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Review

Enantiomer separation of drugs by micellar electrokinetic chromatography using chiral surfactants

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Abstract

A review surveying enantiomer separations by micellar electrokinetic chromatography (MEKC) using chiral surfactants is described. MEKC is one of the most popular techniques in capillary electrophoresis, where neutral compounds can be analyzed as well as charged ones, and the use of chiral micelles enable one to achieve the enantioseparation. The chiral MEKC systems are briefly reviewed according to the types of chiral surfactants along with typical applications. As chiral micelles or pseudostationary phases in MEKC, various natural and synthetic chiral surfactants are used, including several low-molecular-mass surfactants and polymerized surfactants or high-molecular-mass surfactants. Cyclodextrin modified MEKC using chiral micelles is also considered.

Keywords: Reviews; Enantiomer separation; Micellar electrokinetic chromatography; Amino acids; Drugs; Surfactants

Contents

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1. Introduction

Micellar electrokinetic chromatography (MEKC),

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which was first introduced in 1984 [1] as a branch of capillary electrophoresis (CE), has become one of most popular techniques in CE due to its high resolving power and capability of separating both ionic and neutral compounds. Many papers on fundamental characteristics and applications of MEKC have appeared, and a number of reviews as well as books on MEKC are available [2]. In MEKC, an ionic surfactant is used as a pseudostationary phase, which forms ionic micelles in a separation solution. The micelle interacts with an analyte molecule so that the analyte migrates at a different velocity from the surrounding aqueous phase due to the electrophoretic effect through the micelle if the analyte can be incorporated into the micelle. Several pseudostationary phases other than ionic micelles have also been used, in which the separation modes are designated as electrokinetic chromatography (EKC). For example, cyclodextrin (CD) derivatives having an ionic group, microemulsions, and ionic polymers are used as pseudostationary phases.

One of attractive applications of MEKC is enantiomer separations [2]. Enantiomer separations are important objectives especially in pharmaceutical and biomedical fields. Both gas chromatography (GC) and high-performance liquid chromatography (HPLC) have been used for enantiomer separations, where chiral stationary phases or chiral columns are often used to achieve optical recognitions. Several chiral additives to mobile phases are also used instead of chiral stationary phases in HPLC. However, the use of chiral stationary phases as well as chiral additives in GC and HPLC is usually expensive since large amounts of stationary phases or additives are required.

In MEKC, two modes of enantiomer separations are mainly used: one is MEKC using chiral surfactants and the other is CD modified MEKC (CD-MEKC). The former includes (1) the use of ionic chiral surfactants as enantioselective pseudostationary phases and (2) the use of neutral chiral surfactants with ionic achiral surfactants. In the latter or CD-MEKC, several non-derivatized and derivatized CDs are used as chiral selectors and normally achiral ionic micelles as pseudostationary phases. In both cases, the amount of the chiral surfactants or CDs required in MEKC or CD-MEKC is quite small and the costs of the enantioseparations by MEKC or CD-MEKC will be considerably reduced compared with GC or HPLC in total, although a chiral surfactant or derivatized CD is sometimes expensive. Moreover, the other advantage of MEKC for the enantioseparation is that the change of separation solution or running media is easily accomplished by simply altering the solution. It is a useful and helpful property, especially in the method development.

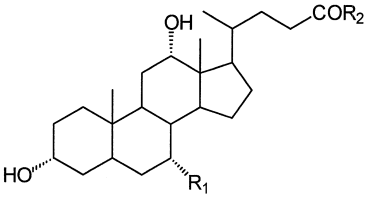
In this article, enantioseparations of drugs by MEKC using chiral surfactants are briefly reviewed. Since review papers on enantiomer separations by EKC [3–15] and on optical resolution of drugs by CE techniques [16–24] have been published, refer to these literatures for detailed discussion and/or fundamentals of enantiomer separations of drugs. Recently, CD-EKC, where charged CDs are used as pseudostationary phases, has become popular especially in enantioseparations of drug components and many enantiomers have been successfully separated by CD-EKC techniques. However, the techniques are actually beyond the MEKC areas, so they are excluded from this article.

