraction (Swartz & Merion, 1993).

Although there are possibilities for automated precapillary derivatisation (Houben *et al.*, 1993) and although a CE conductivity detector has recently been introduced to the market, indirect detection may still be the easiest way to detect analytes lacking both fluorescence and a chromophore. If a UV-absorbing compound of the same charge as the analyte is included in the electrolyte, electroneutrality conditions have to be kept and displacement of the chromophore by the analyte produces negative peaks in the electropherogram (Yeung & Kuhr, 1991). Quantitative aspects of indirect detection in CE have been investigated (Nielen, 1991). Alternatively, temporary association of the analyte with a chromophore may be used to ensure detectability (Kajiwara *et al.*, 1993). Strategies for optimisation of detection sensitivity when applying CE to inorganic anions have been described (Jandik & Jones, 1991).

Validating methods for quantitative analysis

Validation parameters frequently included in CE methods for quantitative analysis include recovery, detection or quantification limits, linearity of calibration curve, precision of peak area and migration time and comparison with other methods of determination.

APPLICATIONS

The application of CE to food analysis clearly demonstrates the versatility of the technique. The types of food that have been analysed range from water to meat, and the analytes are as diverse as metal ions and proteins. This review covers CE applications to food analysis in a broad context, but the emphasis is put on quantitative determinations. Analytes that have been quantitatively determined in food samples are listed in Table 1 together with information on the sample matrix, brief summaries of the methods, typical concentrations and validation parameters. As mentioned above, capillary isotachophoresis has been available for some time and a great number of applications of CITP to food analysis have been published. In order to keep the size of this review within reasonable limits, CITP applications have been excluded and reported applications have been limited to those using novel CE techniques. Textbooks (Everaerts *et al.*, 1976; Bocek *et al.*, 1988) and reviews (Bocek *et al.*, 1985) should provide the interested reader with a number of CITP applications.

Inorganic compounds

The possibility to analyse inorganic ions with capillary ion electrophoresis is discussed above. Using CIE, cations (K, Na, Ca and Mg) were determined in mineral water and apple vinegar (Beck & Engelhardt, 1992), fruit juices (Yang *et al.*, 1994) and pretzels, breadcrumbs, peanut butter, parsley and Parmesan cheese (Morawski *et al.*, 1993). Drinking water and mineral waters were analysed for potassium, sodium, calcium, magnesium and ammonium ions (Šimunicová *et al.*, 1994). Cations were detected in tap water (K, Na, Ca, Mg: Quang & Khaledi, 1994; Morin *et al.*, 1994; K, Na, Ca, Mg, Cu: Weston *et al.*, 1992), mineral water (Morin *et al.*, 1994) and orange juice (K, Na, Ca, Mg: Weston *et al.*, 1992). Zinc was analysed in tap water as a zinc–HQS complex without preconcentration (Timerbaev *et al.*, 1993). The analysis of calcium and magnesium was used to assess the quality of wheat flour (Kajiwara *et al.*, 1993). The effect of temperature on the salt balance of milk was studied by following the availability of cations (K, Ca, Na and Mg) and anions (chloride, sulfate, citrate, phosphate, carbonate and lactate) in ultrafiltrated milk (Schmitt *et al.*, 1993).

CIE was reported to solve separation problems that have restricted the use of IC for the monitoring of anionic disinfection byproducts in drinking water (Jones & Jandik, 1992). Drinking water was also analysed for nitrate and nitrite (Janini *et al.*, 1994) and chloride, sulfate, nitrate and fluoride (Romano & Krol, 1993; Rhemrev-Boom, 1994). Tap water and mineral waters were analysed for chloride, sulfate, nitrate and carbonate content (Li & Li, 1994). Bicarbonate, fluoride, phosphate, nitrate, sulfate and chloride ions were detected in tap water (Avdalovic *et al.*, 1993) and chloride, sulfate, nitrate, phosphate and carbonate ions were detected in a beer sample (Jones & Jandik, 1990). Phosphate content was determined in a carbonated cola drink (Li & Li, 1994). The possibilities for determination of chloride, sulfate and phosphate in brewed coffee was demonstrated (Anonymous, 1990). In one of the earliest applications of CE to quantitative food analysis FSCE with potential gradient detection was used to determine nitrate, chloride and sulfate in drinking water (Gebauer *et al.*, 1983). Orange juice, orange pulpwash and processing plant water samples were analysed for nitrate using direct detection, and for chloride and sulfate using indirect detection (Swallow & Low, 1994). Comparison with IC indicated that FSCE is the method of choice for nitrate analysis in orange juice and orange pulpwash. It was argued that the chloride content may be a useful parameter for the authentication of Brazilian orange juice.

