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Rapid Determination of Carbohydrates in Heroin Drug Seizures Using Capillary Electrophoresis with Short-End Injection*

ABSTRACT: A simple and rapid method for the analysis of carbohydrates in heroin samples by capillary electrophoresis utilizing a borate complexation method is described. Separations were performed using an uncoated fused silica capillary, 50 cm × 50 μm I.D. × 360 μm O.D. with an effective separation length of 9 cm. The system was run at 60°C with an applied voltage of −8 kilovolts. Injection of each sample was for 1 sec at −50 mbar. UV detection was employed with the wavelength set at 195 nm. The background electrolyte consisted of 65 mM borate, pH 12.0. Samples and standards were prepared in the run buffer containing 2 mg/mL of mannose as an internal standard. Under these conditions a test mixture containing glucose, sucrose, lactose, mannitol and mannose as an internal standard was resolved within 5 min. The method was used to determine the concentration of carbohydrates in heroin seizure samples and synthetic heroin samples. The results were in good agreement with the reported values.

KEYWORDS: forensic science, capillary electrophoresis, carbohydrates, heroin seizures, borate, short-end injection

Illicitly produced heroin is never pure, it contains numerous manufacturing by-products, adulterants and diluents. Drug characterization or impurity profiling can establish chemical links between samples from different seizures. This information obtained from an illicit drug sample may be used for evidential purposes or for criminal intelligence to identify drug trafficking patterns and distribution (1,2). Diluents, often carbohydrates, are substances that are added to illicit heroin to expand bulk and increase profits, and usually form a significant part of the drug sample. In a previous paper, we reported the analysis of caffeine and paracetamol in heroin seizures (3). In this paper, we describe the application of capillary electrophoresis to the determination of carbohydrate diluents of illicitly produced heroin in Australia. The most commonly found diluents in illicitly produced heroin samples seized in Victoria and South Australia are glucose, sucrose, lactose, mannitol, caffeine and paracetamol. Inositol, a diluent commonly found in illicitly produced heroin samples in the USA has not been found in heroin samples within Victoria and South Australia, and was not included in this investigation.

The analysis of carbohydrates has found application in foliage analysis (4), urine analysis to diagnose disorders of carbohydrate metabolism (5), and most predominately in food and beverage analysis (6–10). High resolution analytical methodologies for carbohydrate separations include gas chromatography (11–13) and high performance liquid chromatography (9,13,14). Gas chromatography provides good sensitivity and separation efficiency although many carbohydrates are not volatile, are heat-labile or require derivatization (15). High performance liquid chromatography is widely employed for the analysis of carbohydrates, but there is room for improvement in separation efficiency, column equilibrium requirements and analysis costs in respect to solvent consumption and stationary phase material (6,15). The main modes of detection for high performance liquid chromatography include electrochemical (16), refractive index (17), fluorescence (18), mass spectrometry (19) and UV detection (10,20,21).

The potential of capillary electrophoresis to provide rapid and efficient separations for forensic analysis was first demonstrated by Weinberger and Lurie, who applied it to the analysis of a wide range of illicit drugs (22). Since that time a large number of papers have discussed the wider application of capillary electrophoresis to forensic science (23–48).

There are two major obstacles that hinder the use of capillary electrophoresis in carbohydrate analysis. The lack of charge results in difficulties for electrophoretic separation, and the absence of chromophoric groups lead to problems with absorbance detection. The latter issue can be addressed by utilising indirect detection, and this has been used widely (6,8,15,20, 49,50). Ishii et al. (51) determined sugars using capillary electrophoresis with indirect UV detection in illicit cocaine samples. This was achieved using a 85 cm × 75 μm i.d. capillary, an applied voltage of −27 kV and an electrolyte containing 15% (v/v) acetonitrile in 8 mM Na_2HPO_4/5 mM phthalate/10 mM cetyltrimethylammonium bromide (CTAB), pH 12.5, 15°C, 310 nm. When applied specifically to the analysis of illicit cocaine samples, this method was able to resolve the components within 25 min.