2. Enantiomer separation by MEKC with natural chiral surfactants

2.1. Bile salts

Bile salts are natural and chiral anionic surfactants, which form helical micelles of reversed micelle conformation [25,26]. Since the first report on enantiomer separation of dansylated (Dns) DL-amino acids by MEKC with bile salt micelles [27] appeared, several papers have been published [28–33]. Table 1 summarizes the bile salts used in these studies. Non-conjugated bile salts, such as sodium cholate (SC) and sodium deoxycholate (SDC), can be used at pH>5, whereas taurine-conjugated forms, such as sodium taurocholate (STC) and sodium taurodeoxycholate (STDC), can be used in more acidic conditions or pH>3. Chiral separation of diltiazem hydrochloride and related compounds by MEKC using STDC is shown in Fig. 1 [29]. Several enantiomers, such as carboline derivatives [28], trimetoquinol and related compounds [28–30], binaphthyl derivatives [28,29,31], Dns-DL-amino acids [32], mephenytoin and its metabolites [32], and

Table 1
Bile salts employed for enantioseparations in MEKC



Bile salt	Symbol	R_1	R_2	CMC[a] (m*M*)
Sodium cholate	SC	OH	ONa	13–15
Sodium deoxycholate	SDC	OH	ONa	4–6
Sodium taurocholate	STC	H	$NHCH_2CH_2SO_3Na$	10–15
Sodium taurodeoxycholate	STDC	H	$NHCH_2CH_2SO_3Na$	2–6

[a] Critical micelle concentration at 25°C (from Ref. [10]).

3-hydroxy-1,4-benzodiazepins [33], have been successfully separated by MEKC with bile salts. In general, STDC is considered as the most effective chiral selector among the bile salts used in MEKC [10].

The CD-MEKC technique is recognized as one of efficient mode of CE for chiral separations. Since CDs show the enantioselectivities, a CD is usually used with an achiral ionic surfactant, e.g., sodium dodecyl sulfate (SDS), to achieve enantioseparations. However, the use of CDs with bile salt micelles has been also successful for enantiomer separations [32–37]. Dns-DL-amino acids [32,34,35], baclofen and its analogs, mephenytoin and fenoldopam [32], naphthalene-2,3-dicarboxaldehyde (CBI) derivatized DL-amino acids [34], diclofensine, ephedrine, nadolol, and other β-blockers [36], and binaphthyl related compounds [37] were optically resolved by CD-MEKC with bile salts.

Clothier and co-workers investigated the properties of bile salts–polyoxyethylene ethers mixtures, such as SDC–polyoxyethylene-4-dodecyl ether (Brij 30) [38,39]. In an SDC–polyoxyethylene ether solution, larger aggregation numbers and decreased interior hydrophobicity of micelles compared to a solution of a bile salt alone were found.

Enantiomeric resolution of local anesthetic drugs by MEKC with STDC under acidic conditions was studied by Amini et al. [40]. The migration order of the enantiomers could be reversed by using an STDC–polyoxyethylene-23-dodecyl ether (Brij 35) solution, due to a reduced solubilization of the analytes into the micelle.

As an example of environmentally interested chiral compounds, three polychlorinated biphenyls (PCBs), such as PCB 84, 95 and 176, were successfully enantioseparated by MEKC with sodium cholate [41], under alkaline conditions using 2-(*N*-cyclohexylamino)ethanesulfonic acid (CHES) as a buffer constituent and urea as an additive. The enantiomer separations of PCBs 84 and 95 are shown in Fig. 2.

2.2. Digitonin

Digitonin (Fig. 3), which is a glycoside of digitogenin and used for the determination of cholesterol, is a naturally occurred chiral surfactant. Since digitonin is a electrically neutral compound, it is essential to add an ionic micelle to the digitonin solution to form charged micelles or to enable it to be used as a pseudostationary phase. By using a digitonin–SDS solution under acidic conditions, some phenylthiohydantoin (PTH)-DL-amino acids were optically resolved [42]. Three PTH-DL-amino acids were also enantioseparated by MEKC with STDC–digitonin [43].