Free sulfur dioxide was determined in grape juice and wine and advantages of CE over other techniques were discussed (Collins *et al.*, 1993).

Organic acids

Organic acids were determined with CIE in beverages like apple juice (malate, acetate and lactate), tomato juice (citrate, malate, acetate and lactate), dark grape juice (tartrate and malate) and wine (citrate, tartrate, malate, succinate, acetate and lactate) (Kenney, 1991). The levels of organic acids (malate, citrate, succinate, pyruvate, acetate and lactate) in beer were tracked from cold wort to packaged beer (DeVries, 1993). The separation of organic acids (tartrate, malate, citrate, succinate, acetate and lactate) in red wine was demonstrated (Gordon *et al.*, 1988) and the malolactic fermentation in table wine was monitored by assaying the levels of malate, lactate and tartrate (Levi *et al.*, 1993). Organic acids were detected in white wine and coffee (Kelly & Nelson, 1993). Brewed coffee was analysed for oxalate, citrate, tartrate, malate, succinate, acetate and lactate (Anonymous, 1990), while the levels of citrate and isocitrate were determined in orange juice (López Martínez & Rodrígues Roldán, 1993). Acetic, succinic, malic, tartaric, citric and isocitric acid, in addition to sulfate and chloride ions, were identified in grape juice using FSCE with suppressed conductivity detection (Avdalovic *et al.*, 1993). Process juices produced during sugar refinement were assayed for formate, tartrate, succinate, malate, glycolate, acetate, citrate and lactate (chicory root juices) and formate (beet sugar juices) (Lalljie *et al.*, 1993). Soy sauce was analysed for citrate, tartrate, acetate, lactate and butyrate (Kenney, 1991) and propionate was determined in bread (Ackermans *et al.*, 1992a). Lactate was determined in yogurt using conductivity detection and employing butanoate as an internal standard (Huang *et al.*, 1989b).

Other organic compounds

Using more conventional FSCE techniques, often with direct UV detection and not necessarily manipulated EOF, other organic compounds were analysed. Ascorbic acid was determined in fruit and vegetable juices (Koh *et al.*, 1993; Lin Ling *et al.*, 1992; Chiari *et al.*, 1993) and carbonated lemonade (Beck *et al.*, 1993). Sorbic acid was determined in fruit juice concentrates, soft drinks, wine, marmalade and margarine (Kaniansky *et al.*, 1994b). The amount of caffeine was quantified in coffee (Burton *et al.*, 1994) and in brewed coffee and tea, cocoa mix and cola drink (Hurst & Martin, 1993; Jimidar *et al.*, 1993). Aspartame was detected in a diet cola drink (Schlabach & Powers, 1991) and the levels of aspartame and benzoate in diet cola drinks were determined (Jimidar *et al.*, 1993). Benzoate was determined in oyster sauce (Ng *et al.*, 1992) and hippuric and orotic acid were quantified in rennet whey (Tienstra *et al.*, 1992a). Red wine was analysed for compounds containing primary amines and histamine was quantified (Rose & Jorgenson, 1988b). Tap water was assayed for sulfonylurea herbicides like metsulfuron and chlorsulfuron (Dinelli *et al.*, 1993) and for paraquat and diquat after spiking (Kaniansky *et al.*, 1994a). The latter herbicides were also quantitatively determined in potatoes (Wigfield *et al.*, 1993). Drinking water was spiked with herbicides (linuron, metolachlor, atrazine and metsulfuron) at the ng/ml level and analysed with MEKC (Dinelli *et al.*, 1994).

