INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Review Article

FLOW INJECTION-CAPILLARY ELECTROPHORESIS

A. Lakshmi Devi*, G. UshaSree, A. Ajitha and V. Uma Maheshwara Rao

Department of Analysis and Quality Assurance, CMR College of Pharmacy, JNTU(H), Hyderabad, Telangana, India.

INTRODUCTION

Capillary electrophoresis (CE) is a powerful separationtool for examining many types of species including proteins,sugars, cations and anions and DNA[1-10].

CE offers a number of advantages as a separation technique

i) it requiresonly small quantities of material; ii) it is applicable to watersoluble,high molecular-weight species in aqueous buffersolution, and; iii) various separation modes make itapplicable for the analysis of a variety of biological and nonbiologicalspecies.

LIMITATIONS OF CE

Despite the multiple and outstanding advantages of CE as a separation technique, including a wide range of applicable analytes, high column efficiency and resolution, low sample and electrolyte consumption, and short analysis times, some generally recognized limitations still affect its broad acceptance in routine applications. The main limitations of conventional CE may be summarized as:

(a) Discontinuous mode of sample introduction (electro-kinetic, gravitational), even automated, confines the sample throughput and precision.

(b) The electro-kinetic mode can “bias” sample introduction; sample components with higher electrophoretic mobilities are preferentially introduced over those with low mobilities.

(c) Low sensitivity in terms of the concentration with photometric detection owing to the short light path.

(d) Difficulties with samples containing large amounts of proteins and macromolecules when directly injected into the separation capillary, owing to fouling of the capillary walls by adsorption.

PRINCIPLES AND CONCEPTS

Flow Injection

FI has many unique featuresincluding limited sample/reagent consumption, short analysistime, and on-line separation, preconcentration andphysicochemical conversion of analytes into detectable species.

FI is based on three principles

1) reproducible timing;
2) reproducible sample injection, and;
3) partial and controlled dispersion of the sample zone

In FI, the length of the manifold tubing remains constant and carrier and reagent flow rates vary little during transport of the sample zone from injection to detection, thus allowing proper sample zone transport and mixing.As the injectedzone advances, it broadens forming a dispersed form as it moves downstream and changes from an asymmetrical to a more symmetrical shape (although never becoming completely symmetrical in real systems). This continuum of concentrations can be viewed as being composed of individual elements of fluid, each having a certain concentration (Fig. **1**).

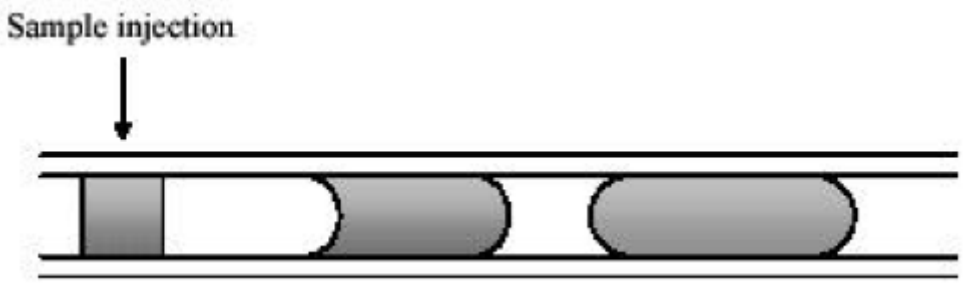


Fig. 1: The advancement of an injected sample zone through a narrow FI tube

Capillary Electrophoresis

CE is a powerful separation technique that has gainedwidespread use in research laboratories because of itsversatility and ease of use. CE separates molecules based ondifferences in electrophoretic mobilities (μ) under theinfluence of an applied field. The direction and velocity ofthe movement of molecules are determined by the sum oftwo vector components, the migration and the electroosmoticflow (EOF). Molecules migrate through the capillary columnbased on their charge-to-mass ratio. In addition, the mobility (μ) of ionic species is directly proportional to the ratio ofcharge to radius (q/r) and reciprocal to the viscosity (□) ofthe solution[11-17]. Thus, small, highly charged ions have high mobilities, whereas large, less charged species have lowmobilities. EOF is a bulk hydraulic flow of liquid in thecapillary driven by the applied electric field and is aconsequence of the surface charge of the capillary. In acapillary column filled with buffer a double layer is formeddue to electrostatic forces. This double layer can bedescribed by the zeta (□) potential. The EOF results from themovement of the layer of electrolyte ions near the capillarywall under the force of the electric field. The basic CEinstrument set-up consists of a high-voltage power supply,two buffer reservoirs, a capillary and a detector (Fig. **2**).

Coupling of the two techniques (example set-uppresented in Fig. **3**) is not without its technical challenges.The FI-CE combined system is based on electrokinetic sample splitting with the bias effect inherent in this type of introduction unavoidable. Proper calibration measuresor use of a non-pressurized sample introduction approach should help minimize such bias. The introduction of airbubbles in the reservoirs and capillary is also of concern inthe combined approach. Upon construction, it is important toposition the platinum electrode with its end to the right of theseparation capillary to avoid interferences from electrolytically generated gas bubbles. The construction of avertical flow cell has been reported to limit the air which caninterfere with the electric current and/or flow conditions. In addition, external high-voltage power sources areused and every effort must be made to effectively ground theinstrument through an appropriate earth contact.