2.3. Saponins

Ishihama and Terabe [44] used saponins,

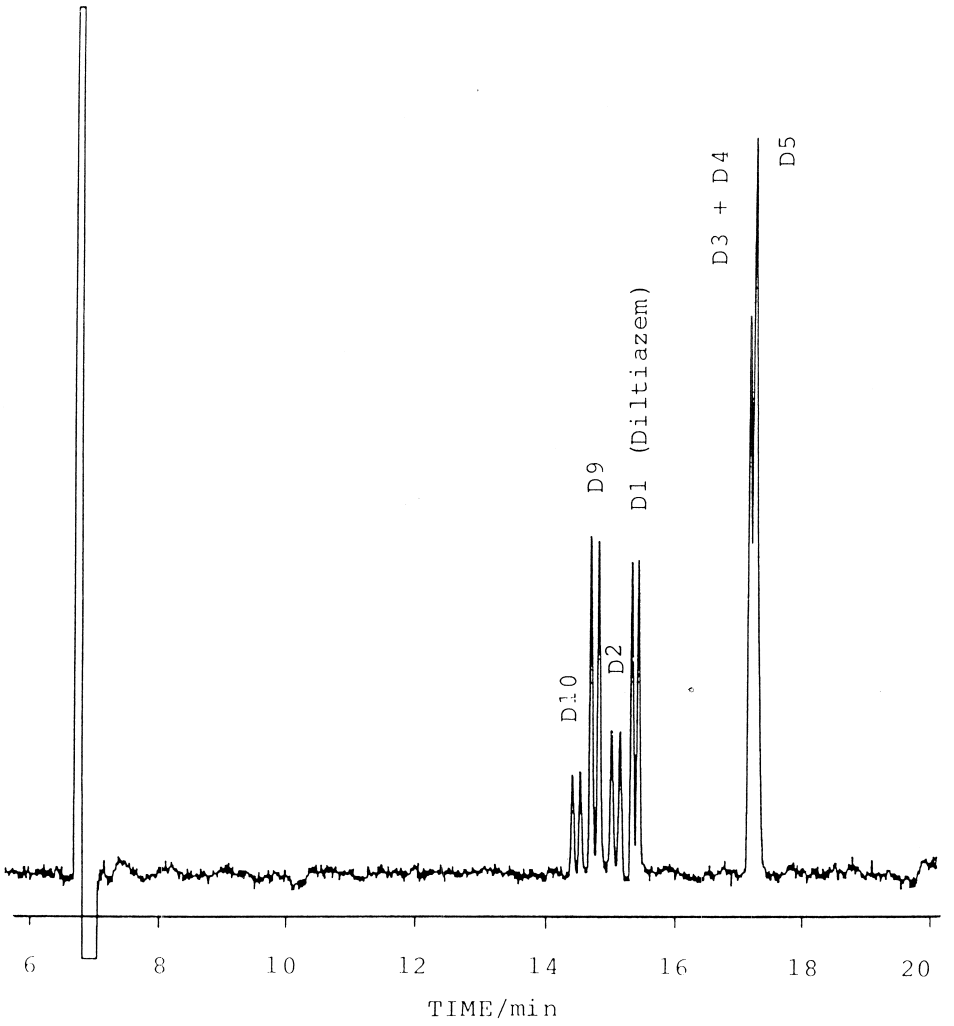


Fig. 1. Chiral separation of diltiazem hydrochloride and related compounds by MEKC using STDC [29]. Separation solution, 50 m*M* STDC in 20 m*M* phosphate–borate buffer (pH 7.0); separation capillary, 65 cm (50 cm effective length)×50 μm I.D.; applied voltage, 20 kV; detection wavelength, 210 nm; temperature, ambient.

glycyrrhizic acid (GRA) and β-escin (Fig. 4), as chiral pseudostationary phases in MEKC. Some Dns-DL-amino acids were optically resolved by a 30 m*M* GRA–50 m*M* octyl-β-D-glucoside–10 m*M* SDS solution (pH 7), but the reproducibility in migration times was not good. A β-escin–SDS system under acidic conditions was effective for enantioseparations of PTH-DL-amino acids, while under neutral conditions insufficient separations were obtained.