Hoffstetter-Kuhn et al. (52) observed a 2–20 fold increase in UV absorbance of underivatized carbohydrates at 195 nm by using a 50 mM borate background electrolyte, pH 9.3 at 60°C (52). This increase in absorbance is due to the borate complexation shifting the

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equilibrium between carbonyl and annular sugar forms toward the carbonyl form (52). Under basic conditions, borate forms a complex with the vicinal hydroxyl groups of a carbohydrate, allowing neutral carbohydrates to acquire a negative charge and to migrate in an electric field. Furthermore, the stability of the sugar-borate complexes depends on the configuration of the carbohydrates, the number of hydroxyl groups, the amount in an open chain form and temperature. High temperatures were preferable for the separation of carbohydrates as the resolution and efficiency of the separations were improved by performing electrophoresis at 60°C, however analysis time was 20 min.

Soga (53) separated sugar-borate complexes by reversing both the polarity to reduce analysis time and the electro-osmotic flow with the addition of CTAB to the buffer. This was achieved using a 64.5 cm × 50 μm i.d (effective length 56 cm) capillary, an applied voltage of −310 V/cm and an electrolyte containing 60 mM tetraborate, pH 9.3, 60°C, 191 nm. When applied specifically to the analysis of orange juice, honey and wine samples, this method was able to resolve the components within 6 min.

In a previous paper, we demonstrated the utility of using short end injection to provide rapid separations for the determination of heroin in heroin seizures (3). In capillary electrophoresis, injection is conventionally performed at the anode with detection at the cathode end of the capillary. If the normal polarity of the electrodes are reversed, such that the anode is at the detector (short) end of the capillary, samples and standards can then be introduced at the detector end, thus yielding a far shorter effective capillary length (54–58). This technique of short-end injection allows for the reduction in analysis time, voltage applied, and a decrease in buffer depletion effects. (54,59). In this current paper, we describe a method to rapidly separate carbohydrates in heroin drug seizure samples using capillary electrophoresis with borate complexation and short-end injection.

Materials and Methods

Chemicals and Reagents

Solutions were prepared with de-ionised water from a Millipore Milli-Q system (Bedford, MA). The heroin standards (99% + purity) were synthesized at Deakin University according to the U.S. Treasury Department method (60). D-glucose, sucrose, lactose, mannitol, D(+)-mannose and caffeine were from BDH (Poole, England). Sodium tetraborate was purchased from Aldrich (Milwaukee). Three heroin samples were provided by the Victoria Police Forensic Services Centre, Australia. All the buffers and samples were filtered with a 0.45 μm membrane filter prior to injection.

Instrumentation

Capillary electrophoresis was performed using a Hewlett Packard HP^{3D} System equipped with a diode array detector. An uncoated fused silica capillary, 50 cm × 50 μm I.D. × 360 μm O.D. with an effective separation length of 9 cm was used for all the experiments. The capillary was conditioned before use by successively washing for 30 min with 0.1 M sodium hydroxide, 15 minutes with deionised water, and 30 min with the run buffer. A 1 min pre wash with the run buffer was performed prior to each injection as was a 1 min post run wash with 0.1 M sodium hydroxide. The running buffer was changed every ten injections.

Sample Preparation

All standards, synthetic and forensic samples were prepared in the run buffer containing 2 mg mL^{-1} mannose as an internal standard. Synthetic samples were prepared by weighing out a know quantity of carbohydrate and heroin. Forensic samples used for analyses were made up as 1 mg mL^{-1} samples.

Electrophoretic Conditions

The run buffer consisted of 65 mM sodium borate, pH 12.0. The system was run at 60°C with an applied voltage of −8 kilovolts, the current did not exceed 100 μA. Injection of each sample was for 1 sec at −50 mbar with a five minute run time. UV detection was employed with the wavelength set at 195 nm. All analyses were carried out in a temperature-controlled room, set at 20°C.

Results and Discussion

Method Development

The initial conditions used for the background electrolyte were that by Hoffstetter-Kuhn et al. (52) and applied to short end injection. Unfortunately, lactose and sucrose co-migrated, and the peak shapes observed for all carbohydrates were poor.

Migration times, resolution and absorbance for a test mixture of carbohydrates with varying borate concentrations were examined. Increasing the borate concentration from 25 mM to 85 mM, in 10 mM increments, improved resolution and detector response, however peak shape deteriorated. However, at elevated buffer concentrations, the generated current was very high, affecting the separation performance. As a result, a final borate concentration of 65 mM was employed as the best compromise between detector response, resolution and current.