Also more complex food matrices were analysed. An alternative method to determine levels of histamine in fish was presented (Mopper & Sciacchitano, 1994) and soy-beans were assayed for phytate using indirect detection (Nardi *et al.*, 1992). Paralytic shellfish toxins (saxitoxin and neosaxitoxin) were analysed in clam, oyster and scallop (Thibault *et al.*, 1991; Sciacchitano & Mopper, 1993; Locke & Thibault, 1994). Okadaic acid was detected in cooked mussels with MEKC coupled to a liquid chromatography-linked protein phosphatase bioassay (Boland *et al.*, 1993) whereas domoic acid was determined in mussels with FSCE and UV detection (Nguyen *et al.*, 1990a). Fish freshness was assessed by measuring nucleotide degradation products (inosine monophosphate, inosine and hypoxanthine) in fish extracts (Nguyen *et al.*, 1990b; Luong *et al.*, 1992). Several sulfonamide antibiotics added to pork meat extracts were determined (Ackermans *et al.*, 1992b) and sulfadimethoxine was analysed in fortified oyster extract (Pleasance *et al.*, 1992). Xylazine, haloperidol, trimethoprim, sulfadiazine and sulfamethoxazol were detected in fortified pork meat (Hoogland & Tomassen, 1992).

Carbohydrates were identified in a purified pea extract (sucrose, raffinose, stachyose, verbascose and ajugose) with lactose and melibiose as internal standards (Arentoft *et al.*, 1993), in carbonated soft drinks (glucose and fructose) (Colón *et al.*, 1993), and in a sorghum hydrolysate (xylose, arabinose, glucose and galactose) after reductive amination (Delgado *et al.*, 1993). Orange juice was analysed for carbohydrates (saccharose, glucose and fructose) with indirect detection (Vorndran *et al.*, 1992). Quantitative determinations of glucose, fructose and saccharose in fruit juices by CE using glucuronic acid as an internal standard were found not to be statistically different from HPAEC–DAD analysis of the same samples (Klockow *et al.*, 1994a). The carbohydrate fraction of *Gummibärchen* (jelly beans) was extracted and analysed after derivatisation with ANTS (Klockow *et al.*, 1994b). The separation of glucosinolates and desulfoglucosinolates in rape-seed by MEKC was reported (Bjergegaard *et al.*, 1991; Michaelsen *et al.*, 1992). Flavonoids from rape-seed, yellow mustard and broccoli were separated (Bjergegaard *et al.*, 1993b). Flavonoids were also quantitatively analysed in sugarcane (McGhie, 1993) and characterised in honey to permit the determination of botanical and geographical origin (Delgado *et al.*, 1994; Ferreres *et al.*, 1994). Isoflavones were analysed in soybean products (Shihabi *et al.*, 1994). Phenolic carboxylic acids (4-hydroxybenzoic acid, sinapic acid, ferulic acid and coumaric acid) were determined in insoluble dietary fibres from whole rape-seed and rye (Bjergegaard *et al.*, 1992) and aromatic choline esters were analysed in seeds from white mustard (Bjergegaard *et al.*, 1993a). The

determination of trigonelline, isoxazoline, tryptophan and tyrosine in germinating pea seeds was performed (Bjergegaard *et al.*, 1994). Much work was devoted to the analysis and characterisation of lupulones and humulones in hop extract (Vindevogel *et al.*, 1990; Verschuere *et al.*, 1992; Szücs *et al.*, 1994) and beer (Vindevogel *et al.*, 1991; Szücs *et al.*, 1993). Aflatoxins were separated in a spiked corn meal extract (Cole *et al.*, 1992) and the phospholipid composition of soy-bean and rape-seed lecithins was analysed (Ingvardsen *et al.*, 1994).

The very high resolving power of CE was used to monitor citrus juice composition (phenolic amines, amino acids, flavonoids, polyphenols and ascorbic acid) for the possible detection of fruit juice adulteration (Cancalon & Bryan, 1993; Cancalon, 1993, 1994). Quality deterioration in grapefruit juice was monitored in a MEKC system without sample pretreatment by measuring the indicators 5-hydroxymethyl-2-furaldehyde and 2-furaldehyde (Corradini & Corradini, 1992). A similar system was used to quantify 5-hydroxymethyl-2-furaldehyde in aged and heat-treated honey using 2-furylmethylketone as an internal standard (Corradini & Corradini,, 1994). Several compounds including nitrate, gallic acid, chlorogenic acid, gallotannin, quercetin, rutin and (+)–catechin were detected in camomile tea, and complexing agents in mate tea were analysed before and after decomplexation with CDTA (Harms & Schwedt, 1994).