3. Enantiomer separation by MEKC with synthetic chiral surfactants

3.1. N-Alkanoyl-L-amino acids

Dobashi et al. [45,46] first introduced sodium *N*-dodecanoyl-L-valinate (SDVal) and sodium *N*-dodecanoyl-L-alaninate (SDAla), chemical structures are shown in Table 2 along with several other *N*-

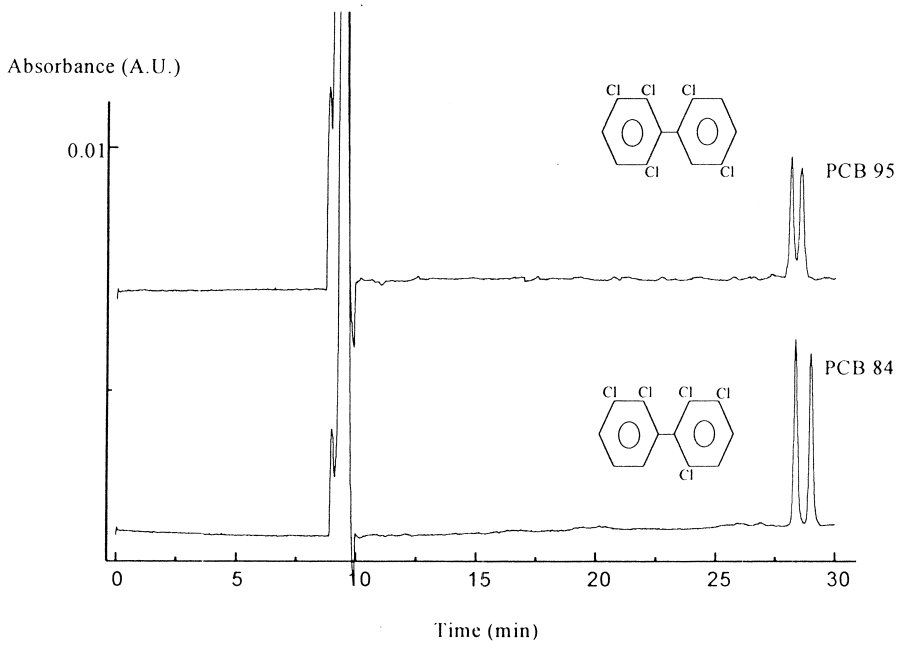


Fig. 2. Chiral separations of PCBs 84 and 95 by MEKC with SC [41]. Separation solution, 150 m*M* SC–2 *M* urea in 50 m*M* CHES buffer (pH 10.0); separation capillary, 65 cm (50 cm effective length)×50 μm I.D.; applied voltage, 15 kV; detection wavelength, 235 nm; temperature, 25°C.