The effect of pH was investigated between pH 10.5 to 12.5, in increment increases of 0.5 pH units. Operating at a higher pH improved detector response whereas a response from glucose and mannitol were not observed while operating at pH 10.5. It was found that pH 12.0 was optimal for the separation of the test mixture. Operation in basic conditions ensures the ionization of the weakly acidic hydroxyl groups of the carbohydrates, allowing for complexation in solution with borate ions, and migration of these complexes as anions.

The applied voltage, which affects the speed and quality of a separation (61) was also investigated. A voltage of −8 kV was found to provide an optimal separation, above which further increases in voltage resulted in a current in excess of 100 μA, which would adversely affect the separation performance.

It has been reported that temperature considerably affects resolution, efficiency and analysis time of carbohydrates when using borate complexation (52). This variable was investigated between 15°C to 60°C using a 65 mM tetraborate buffer, pH 12.0. Glucose and mannitol were not fully resolved below a temperature of 25°C, peak shapes broadened and furthermore the baseline was unstable. Both resolution and baseline improved as the temperature was increased from 15°C to 60°C. The use of a higher temperature also resulted in a shorter analysis time and provided increased sensitivity. This increased sensitivity can firstly be attributed to the faster complexation reaction equilibrium attained at higher temperatures, resulting in sharper peaks and the amount of carbohydrates present in an open chain form (52). Secondly, an increase in sensitivity was observed due to the increased injection volumes as a result of a decrease in run buffer viscosity. Hence, temperature was fixed at 60°C for rapid and baseline separation of all carbohydrates.

The final background electrolyte conditions were 65 mM sodium borate, pH 12.0, 60°C. These conditions were used for all subsequent experiments. A separation of four carbohydrates in a test mixture was attained within five minutes and migration was in the

order of sucrose, lactose, mannitol and glucose, as expected. In conventional capillary electrophoresis, i.e. migration is from the anode to cathode, solute migration is based on the charge to mass ratio of the species. Therefore monosaccharides would migrate before disaccharides in the order of glucose, mannitol, lactose and sucrose, as observed by Soga (53). As the polarities are reversed in short-end injection, so is the order of migration for the carbohydrates, hence the expected order of migration.

The importance of using an internal standard in quantitative analysis was discussed in our previous paper (3). A range of potential internal standards were also investigated and mannose was selected as it dissolved in the background electrolyte, did not co-migrate with the carbohydrates in a test mixture and provided satisfactory quantitative results.

Analysis of Cut Heroin Seizures

A series of calibrations for glucose, sucrose, lactose and mannitol over the linearity range of 0.1 to 2.5 mg mL^{-1} for each analyte was performed. The analytical figures of merit are presented in Table 1. The limits of detection for all carbohydrates were between 0.1 to 0.5 mg mL^{-1} at a signal-to-noise ratio of three.

Good reproducibility was obtained when the capillary was flushed with buffer prior to analysis for one minute, and a post separation washing of the capillary with 0.1 M sodium hydroxide was also employed for one minute. Increasing the sodium hydroxide wash period resulted in poor reproducibility. The background electrolyte was also replaced every ten injections to avoid the affects of buffer depletion (62). The migration time and peak area reproducibility for a 1.0 mg mL^{-1} test mixture is shown in Table 2. Satisfactory migration time and peak area reproducibilities for intra-day and between-day were also obtained.

Three heroin seizures and six synthetic samples were diluted with the background electrolyte containing the internal standard and the carbohydrate content of each was determined. An electropherogram of a separation of a test mixture containing the internal standard is presented in Fig. 1. An electropherogram of a synthetic and seized heroin sample are presented in Figs. 2 and 3 respectively. The quantification of carbohydrates in heroin samples incorporating mannose as an internal standard is shown in Table 3. The results obtained were in good agreement with the reported values of the heroin seizures and the composition of the synthetic seizures. As this method is a screening technique for the determination of carbohydrates, the poor peak shape observed for heroin, as can be seen in Figs. 2 and 3, is not an issue. It would appear from its peak shape that heroin is migrating as a charged species, possibly as a