Proteins and peptides

Proteins have been analysed mainly in milk. Whey proteins (β-lactoglobulin A, β-lactoglobulin B, α-lactalbumin, bovine serum albumin and immunoglobulin G) were analysed (Cifuentes *et al.*, 1993; Cifuentes *et al.*, 1994; Otte *et al.*, 1994a) and the composition of whole casein was monitored as was the chymosin hydrolysis of purified caseins (Kristiansen *et al.*, 1994). In addition, the purity of reversed-phase HPLC fractions of the hydrolysate was assayed by CE. The possibility to separate both whey proteins and casein proteins as opposed to HPLC was demonstrated and used to detect fresh milk adulteration by measuring the ratio of β-casein to α-lactalbumin (Chen & Zang, 1992). The detection of 1% goat milk in cow milk by determination of casein and whey proteins was demonstrated (Tienstra *et al.*, 1992b). Genetic variants of bovine milk proteins were separated (de Jong *et al.*, 1993). In the same study the separation patterns of goat, cow and sheep milk were compared, and the detection of heat-damaged caseins was monitored. The latter could provide a possibility to detect the addition of milk powder to fresh milk and heat treatment of milk more intensive than pasteurisation. In another study, the separation pattern of human milk proteins was compared to those of goat, sheep and cow milk and soy proteins were also analysed (Kanning *et al.*, 1993). Glycated forms of caseinomacropeptide(s) (CMP) were analysed before and after neuraminidase treatment, which made possible the identification of a rennet whey CMP containing *N*-acetyl neuraminic acid (Otte *et al.*, 1994b). FSCE was used to analyse multiple phosphoseryl-containing casein peptides in purified enzymic digests of casein (Adamson *et al.*, 1993). The major proteins in chicken eggs and cow milk were separated (Chen & Tusak, 1994). Lysozyme, conalbumin and ovalbumin were analysed in egg white (McCulloch, 1993). Fractionation of wheat proteins with MEKC was reported (Bietz & Simpson, 1992) and wheat varieties were identified by analysis of gliadins and glutenin subunits using FSCE in the reversed mode and CGE with an entangled polymer network (Werner *et al.*, 1994a, 1994b). The possibility to use CE in species and cultivar determination was investigated (Dinelli & Bonetti, 1992). Proteins from mature and immature peanuts were characterised by peptide mapping, where FSCE was used to analyse protein digests fractionated on reversed-phase or affinity columns with immobilised anhydrotrypsin (Chung *et al.*, 1994). Peptide analysis of raw and dry-cured ham was performed with FSCE in order to monitor proteolytic changes (Toldrá & Aristoy, 1993).

CONCLUSIONS AND FUTURE PROSPECTS

Applications of CE to food analysis have not been common in the literature until the past few years. Of the 105 applications cited in the section above, 14 appeared before 1992, 22 in 1992 and 37 in 1993. It can be seen that CE techniques can be used with advantage in food analysis for a diversity of analytes and matrices, and with increasing awareness among food scientists of the analytical capabilities of CE it is anticipated that the number of reported publications in the area will continue to increase.

With the advent of commercial CE instruments, an increasing number of quantitative applications have been published. Although quantitative analysis is possible and the performance can be comparable to that achieved with chromatographic techniques, care has to be taken in order to achieve reliable results.

The potential for highly efficient separations often makes method development relatively straightforward because it allows the use of closely related compounds as internal standards and diminishes the need for extensive sample clean-up. The possibility to automate slab-gel electrophoretic methods will probably further increase the use of CE in food analysis. The concentration sensitivity of HPLC is yet to be achieved, and much work is devoted to improving detectors and capillary geometries in order to close this gap.

Finally, it should be noted that CE can be utilised in the development and validation of other methods of analysis. The high resolving power and orthogonality to different modes of chromatography make CE an appropriate technique for the purity control of calibrants, HPLC fractions, etc. Isoelectric points for proteins and dissociation constants for smaller molecules can be conveniently determined with CE (Kilár, 1991;

Gluck & Cleveland, 1994a; Gluck & Cleveland, 1994b), which in turn will assist in choosing strategies for analysis.

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