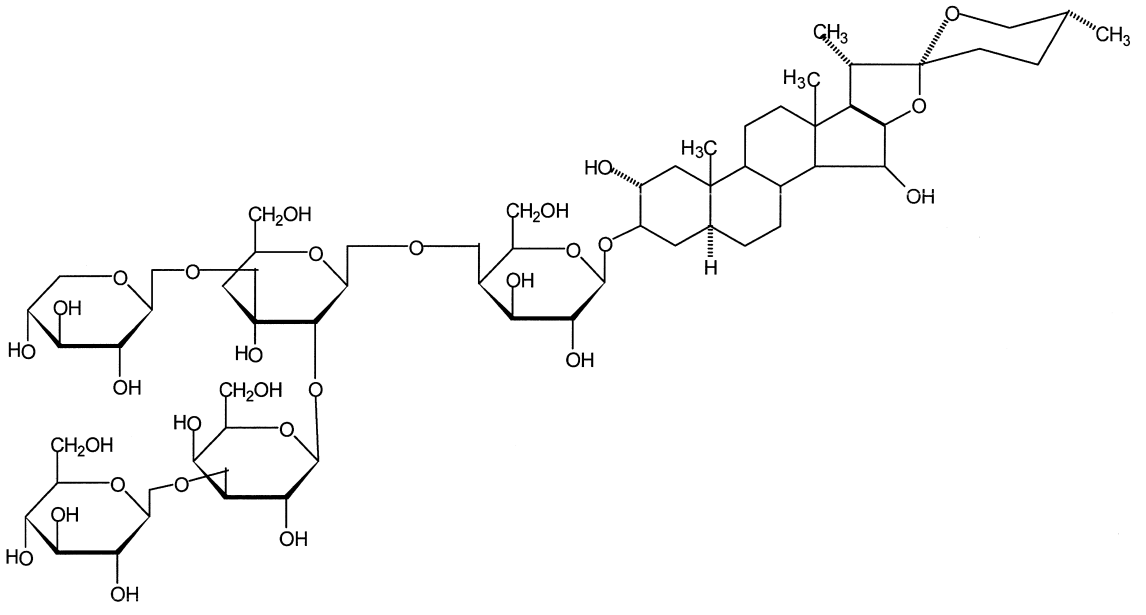


Fig. 3. Chemical structure of digitonin.

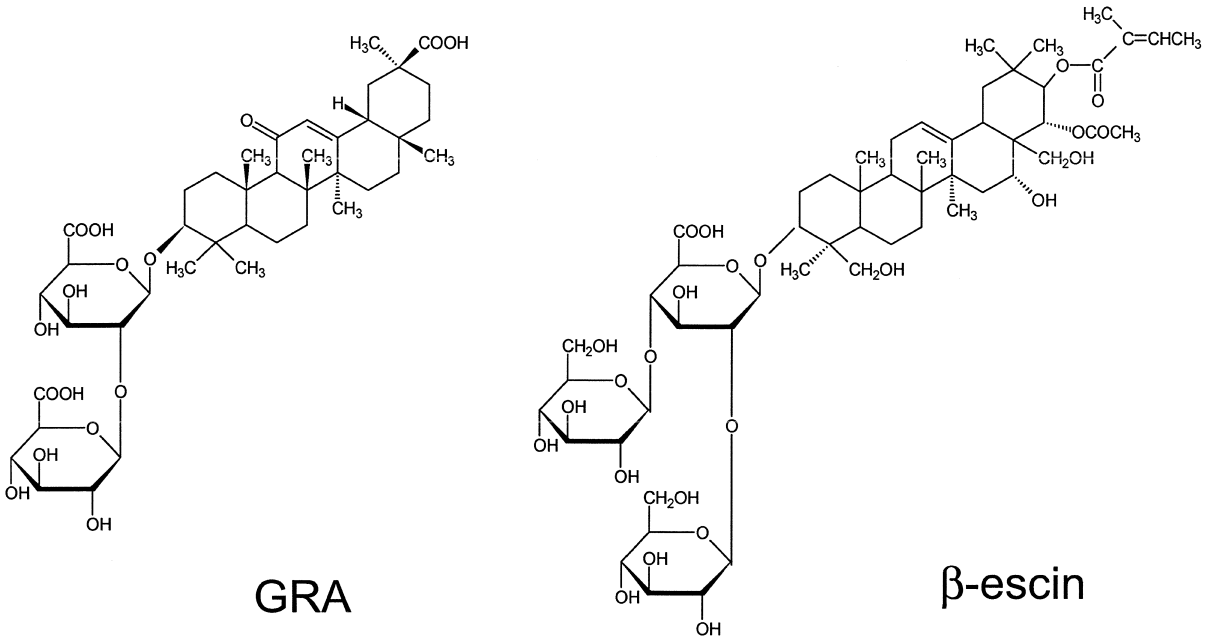


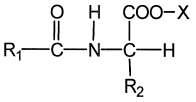
Fig. 4. Chemical structures of glycyrrhizic acid (GRA) and β-escin.

alkanoyl-L-amino acid surfactants, as synthetic chiral surfactants into MEKC, and showed the enantioseparations of *N*-acetylated amino acid esters and 3,5-dinitrobenzoylamino acid derivatives, although the efficiency was not high.