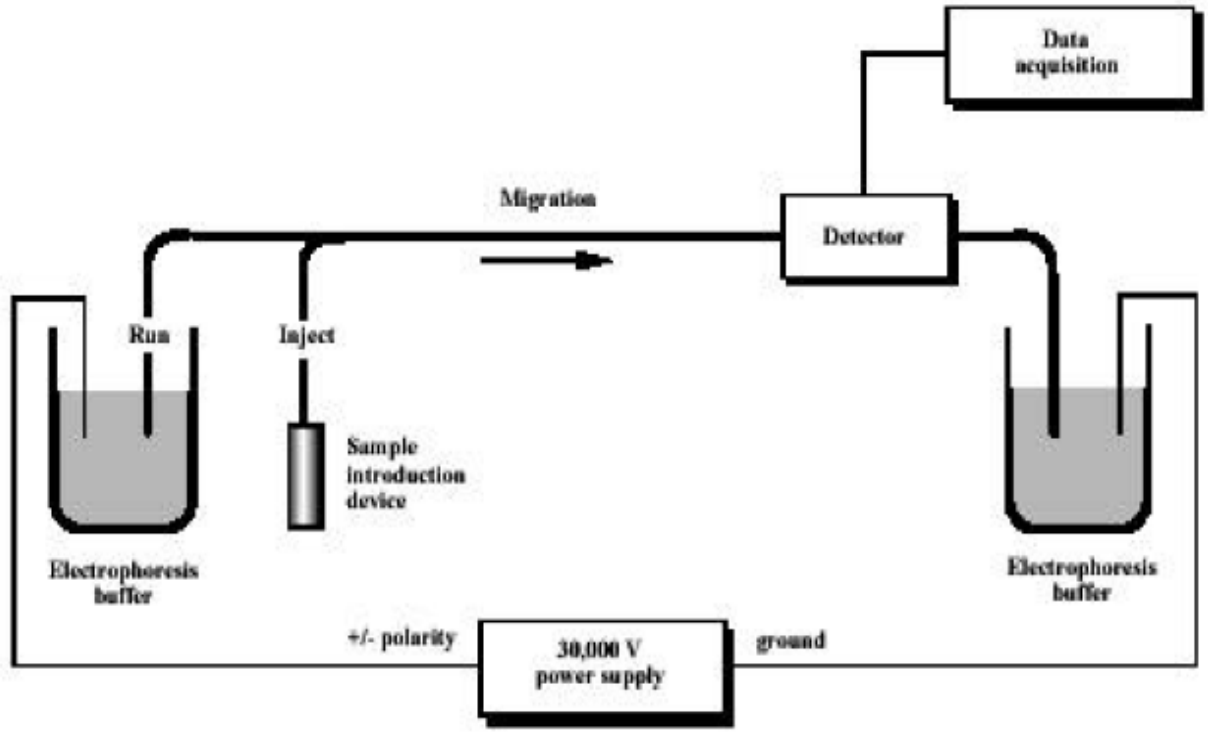


Fig. 2: The basic CE instrument set-up

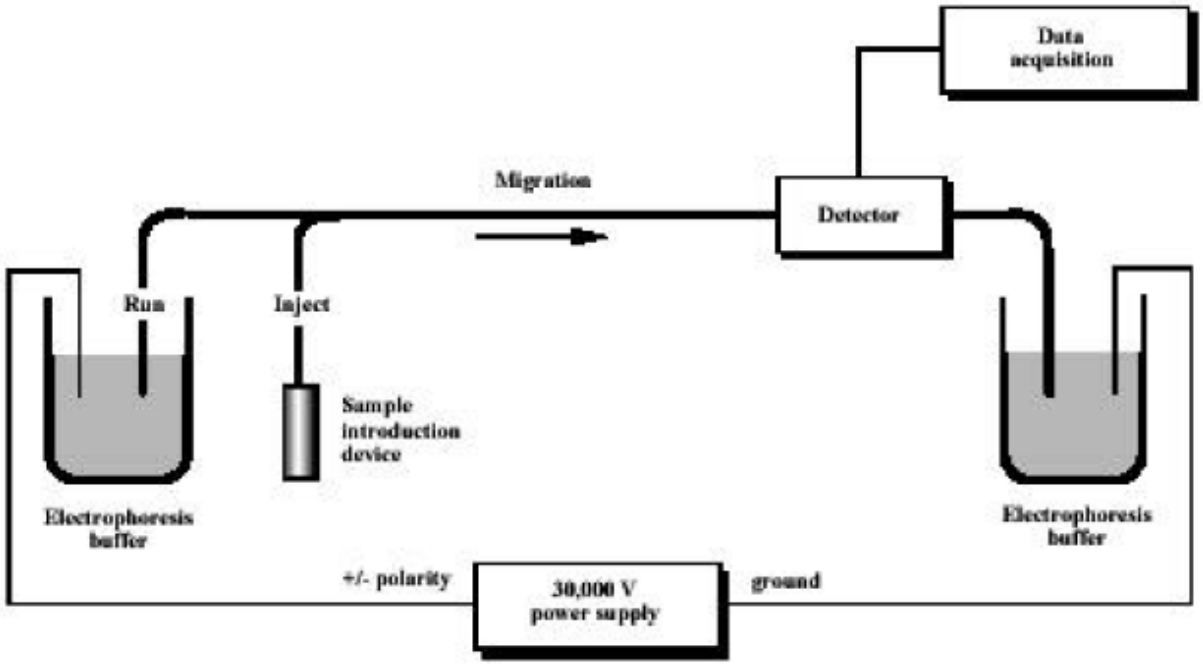


Fig. 3: The basic CE instrument set-up

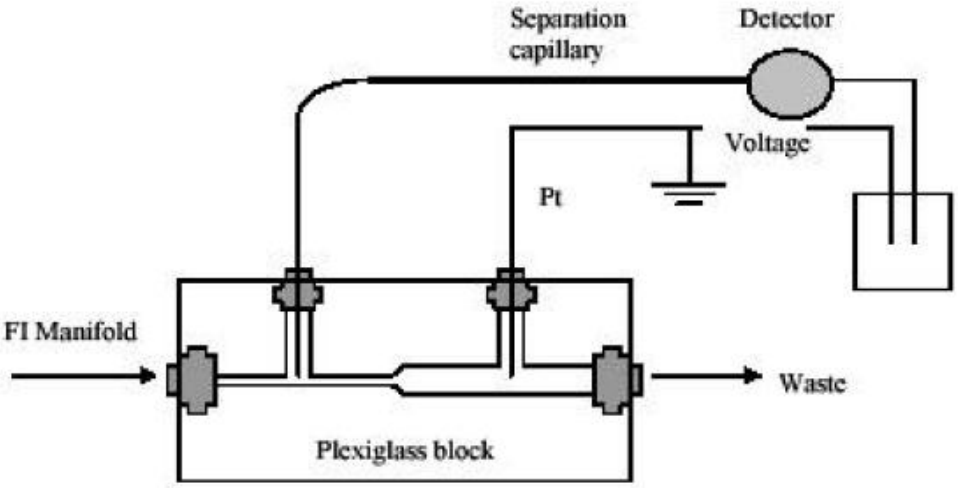


Fig. 4: A basic FI-CE interface set-up

The FI-CE Split-flow Interface and Basic FI-CE System

The mixed hydrodynamic-electrokinetic split-flow interfaces developed by Karlberg's group and the most recent version developed by group are shown schematically in Fig. 4.