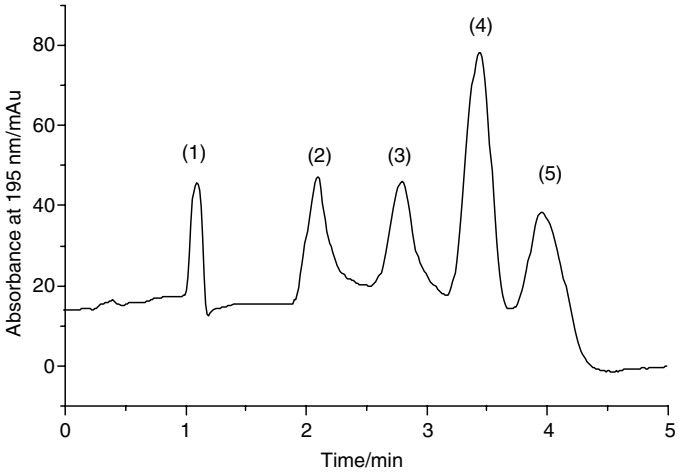

FIG. 1—*Electropherogram showing the separation of a test mixture containing: (1) sucrose, (2) lactose, (3) mannose (ISTD), (4) mannitol and (5) glucose. UV absorbance at 195 nm, uncoated fused silica capillary 50 cm × 50 μm I.D. × 360 μm O.D., effective separation length 9 cm, background electrolyte: 65 mM sodium borate pH 12.0, 60°C, −8 kV, hydrodynamic injection: 1 second at −50 mbar.*

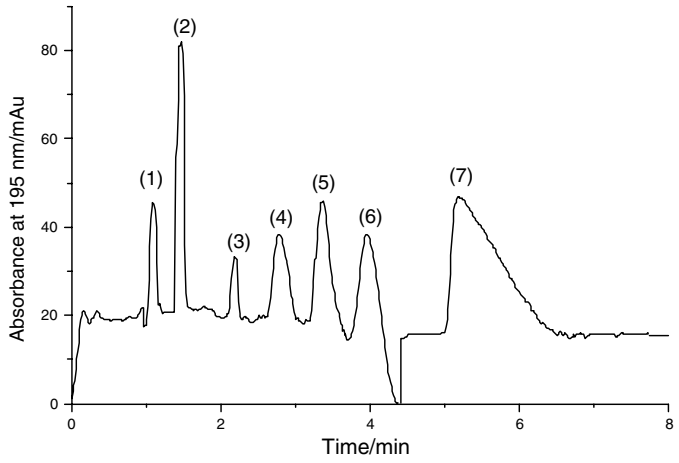

FIG. 2—*Electropherogram showing the separation of a synthetic heroin sample containing: (1) sucrose, (2) caffeine, (3) lactose, (4) mannose (ISTD), (5) mannitol, (6) glucose and (7) heroin. UV absorbance at 195 nm, uncoated fused silica capillary 50 cm × 50 μm I.D. × 360 μm O.D., effective separation length 9 cm, background electrolyte: 65 mM sodium borate, pH 12.0, 60°C, −8 kV, hydrodynamic injection: 1 second at −50 mbar.*

TABLE 1—*Analytical figures of merit.*

Analyte	Calibration Function*	Correlation Coefficient (r^2)	Limit of Detection (mg mL^{-1})
Sucrose	y = 0.69x – 0.456	0.9996	0.5
Lactose	y = 0.85x – 0.173	0.9992	0.25
Mannitol	y = 3.70x – 0.671	0.9996	0.1
Glucose	y = 1.87x – 0.371	0.9997	0.25

* y = peak area (mAu), x = concentration (M).