The use of SDVal for enantioseparation in MEKC was also investigated [42], and the effects of the addition of urea and methanol on the enantioselectivity and peak shapes were studied [47]. Basic studies on urea addition in MEKC were also reported [48]. By using an SDVal–SDS solution containing urea and methanol [49], six PTH-DL-amino acids were enantioseparated simultaneously, as well as warfarin and benzoin.

Sodium *N*-dodecanoyl-L-glutamate (SDGlu) [43], *N*-dodecanoyl-L-serine (DSer), *N*-dodecanoyl-L-aspartic acid (DAsp) [50], sodium *N*-tetradecanoyl-L-glutamate (STGlu) [50,51] were also employed for the enantioseparations of PTH-DL-amino acids. In each case, the addition of SDS, urea and organic modifiers such as methanol and 2-propanol were essential to obtain improved peak shapes and en-

Table 2
N-Alkanoyl-L-amino acid surfactants employed for enantioseparations in MEKC



Surfactant	Symbol	R_1	R_2	X
N-dodecanoyl-L-aspartic acid	DAsp	$C_{11}H_{23}$	CH_2COOH	H
N-dodecanoyl-L-serine	DSer	$C_{11}H_{23}$	CH_2OH	H
Sodium *N*-dodecanoyl-L-alaninate	SDAla	$C_{11}H_{23}$	CH_3	Na
Sodium *N*-dodecanoyl-L-glutamate	SDGlu	$C_{11}H_{23}$	$(CH_2)_2COONa$	Na
Sodium *N*-dodecanoyl-L-threoninate	SDThr	$C_{11}H_{23}$	$CH(OH)CH_3$	Na
Sodium *N*-dodecanoyl-L-valinate	SDVal	$C_{11}H_{23}$	$CH(CH_3)_2$	Na
Sodium *N*-tetradecanoyl-L-glutamate	STGlu	$C_{13}H_{27}$	$(CH_2)_2COONa$	Na

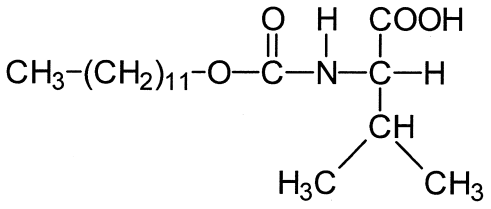


Fig. 5. Chemical structures of *N*-dodecoxycarbonylvaline (DDCV).

hanced enantioselectivity. The separation characteristics observed were not substantially different among these MEKC systems using *N*-alcanoyl-L-amino acid surfactants as chiral pseudostationary phases. Dobashi et al. [52] have also introduced sodium *N*-dodecanoyl-L-threoninate (SDThr).

3.2. N-Dodecoxycarbonyl amino acids

Mazzeo et al. [53] synthesized the novel chiral surfactants of amino acid derivatives, i.e., (*S*)- and (*R*)-*N*-dodecoxycarbonylvaline (DDCV), the chemical structure in Fig. 5, and achieved enantioseparations of several pharmaceutical amines. The enantioselectivities for the pharmaceutical amines obtained with DDCV were superior to those with *N*-dodecanoylvaline (DVal). DDCV and DVal have almost the same structures or there is only one difference: an amide group in DVal is replaced with a carbamate group in DDCV. DDCV has also an advantage of a low UV absorbance in lower wavelength compared to DVal. By using DDCV, several benzoylated amino acid methyl ester derivatives [54] and piperidine-2,6-dione enantiomers [55] were also successfully resolved. In Fig. 6, the enantiomeric resolution of 1-phenyl-3-methyl-5-pyrazolone (PMP) derivatives of four aldose enantiomers is shown [56], where (*R*)-DDCV is employed.

It is useful that both enantiomeric forms of DDCV are available, since the migration order of an enantiomeric pair can be reversed by using both forms. (*S*)- and (*R*)-forms: the inversion of the migration order of benzoin enantiomers were shown [53].