Both are characterized by an electrically grounded low dead- volume split-flow cell, in which a small fraction of the sample is electro-kinetically introduced into the separation capillary located in the cell when an injected sample zone in themicroliter range is transported past the capillary tip by a carrier buffer using peristaltic pumps. The main differences between the two interfaces are the flow direction

of the carrier in relation to the electrode and separation capillary and the mode for maintaining a constant hydrostatic level in the cell. A separation capillary and a grounded electrode were vertically inserted into the channel. Our split-flow interface (Fig. 5) was

composed of a vertically positioned conical open-cell, through which the carrier buffer was introduced from the lower end and expelled by forced outflow via an upper outlet. By employing an outflow rate higher than the inflow, the liquid level was maintained constant higher than the inflow, the liquid level was maintained constant and identical with that of the capillary outlet. Thus, hydro-dynamic flow in the capillary owing to differences in the liquid levels at its two ends was kept to a minimum. The separation capillary was inserted into the cell with its tip positioned a few millimeters above the inlet, and the grounded electrode was positioned with its end above the tip of the capillary so as to avoid possible interferences from gas bubbles generated at the electrode surface (Fig. 6).

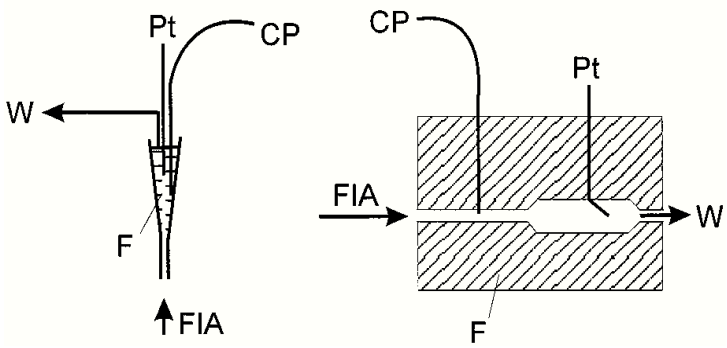
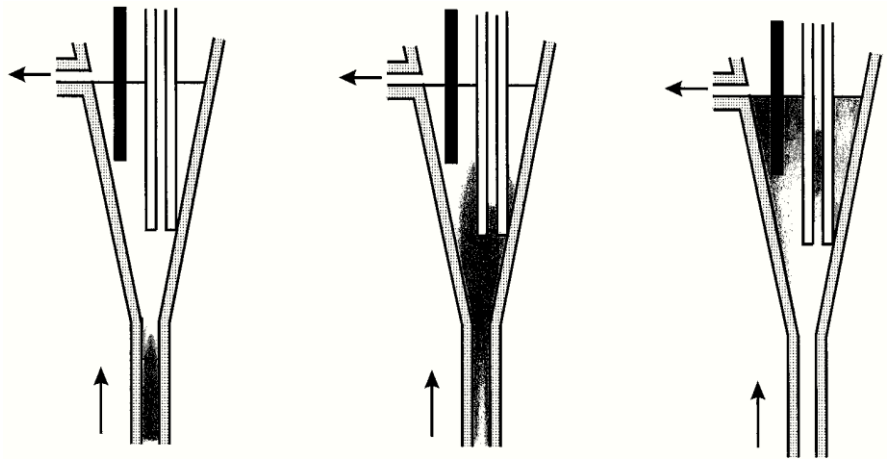


Fig. 5: Schematic diagram of split-flow interfaces for coupling FI to CE: (a) vertical design; (b) horizontal design. F, flow-cell; Pt, platinum electrode; CP, separation capillary; W, waste



Flow-cell working

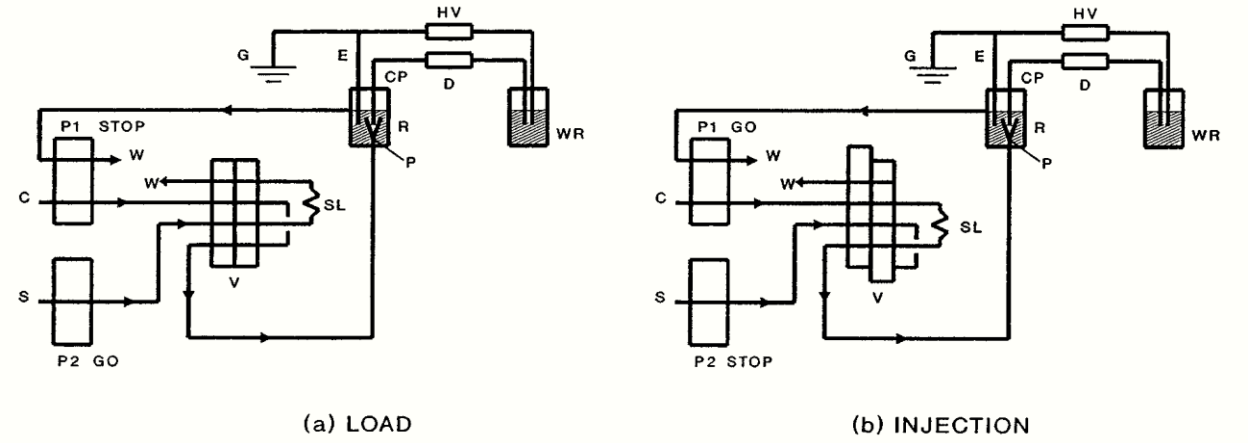


Fig. 6: Working principles of the vertical FI-CE interface. b: basic manifold configuration of FI-CE system

ADVANTAGES OF FI-CE OVER CONVENTIONAL METHODS

(a) Outstanding reproducibility in retention time, peak area and peak height (RSDs of better than 2.5% for the peak height were reported.
(b) Enhanced sample throughput through a simplification in operation, usually by at least a factor of two, when separations are effected within a few minutes.
(c) To further increase the sampling frequency, more than one electropherogram may be overlapped, provided peaks of interest, do not overlap,i.e, one or two more samples may be injected before the last peak of the first sample has been detected.
(d) Large potentials in coupling FI on-line separation and preconcentration techniques to CE to enhance the selectivity and sensitivity.