TABLE 2—*Migration time and peak area reproducibility for a 1.0 mg mL^{-1} test mixture for a run buffer consisting of 65 mM borate, pH 12.0. RSD calculated from 10 replicate injections.*

Analyte	Migration Time (mins.)	RSD of Migration Time for Intra-Day (%)	RSD of Migration Time for between-Day (%)	RSD of Peak Area for Intra-Day (%)	RSD of Peak Area for between-Day (%)
Sucrose	1.10	0.2	0.8	1.1	1.4
Lactose	2.12	0.3	1.0	1.0	2.7
Mannitol	3.46	0.5	0.8	2.4	2.1
Glucose	4.00	0.6	0.9	1.1	2.9

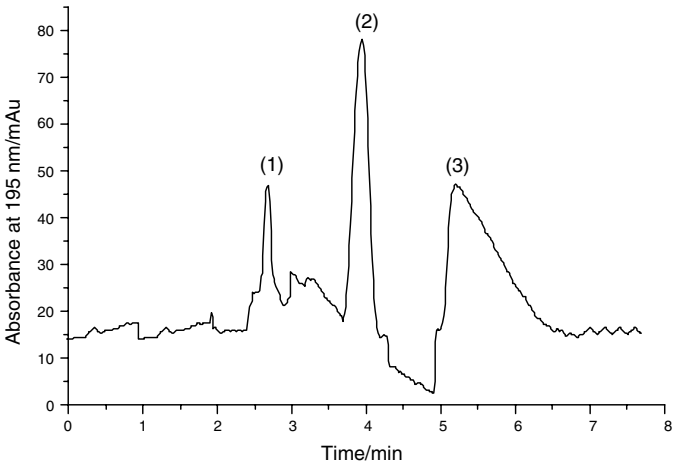

FIG. 3—*Electropherogram showing the separation of a heroin seizure sample containing (1) mannose (ISTD), (2) glucose and (3) heroin. UV absorbance at 195 nm, uncoated fused silica capillary 50 cm × 50 μm I.D. × 360 μm O.D., effective separation length 9 cm, background electrolyte: 65 mM sodium borate, pH 12.0, 60°C, −8 kV, hydrodynamic injection: 1 second at −50 mbar.*

TABLE 3—*Quantification of carbohydrates in heroin seizure samples. CE Conditions: Mannose (internal standard), UV absorbance at 195 nm, uncoated fused silica capillary 50 cm × 50 μm I.D. × 360 μm O.D., effective separation length 9 cm, background electrolyte: 65 mM sodium borate, pH 12.0, 60°C, −8 kV, hydrodynamic injection: 1 second at −50 mbar, n = 2.*

Sample	Analyte	Actual Amount (% by mass)	CE Amount (% by mass)
1*	Glucose	64.9	61.9
2†	Sucrose	59.6	61.8
3*	Sucrose	25.7	24.8
	Mannitol	40.0	39.1
4*	Sucrose	50.0	48.2
	Glucose	29.1	29.3
5†	Sucrose	37.9	36.2
	Lactose	21.4	22.5
	Glucose	15.3	15.8
6†	Sucrose	17.8	18.1
	Lactose	4.3	4.5
	Mannitol	18.5	18.6
	Glucose	20.3	21.2
7†	Glucose	51.9	54.2
8†	Sucrose	23.3	22.2
	Glucose	45.5	47.4
9†	Sucrose	35.3	36.9
	Lactose	25.6	26.8
	Mannitol	20.6	21.5

* = forensic sample, † = synthetic sample.

complex with borate. Zone broadening is also more pronounced at higher capillary temperatures owing to an increase in longitudinal diffusion (63). However, this was not further investigated as a rapid method for heroin has been previously reported (3).

Conclusion

A rapid method for the determination of carbohydrates in heroin seizures by capillary electrophoresis is described. A simple borate complexation method with the addition of an internal standard to the buffer provided satisfactory results for synthetic and seized heroin samples. This paper along with our previous paper (3) demonstrates the utility of the short end technique to rapid forensic analysis. Such an approach has the potential to greatly improve sample throughput. In addition, as in this case, if the underlying method is robust enough, conversion of existing capillary electrophoresis methodology to a short end approach is relatively straightforward.

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References

1. Besacier F, Chaudron-Thozet H. Chemical profiling of illicit heroin samples. Forensic Sci Rev 1999;11(2):105–19.
2. O'Neil PJ, Baker PB, Gough TA. Illicitly imported heroin products: Some physical and chemical features indicative of their origin. J Forensic Sci 1984;29(3):889–902. [PubMed]
3. Anastos N, Lewis SW, Barnett NW, Pearson JR, Kirkbride KP. The rapid analysis of heroin drug seizures using micellar electrokinetic chromatography with short-end injection. J Forensic Sci 2005;50(1):37–42. [PubMed]
4. Warren CR, Adams MA. Capillary electrophoresis for the determination of major amino acids and sugars in foilage: Application to the nitrogen nutrition of sclerophyllous species. J Exp Botany 2000;51(347):1147–57.
5. Jin LJI, Li SFY. Screening of carbohydrates in urine by capillary electrophoresis. Electrophoresis 1999;20:3450–54. [PubMed]
6. Klockow A, Paulus A, Figueiredo V, Amado R, Widmer HM. Determination of carbohydrates in fruit juices by capillary electrophoresis and high performance liquid chromatography. J Chromatogr A 1994;680:187–200.
7. Soga T, Tajima I, Heiger D. Capillary electrophoresis for the determination of forensic anions in adulterated foods and beverages. American Laboratory 2000;32:124–28.
8. Soga T, Serwe M. Determination of carbohydrates in food samples by capillary electrophoresis with indirect UV detection. Food Chemistry 2000;69:339–44.
9. Cabalkova J, Zidkova J, Pribyla L, Chmelik J. Determination of carbohydrates in juices by capillary electrophoresis, high performance liquid chromatography and matrix-assisted laser desorption/ionization-time of flight-mass spectrometry. Electrophoresis 2004;25:487–93. [PubMed]
10. Cortacero-Ramirez S, Segura-Carretero A, Cruces-Blanco C, Hernainz-Bermudez de Castro M, Fernandez-Gutierrez A. Analysis of carbohydrates in beverages by capillary electrophoresis with precolumn derivatization and UV detection. Food Chemistry 2004;87(3):471–76.
11. Miller MD. Determination of excipient sugar diluents in illicit preparations containing heroin by gas chromatography. J Forensic Sci 1972;17:150–63. [PubMed]
12. Chaplin MF. A rapid and sensitive method for the analysis of carbohydrates components in glycoproteins using gas-liquid chromatography. Anal Biochem 1982;123(2):336–41. [PubMed]
13. Molnar-Perl I. Role of chromatography in the analysis of sugars, carboxylic acids and amino acids in food. J Chromatogr A 2000;891:1–32. [PubMed]
14. White PC, Jane I, Scott A, Connett BE. Use of high-performance liquid chromatography to quantitate the opiate and sugar content of illicit heroin preparations. J Chromatogr 1983;265:293–300. [PubMed]
15. Lee YH, Lin TI. Determination of carbohydrates by high performance capillary electrophoresis with indirect absorbance detection. J Chromatogr B 1996;681:87–97.
16. Zhang X, Cao Y, Ye J. Determination of lactose in sugar-free milk powder by capillary electrophoresis with electrochemical detection. Food Chem 2001;72:385–88.
17. Ivanov AR, Nazimov IV, Lobazov AP, Popkovich GB. Direct determination of amino acids and carbohydrates by high-performance capillary electrophoresis with refractive detection. J Chromatogr A 2000;894:253–57. [PubMed]
18. Garner TW, Yeung ES. Indirect fluoresence detection of sugars separated by capillary zone electrophoresis with visible laser excitation. J Chromatogr 1990;515:639–44.
19. Zidkova J, Chmelik J. Determination of saccharides in fruit juices by capillary electrophoresis and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. J Mass Spectrom 2001;36:417–21. [PubMed]