SHORTCOME OF FI-CE

The main short come in FI-CE spilt flow interface lies in relatively large sample consumption of few decade microlitres which is more than the volume required for conventional CE. Further drawback in interface design is the limitation associated with bias effects inherent
In electrokinetic injections.
To overcome this bias an interface based on hydrodynamic injection in which the carrier flowing out of the interface was controlled by a pinch valve. When the sample plug in the carrier passed the capillary inlet in the FI-CE interface, with high voltage supply disconnected, the pinch valve was shut off for a defined period of time (usually0.1 – 1 s), during which a fraction of the sample was forced into the capillary under the developed pressure. High voltage was resumed across the separation capillary after the injection, and separation was initiated. With two programmable time relays, one controlling the pinch valve and the other the voltage supply, synchronously with an injection valve, repetitive sample injections during the course of one electrophoretic run was achieved. However, this created hydrodynamic flows within the capillary which deteriorated the separation efficiency to some extent.
A bias-free split-flow sample introduction interface for FI-CE based on introducing the sample into the capillary by electro osmotioc flow traction instead of electrophoretic migration of analytes. A Nafion joint, which only allowed ions to penetrate, was implemented at a capillary fracture about 2 cm downstream of the capillary inlet. The joint was immersed in a buffer solution contained in a plastic vial in which a platinum electrode was inserted. The capillary inlrt was threaded through the bottom of the vial, and inserted into the conical flow-cell through which the carrier and injected sample were transported. The complete FI-CE system is shown schematically (Fig. 7 & 8).

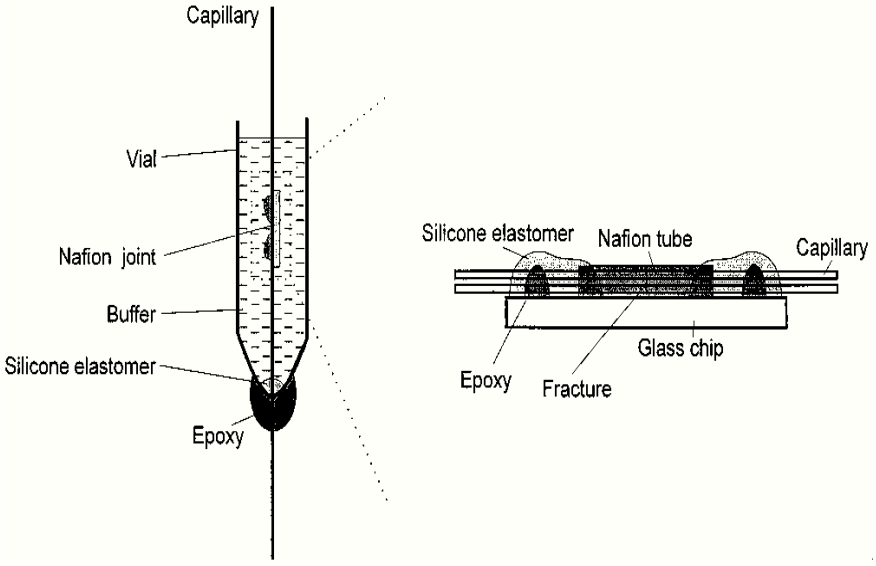


Fig. 7: Structure of the Nafion joint

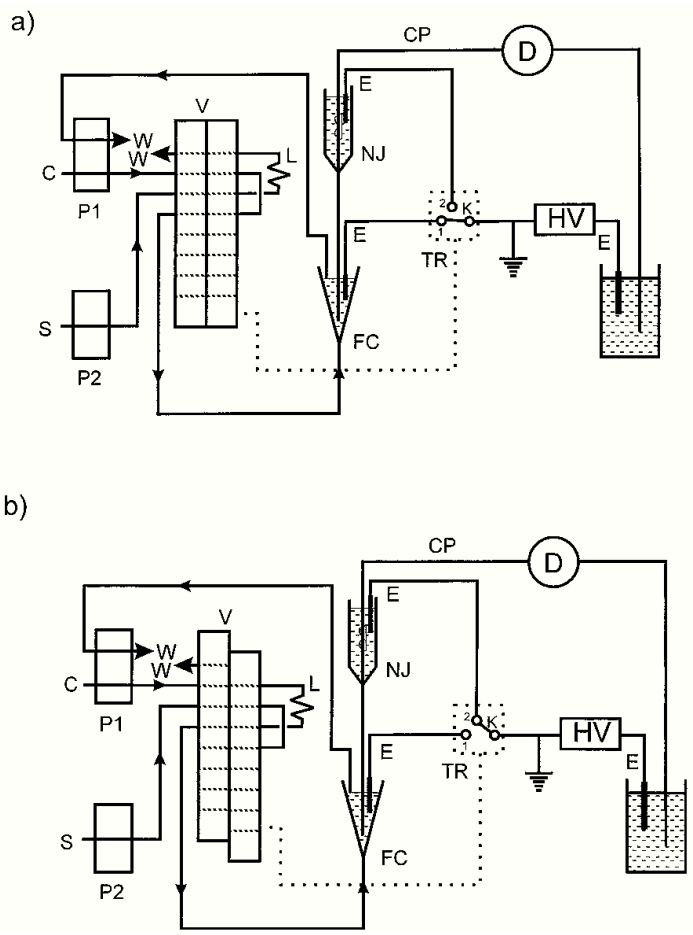


Fig. 8: The FI-CE system with EOF traction injection. (a) Fill position; (b) injection position P1, P2, peristaltic pumps; V, injection valve; L, sample loop; C, carrier (buffer), S, sample; W, waste; CP, separation capillary; E, platinum electrode; K, microswitch; FC, flow-cell; NJ, Nafion joint; HV, high voltage supply; D, detector; R, buffer reservoir; TR, time relay.

When a sample plug reached the flow-cell, the electrode in the Nafion joint vial was automatically connected to the high-voltage supply, and the electro-osmotic flow generated by the voltage applied across the capillary fracture and its outlet drew into its inlet a fraction of the sample plug flowing pass the inlet. Since electrical fields were almost absent in the split-flow interface, bias effects owing to electromigration of the analytes were avoided. After the sample zone had passed the interface, the high-voltage supply was applied across the inlet and outlet of the capillary and electrophoretic separation was initiated. With this arrangement the peak-area ratios of two model compounds, dimethyl sulfoxide and benzoic acid, obtained with gravity injection. The FI-CE system with a bias-free split-flow interface was applied to the separation and the determination of caffeine, theobromine and theophylline in various beverage samples with satisfactory recoveries in 92-107% range.

DEVELOPMENTS IN FI-CE

Micro-chip Based FI-CE System

A micro-volume sequential injections (SI) sample-injection system is employed inorder to further minimize the injected sample volume.An H-configuration arrangement was adopted in this case to accommodate the split-flow interface and short separation cspillsry on a single 20x70x1 mm glass chip. With short separation capillary of 60 mm the continuous delivery of microliter samples by a suitable carrier was shown to be feasible at throughputs of 40-60 per hour with less than 3% carryover between neighbouring samples (Fig. 9).

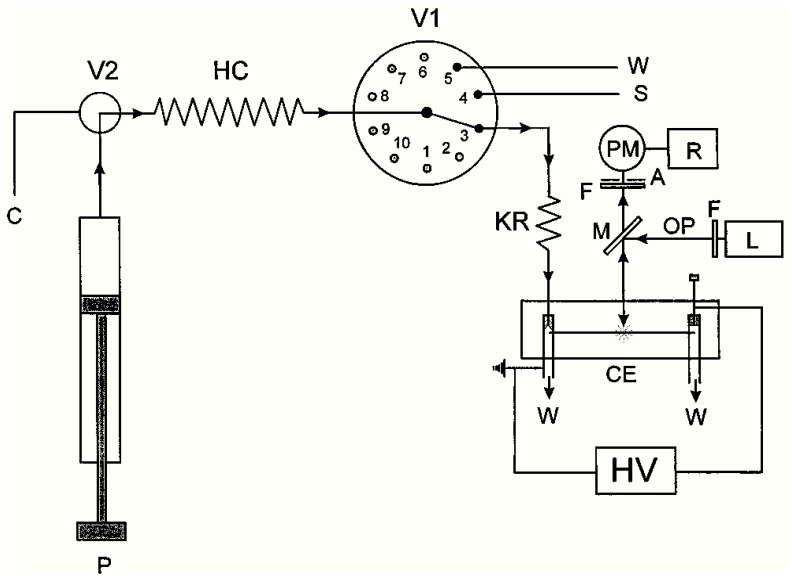


Fig. 9: Schematic diagram of the SI-sample introduction microfluidic CE system. P, syringe pump; V1, multi-position selector valve; V2, two-way valve; HC, holding coil; C, carrier (buffered working electrolyte); S, sample; W, wastes; KR knotted reactor; CE, microfluidic CE system; HV, high voltage power supply; L, laser source; M, dichroic mirror; OP, optical fiber; F, filters; A, pinhole aperture; PM, photomultiplier; R, chart recorder

FI-CE Systems Involving On-line Separation and Pre-concentration

Advantage of combines FI-CE system is the possibility of readily employing well-documented on-line FI sample pretreatment techniques, mainly involving on-line separations and pre-concentrations, to enhance the performance of CE procedures. Various processes are involved in this such as on-line sample filtration, dialysis, gas-diffusion and column sorption. A common feature of such systems is that the sample pretreatment may be operated independently, and in parallel with the CE separation; sample wastes resulting from the pretreatment are not introduced into the separation capillary.

i. **FI-CE System with on-line filtration**
On-line filtration can be readily incorporated in the combined FI-CE system for monitoring a drug dissolution process by incorporating a 75 sq.mm membrane filter at the tip of the sampling probe of the injection valve, a fully automated dissolution testing system produced for multi-component monitoring, capable of a high-resolution dissolution process.

ii. **FI-CE System with on-line dialysis**
The inner surface of the capillary tends to absorb bio-macromolecules in biological samples, leading to changes in the surface properties, and hence the electro-osmotic flow. Interfering macromolecular constituents may be separated by dialysis, which is similar to filtration.

iii. **FI-CE System with on-line gas-diffusion**
On-line gas diffusion coupled to a FI-CE system for separating volatile analytes from complicated sample matrices. The gas diffusion process usually requires conversion of ionic analytes into their respective gaseous species, which can penetrate a semi-permeable membrane. The separated analytes species are then trapped in the acceptor phase by conversion of the gaseous species into ions.

iv. **FI-CE System with on-line solid phase extraction pre-concentrations**
FI on-line ion-exchange and solid phase extraction (SPE) using mini-columns have proved to be efficient means for pre-concentration purposes applicable to a wide range of analytes. On-line column pre-concentration system for FI-CE based on sorption extraction using micro-column packed with C18, which was incorporated in a multi-channel injector valve. During sample loading, the micro-column was switched out of connection with the split-flow interface. The analyte was sorbed on the column while sample effluent was directed to waste, so that no sample matrix was allowed to reach the CE system (Fig. 10).