20. Zemann A, Nguyen DT, Bonn G. Fast separation of underivatized carbohydrates by coelectroosmotic capillary electrophesis. Electrophoresis [PubMed] 1997;18:1142–47.
21. El Rassi Z. Recent developments in capillary electrophoresis and capillary electrochromatography of carbohydrate species. Electrophoresis [PubMed] 1999;20:3134–44.
22. Weinberger R, Lurie IS. Micellar electrokinetic capillary chromatography of illicit drug substances. Anal Chem 1991;63:823–27.
23. Lurie IS, Hays PA, Parker K. Capillary electrophoresis analysis of a wide variety of seized drugs using the same capillary with dynamic coatings. [PubMed] Electrophoresis 2004;25:1580–91.
24. Lurie IS, Hays PA, Garcia AE, Panicker S. Use of dynamically coated capillaries for the determination of heroin, basic impurities and adulterants with capillary electrophoresis. [PubMed] J Chromatogr A 2004; 1034:227–35.
25. Bortolotti F, De Paoli G, Gottardo R, Trattene M, Tagliaro F. Determination of γ-hydroxybutyric acid in biological fluids by using capillary electrophoresis with indirect detection. J Chromatogr B 2004;800:239–44.
26. Cabovska B, Norman AB, Stalcup AM. Separation of cocaine stereoisomers by capillary electrophoresis using sulfated cyclodextrins. Anal [PubMed] Bioanal Chem 2003;376:134–37.
27. Huang YS, Liu JT, Lin LC, Lin CH. Chiral separation of 3,4-methylenedioxymethamphetamine and related compounds in clandestine tablets and urine samples by capillary electrophoresis/fluorescence [PubMed] spectroscopy. Electrophoresis 2003;24:1097–104.
28. Kelly T, Doble P, Dawson M. Chiral separation of methadone, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP) and 2-ethyl-5-methyl-3,3-diphenyl-1-pyrroline (EMDP) by capillary electrophoresis [PubMed] using cyclodextrin derivatives. Electrophoresis 2003;24:2106–10.
29. Liau AS, Liu JT, Lin LC, Chiu YC, Shu YR, Tsai CC, Lin CH. Optimisation of a simple method for the chiral separation of methamphetamine and related compounds in clandestine tablets and urine samples by β-cyclodextrin modified capillary electrophoresis: a complementary [PubMed] method to GC-MS. Forensic Sci Int 2003;134:17–24.
30. Piette V, Parmentier F. Analysis of illicit amphetamine seizures by capillary zone electrophoresis. [PubMed] J Chromatogr A 2002;979:345–52.
31. Plaut O, Staub C. Capillary electrophoresis in forensic toxicology. Chimia 2002;56:96–100.
32. Hilhorst MJ, Somsen GW, de Jong GJ. Capillary electrokinetic separation techniques for profiling of drugs and related products. Electrophoresis [PubMed] 2001;22:2542–64.
33. Lemos NP, Bortolotti F, Manetto G, Anderson RA, Cittadini F, Tagliaro F. Capillary electrophoresis: A new tool in forensic medicine [PubMed] and science. Sci Justice 2001;41:203–10.
34. Thormann W, Lurie IS, McCord B, Marti U, Cenni B, Malik N. Advances of capillary electrophoresis in clinical and forensic analysis (1999–2000). [PubMed] Electrophoresis 2001;22:4216–43.
35. Backofen U, Matysik FM, Hoffman W, Lunte CE. Analysis of illicit drugs by nonaqueous capillary electrophoresis and electrochemical detection. [PubMed] Fresenius J Anal Chem 2000;367:359–63.
36. Di Pietra AM, Gotti R, Del Borrello E, Pomponio R, Cavrini V. Analysis of amphetamine and congeners in illicit samples by liquid chromatography and capillary electrophoresis. [PubMed] J Anal Toxicol 2001;25:99–105.
37. Chiarotti M, Fucci N. Comparitive analysis of heroin and cocaine seizures. J Chromatogr B 1999;733:127–36.
38. Thormann W, Wey AB, Lurie IS, Gerber H, Byland C, Malik N, Hochmeister M, Gehrig C. Capillary electrophoresis in clinical and forensic analysis: Recent advances and breakthrough to routine applications. [PubMed] Electrophoresis 1999;20:3203–36.
39. Bjornsdottir I, Hansen SH. Fast separation of 16 seizure drug substances using non-aqueous capillary electrophoresis. J Biochem Biophys Meth- [PubMed] ods 1999;38:155–61.
40. Altria K. Overview of capillary electrophoresis and capillary chromatog- [PubMed] raphy. J Chromatogr A 1999;856:443–63.