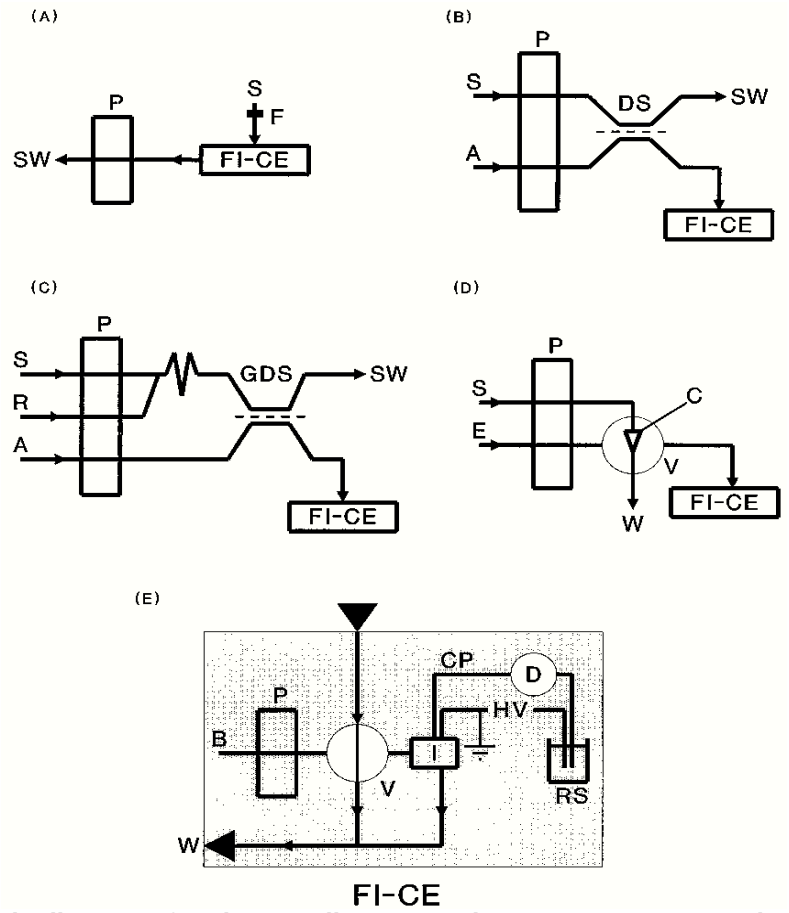


Fig. 10: Schematic diagram of various on-line separation systems connected to FI-CE. (A), on-line filtration mode; B) on-line dialysis mode; (C) on-line gas diffusion mode; (D) on-line column sorption mode; (E) FI-CE basic system. P, pump, S, sample; SW, sample waste; FI-CE, combined FI-CE system; F, membrane filter; DS, on-line dialysis membrane separator; A, acceptor stream; R, reagent for generation of gas phase; GDS; on-line gas diffusion membrane separator; C, sorption column; E, eluent; V, injector valve; W, waste; B, buffer/carrier; I, interfacing flow-cell (see Fig.1); CP, separation capillary; HV, high voltage supply; RS, outflow electrolyte reservoir; D, detector

APPLICATIONS

The coupling of CE with FI has resulted in enhancedseparation techniques with advanced sample introduction/pretreatment capabilities of a wide range of analytes. Table **1** gives specific applications and quantitativedetails in selected FI-CE systems in the last five years.

Biological/Food Samples

Over the past two decades CE has become a musttechnique in many biological laboratories and, in some cases,is the technique of choice when analyzing small quantities of materials. Because of the versatility afforded by the CEformat, it was a natural choice for coupling to otheranalytical techniques. Mass spectrometry (MS) and nuclearmagnetic resonance (NMR) are but two techniques, thatwhen coupled to CE, have yielded critical data on biologicalspecies and their physicochemical properties. Thisexamination of biomaterials has continued with the recentcoupling of FI and CE. Simonet *et al*. coupled FI to a commercial CEinstrument with indirect photometric detection to examine myo-inositol phosphates in food samples. The FI systemserved to clean-up and preconcentrate myo-inositol phosphates while the commercial instrument allowed forincreased selectivity and programmability. The lower limit of detection for myo-inositol phosphate ranged from 11-26µM with a coefficient of variation of 3.9-5.0%. The method determined the content of myo-inositol hexakisphosphate innuts to be 2-3 times higher than that found in legumes.

Kubán*et al*. showed that small inorganic cations in proteinaceous samples could be directly determined using FI-CE. Using a buffer containing 4-aminopyridine (PAP) and cetyltrimethylammonium bromide (CTAB) at pH 4.5potassium, sodium calcium, magnesium, and lithium couldbe detected in milk and blood plasma samples.

Electropherograms of 20 consecutive direct injections ofmilk and blood samples are shown in (Fig. 11).Wang *et al*. described a low cost FI-CE system with fluorometric detection using light emitting diodes (LED).Continuous introduction of 30 µL samples containing fluorescein isothiocyanate (FITC)-labeled amino acids was conducted with a throughput rate of 144 samples/hour andgood precision (3.2% RSD). Baseline resolution wasachieved for FITC-arginine, phenylalanine, glycine, and FITC in sodium tetraborate buffer (pH 9.5). The limits of detection of the amino acids was 1.3 µM (FITC-arginine) and 1.3 µM (FITC-phenylalanine and glycine) correspondingto 1.6 and 2.3 fmol, respectively. Recently, a rapid and accurate method for separating and determining the bis-alkoloidsaloperine (ALP), sophordine (SRI), matrine (MT), and oxymatrine (OMT) was developed by combining FI and CE. Although the authors called their instrument set-up FI-micro-fluidic CE, separation ofanalytes was still conducted in a capillary format and, hence,this system cannot be considered a true "lab-on-a-chip"device. In this work an H-channel structure was produced and a capillary was placed across two vertical side arm tubes placed on either side of the channel. Complete separation ofthe four bis-alkaloids was readily achieved in 50 mm boratebuffer (pH 8.8) at 0.6-1.8 kV.A novel electrode design in FI-CE was recently described by Samskog*et al*.. Here, the electrode consisted of a conductive on-column graphite/polyimide coating immobilized onto the CE column inlet. The on-line FI-CE system was coupled to electro-spray ionization (ESI)-time offlight (TOF)-MS detection. The authors demonstrated separation of three peptides (methionine-enkephalin, neurotensin, and substance P) in an electrolyte consisting of50% formic acid/ammonia and 50% acetonitrile. This electrode configuration shows a high mechanical and electrochemical stability and performance comparable to normal platinum electrodes.

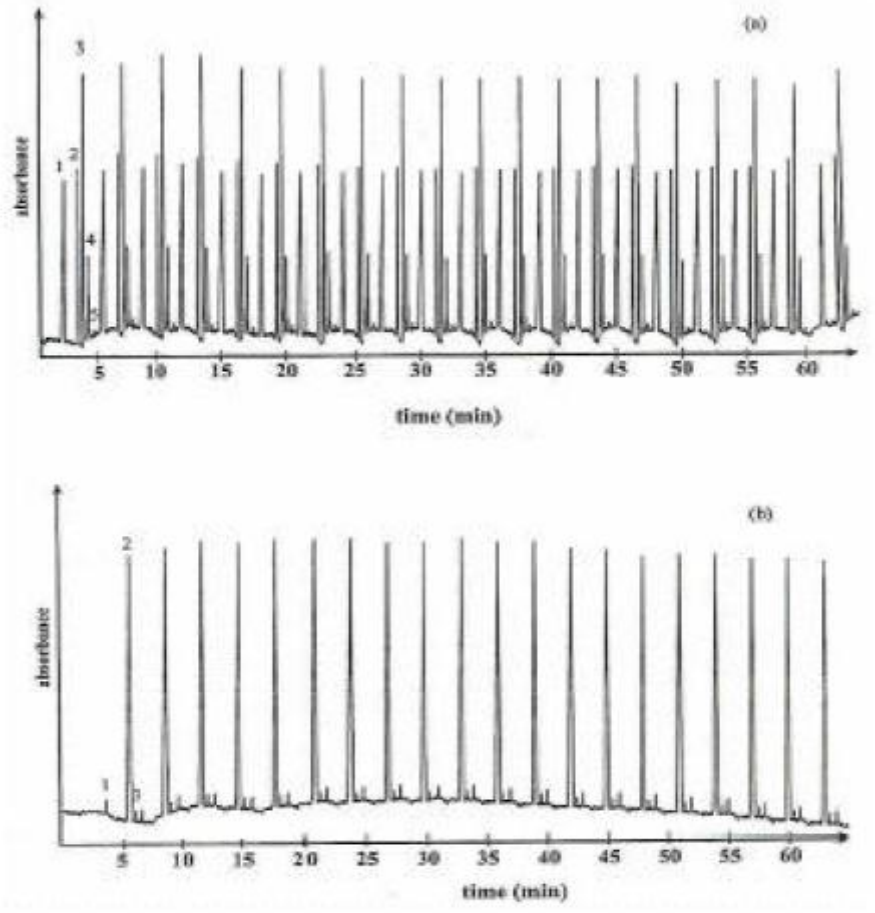


Fig. 11: Electropherograms of 20 consecutive direct injections of milk (a) and blood samples (b) (from reference with permission)

Table 1. Applications and quantitative details of advances in selected FI-CE systems in the last five years

Application	Measured Species	Detection method	LOD (unit as reported)	Notes	Reference
Biological/Food Samples	Sucrose, glucose	Amperometric detection	2 μM (sucrose) 1 μM (glucose)	Microchip-based CE system coupled to conventional FI technology.	[23]
Biological/Food Samples	Myo-inositol phosphates	Indirect photometric at 510 nm	11-26 μmol L^{-1}	System included a micro-column anionic exchange resin for solid phase extraction of myo-inositol phosphates.	[40]
Biological/Food Samples	Arginine, phenylalanine, glycine	Fluorometric detection	1.3 μM (arginine) 1.9 μM (phenylalanine & glycine)	Miniaturized liquid core waveguide-CE system with FI introduction.	[42]
Biological/Food Samples	Aloperine, sophoridine, matrine , oxymatrine	UV detection at 215 nm	3.28 μg ml^{-1} (ALP) 2.13 μg ml^{-1} (SRI) 2.23 μg ml^{-1} (MT) 3.11 μg ml^{-1} (OMT)	Combination FI with microfluidic capillary electrophoresis.	[43]
Biological/Food Samples	Peptide samples	Amperometric detection	Not reported	On-column polymer-imbedded graphite inlet electrode for FI-CE in a poly(dimethylsiloxane) interface.	[44]
Biological/Food Samples	Proline, valine, phenylalanine	Electrogenerated chemiluminescence	1.2 μM (proline) 50 μM (valine) 25 μM (phenylalanine)	System developed on a chip platform to provide easy FI sample introduction and ECL detection.	[45]
Environmental	Phenol pollutants	UV detection at 210 nm	2.12 ng mL^{-1} (PCP) 1.21 ng mL^{-1} (2,4,6-TCP) 1.06 ng mL^{-1} (2-NP) 4.52 ng mL^{-1} (2,4-DMP)	On-line flow stacking in a FI-CE system.	[47]
Environmental	Copper, cobalt	Chemiluminescence detection	1.2 x 10^{-8} mol dm^{-3} (Co^{2+}) 2.3 x 10^{-8} mol dm^{-3} (Cu^{2+})	FI-CE with chemiluminescence on a chip platform.	[48]
Environmental	Inorganic ions	Contactless conductivity detection	Range: 20-200 μg L^{-1} for all ions including: Cl^-, NO_3^-, SO_4^-,HPO_4^{2-} K^+, Ca^{2+}, Na^+, Mg^{2+}	On-site determination with an automated FI-CE method.	[49]

(Table 1). Contd.....

Environmental	Nitrate, sulfate	UV detection at 372 nm	124 ppb (nitrate) 77 ppb (sulfate)	Microsequential injection coupled to CE using electrokinetic injection.	[50]
Environmental	Lead, cadmium, cobalt, nickel, zinc	UV-Vis detection at 570 nm	2.0 x 10^{-6} mol dm^{-3} (Pb^{2+}) 8.0 x 10^{-6} mol dm^{-3} (Cd^{2+}) 8.0 x 10^{-6} mol dm^{-3} (Co^{2+}) 4.0 x 10^{-6} mol dm^{-3} (Ni^{2+}) 4.0 x 10^{-6} mol dm^{-3} (Zn^{2+})	Separation of heavy metal ions by FI-CE using xylenol orange.	[51]
Environmental	Se(IV), Se(VI)	Contactless conductivity detection	190 μg L^{-1} (Se(IV)) 7.5 μg L^{-1} (Se(VI))	FI-CE system with contactless conductivity detection.	[52]
Environmental	Nitrate, nitrite	UV detection	10 ng ml^{-1}	On-line ion-exchange preconcentration.	[53]
Medicinal/ Pharmaceuticals	Artemisinin	UV detection at 292 nm	5.93 μg mL^{-1}	On-line conversion of anti-malarial artemisinin using FI-CE. Artemisinin converted to a strongly UV-absorbing compound by treating it with NaOH.	[54]
Medicinal/ Pharmaceuticals	Sulphamethozazole Trimethoprim	UV-Visible detection at 254 nm	1 mg L^{-1} 0.5 mg L^{-1}	Miniaturized FI-CE system with ultraviolet photometric detection incorporating a modified falling-drop interface.	[56]
Medicinal/ Pharmaceuticals	Aspirin	UV detection at 214 nm	1.0 μg mL^{-1}	Splitting-flow interface used for on-line electrokinetic injection.	[57]
Medicinal/ Pharmaceuticals	Aspirin	UV detection at 254 nm	3.71 μg mL^{-1}	Acetylsalicylic acid (ASA) converted to salicylic acid (SA) by on-line alkaline hydrolysis with ASA indirectly quantified by determining the hydrolysis product of SA.	[58]
Medicinal/ Pharmaceuticals	Aspartic acid	UV detection at 214 nm	0.12 μg mL^{-1} (L-Asp) 0.11 μg mL^{-1} (D-Asp)	Separation and determination of aspartic acid enantiomers by on-line derivatization with *o*-phthalaldehyde and mercaptoethanol.	[59]
Medicinal/ Pharmaceuticals	Trimethoprim Sulfamethoxazole	UV detection at 214 nm	0.31 μg mL^{-1} (TMP) 0.70 μg mL^{-1} (SMZ)	Microfluidic CE combined with FI. Continuous on-line concentration based on dynamic pH junction.	[60]