41. Tagliaro F, Turrina S, Pisi P, Smith FP, Marigo M. Determination of illicit and/or abused drugs and compounds of forensic interest in biosamples by capillary electrophoretic/electrokinetic methods. J Chromatogr B 1998;713:27–49.
42. Deyl Z, Miksik I, Tagliaro F. Advances in capillary electrophoresis. Forensic Sci Int 1998;92:89–124. [PubMed]
43. Thormann W, Caslavska J. Capillary electrophoresis in drug analysis. Electrophoresis 1998;19(16–17):2691–94. [PubMed]
44. Lurie IS. Application of micellar electrokinetic capillary chromatography to the analysis if illicit drug seizures. J Chromatogr A 1997; 780:265–84. [PubMed]
45. Lurie IS. Application of capillary electrophoresis to the analysis of seized drugs. Int Lab 1996:21–8.
46. Tagliaro F, Smith FP. Forensic capillary electrophoresis. Trends Anal Chem 1996;15(10):513–25.
47. Lurie IS. Analysis of seized drugs by capillary electrophoresis. In: Adamovics J, Editor. Analysis of addictive misused drugs. New York: Marcel Dekker, Inc, 1995; 151.
48. Thormann W, Molteni S, Caslavska J, Schmutz A. Clinical and forensic applications of capillary electrophoresis. Electrophoresis 1994; 15:3–12. [PubMed]
49. Vorndran AE, Oefner PJ, Scherz H, Bonn GK. Indirect UV detection of carbohydrates in capillary zone electrophoresis. Chromatogr 1992;33(3/4):163–68.
50. Oefner PJ, Vorndran AE, Grill E, Huber C, Bonn GK. Capillary zone electrophoretic analysis of carbohydrates by direct and indirect UV detection. Chromatogr 1992;34(5–8):308–16.
51. Ishii H, Morishita M, Yamad H, Iwasa S, Yajima T. Simultaneous analysis of cocaalkaloids and sugars in illicit cocaine using capillary electrophoresis. J Forensic Sci 2001;46(3):490–94.
52. Hoffstetter-Kuhn S, Paulus A, Gassman E, Widmer M. Influence of borate complexation on the electrophoretic behaviour of carbohydrates in capillary electrophoresis. Anal Chem 1991;63:1541–47.
53. Soga T. Capillary zone electrophoresis of carbohydrates by borate complexation utilizing EOF reversal. Hewlett Packard Application Note, Publication number 12–5964–1817E, Germany: Hewlett Packard Company, 1995.
54. Altria KD, Kelly MA, Clark BJ. The use of a short-end injection procedure to achieve improved performance in capillary electrophoresis. Chromatogr 1996;43(3):153–58.
55. Euerby M, Johnson C, Cikalo M, Bartle K. 'Short-end injection' rapid analysis capillary electrochromatography. Chromatogr 1998;47:135–40.
56. Fabre H, Mesplet N. Robustness testing for a capillary electrophoresis method using the 'short-end injection' technique. J Chromatogr A 2000;897:329–38. [PubMed]
57. Bergholdt AB, Jorgensen KW, Wendel L, Lehmann SV. Fast chiral separations using sulfated β-cyclodextrin and short-end injection in capillary electrophoresis. J Chromatogr A 2000;875:403–10. [PubMed]
58. Wan H, Holem A, Nagard M, Lindberg W. Rapid screening of pKa values of pharmaceuticals by pressure assisted capillary electrophoresis combined with short end injection. J Chromatogr A 2002;979:369–77. [PubMed]
59. Perrett D, Ross G. Rapid determination of drugs in biofluids by capillary electrophoresis. Measurement of antipyrine in saliva for pharmacokinetic studies. J Chromatogr A 1995;700:179–86. [PubMed]
60. Small LF, Lutz RE. Chemistry of the opium alkaloids. Vol. Supplement No. 103 to the Public Health Reports, Part II. Washington: U.S. Government Printing Office, 1932; 153–54.
61. Altria K, Bestford J. Main component assay of pharmaceuticals by capillary electrophoresis: Considerations regarding precision, accuracy, and linearity data. J Capillary Electrophor 1996;3(1):13–23. [PubMed]
62. Kelly MA, Altria KD, Clark BJ. Approaches used in the reduction of buffer electrolysis effects for routine electrophoresis procedures in pharmaceutical analysis. J Chromatogr A 1997;768:73–80.
63. Oefner P, Scherz H. Capillary electrophoresis and thin-layer electrophoresis of carbohydrates. In Chrambach A, Dunn MJ, Radola BJ, Editors. Advances in electrophoresis, Vol. 7. New York: VCH Publishers, 1994;157–220.

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