Environmental

Timerbaev*et al*. extensively reviewed the growingacceptance of using CE technology for environmentalanalysis. This trend has continued over the past five yearswith major improvements in sample introduction andpre-concentration by incorporating FI technology. Kubán *et al*., for example, developed a novel FI-CE on-line flowstacking system for use in the detection of eleven USEnvironmental Protection Agency priority pollutants. Thisunique system (Fig. **5**) continuously delivered lowconcentrations of phenols dissolved in distilled water to thecapillary by means of a peristaltic pump. This innovativedelivery system, one in which the sample temporarilyreplaced the electrolyte solution forming a water pre-plug,allowed optimized stacking conditions and achieved a 2000-fold pre-concentration of phenolic pollutants.

Huang *et al* enhanced the monitoring capabilities ofFI-CE by incorporating chemiluminescence (CL) detectionon a chip platform for the determination of Co2+ and Cu2+. Afalling-drop interface was applied for FI split-flow sampleintroduction and the CE microchipapproach furtherenhanced sample throughput efforts. The performance of thesystem was studied using the luminal-hydrogen peroxide CLreaction and achieved overall detection limits of 1.25 x 10-8and 2.3 x 10-6 mol dm-3 for Co2+ and Cu2+, respectively.

More recent advances by Kubán*et al*. paved the wayfor a fully automated field-based FI-CE system for thedetermination of inorganic ions (e.g., Cl-, NO3-, SO4-, K+,

Ca2+, Na+, Mg2+). This system employed dual injection atopposite ends of the separation capillary which allowedconcurrent anion and cation determinations at 10 minintervals with detection limits in the range of 20-200 µg L-1for all ions.

PHARMACEUTICAL APPLICATIONS

Chiral separations

The performance of the FI-CE combined system was tested by applying it to the chiral separation of intermediate enantiomers in chloramphenicol synthesis. Cyclodextrin and derivatives, used as chiral selectors, were added to the separation buffer, which also functioned as the FI carrier. Baseline resolution of enantiomers of the rac-threo bases 2-amino-1-(*p*-nitrophenyl-1,3-propanediol) was achieved with a theoretical plate number of 1.2x10, and a sample throughput of 15h, which was higher than conventional than bya factor of five. The peak-height reproducibility was 2 – 3% RSD, which was also significantly better than that obtained by conventional CE (7 – 10% RSD).

Continuous monitoring of multi-components in drug dissolution process

The high sampling frequencies of FI-CE systems make it possible to use CE in process analysis for the simultaneous monitoring of multi-analytes. The on-line separation capabilities are extremely useful in dealing with process samples with complicated matrices. Such potentials were demonstrated by applying the on-line filtration FI-CE system described previously regarding drug dissolution studies.

Determination of pseudoephedrine in plasma samples with on- line separation and pre-concentration

The potentials of FI-CE in providing sensitive and rapid methods for the analysis of bio-samples with complicated matrices were recently demonstrated by a determination of pseudoephedrine in human plasma.

REFERENCES

1. Landers JP. Handbook of Capillary Electrophoresis, CRC Press LLC: Boca Raton, FL, 1997.
2. Flurer CL. Electrophoresis. 2001;22:4249.
3. Thormann W, Molteni S, Caslavska J and Schmutz A. Electrophoresis. 1994;15:3.
4. Dacaronnet A, Cheregi M, Calatayud JM, Garcia Mateo JV and Aboul EH. Crit Rev Anal Chem. 2001;31:191.
5. Wang J and Hansen EH. Trends Anal Chem. 2003;22:836.
6. Nan J, Jiang Y and Yan XP. J Anal At Spectrom. 2003;18:946.
7. Kubán P, Berg M, García C and Karlberg B. J Chromatogr A. 2001;912:163.
8. Cao XD, Fang Q and Fang ZL. Anal Chim Acta. 2004;513:473.
9. Chen HL, Fan LY, Hu ZD, Zhao ZF and Hooper M. J Sep Sci. 2003;26:863.
10. Terabe S, Otsuka K, Ichikawa K, Tsuchiya A and Ando T. Anal Chem. 1984;56:111.
11. Tagliaro F, Smith FP, de Battisti Z, Manetto G and Marigo M. J Chromatogr B. 1997;689:261.
12. Novotny MV. J Chromatogr B. 1997;689:55.
13. Balchunas AT and Sepaniak MJ. Anal Chem. 1987;59:1466.

14. Otsuka K, Higashimori M, Koike R, Karahuha K, Okada Y and Terabe S. Electrophoresis. 1994:15.
15. Palmer CP and Terabe S. J Microcolumn Separ. 1996;8:115.
16. Terabe S, Ozaki H and Tanaka Y. J Chin Chem Soc. 1994;41:251.
17. Von Heeren F, Verpoorte E, Manz A and Thormann W. Anal Chem. 1996;68:2044.