Swartz et al. synthesized another similar chiral surfactant, *N*-dodecoxycarbonylproline (DDCP) and demonstrated the enantioseparation of glutethimide enantiomers among piperidine-2,6-dione enantiomers [55].

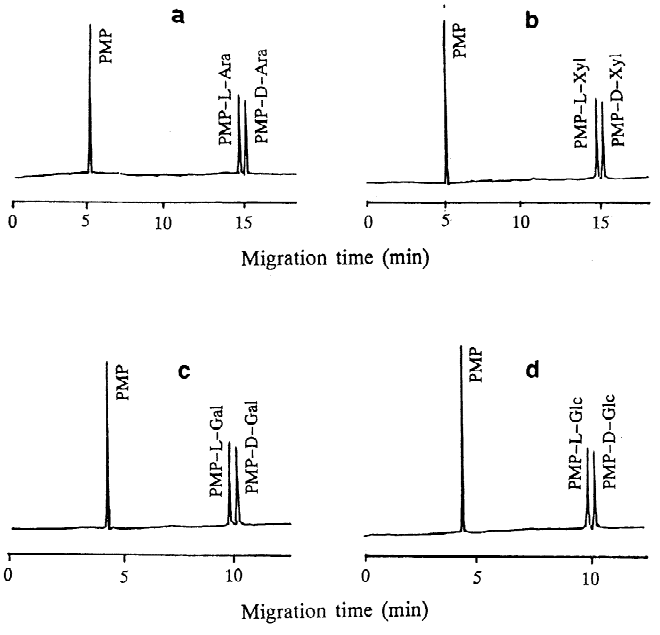


Fig. 6. Enantiomer separations of PMP derivatives of (a) Ara, (b) Xyl, (c) Gal, and (d) Glc by MEKC using DDCV [56]. Separation solution, 50 m*M* (*R*)-DDCV in 50 m*M* phosphate buffer (pH 7.0); separation capillary, 54 cm×50 μm I.D.; applied voltage, 20 kV; detection wavelength, 254 nm; temperature, 25°C.

A validation study on enantiomeric separations of ephedrine by MEKC with DDCV was carried out by Swartz et al. [57] according to the US Pharmacopeia protocol.

Peterson and Foley [58] investigated the influence of inorganic counterion on thermodynamic quantities, such as the entropy, enthalpy and Gibbs free energy changes, of micellar solubilization in MEKC with DDCV.

3.3. Alkylglucoside chiral surfactants

Anionic alkylglucoside chiral surfactants (Fig. 7), dodecyl β-D-glucopyranoside monophosphate and monosulfate, were introduced by Tickle et al. [59]. These surfactants can provide the good enantioselectivity, as shown in Fig. 8, as well as the structural recognition. The structure and chiral selectivity in MEKC with two isomeric D-glucopyranoside based surfactants was investigated [60].

Several neutral alkylglucoside surfactants, such as heptyl-, octyl-, nonyl- and decyl-β-D-glucopyranosides [61,62], were used for the enantiomer separation of phenoxy acid herbicides and amino acid derivatives. For the optical resolution of phenoxy acid herbicide enantiomers, octylmaltopyranoside was also employed [63,64].

For the enantiomeric separations of Dns-DL-amino acids, 1,1′-bi-2-naphthyl-2,2′-diyl hydrogenphosphate (BNP), warfarin and bupivacaine, the difference in enantioselectivity among three alkylglucosides, i.e., octyl- and nonyl-β-D-glucopyranosides and octylmaltopyranoside, was investigated [65].

The use of some other alkyl D-glucopyranoside surfactants, such as sodium hexadecyl D-glucopyranoside 6-hydrogensulfate, was also investigated [66,67], where some PTH-DL-amino acids and binaphthol were resolved.

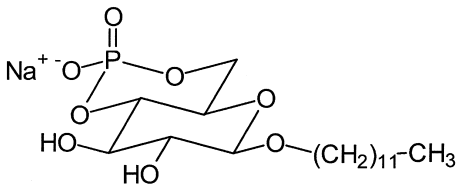
3.4. Tartaric acid based surfactants

Dalton and co-workers [68,69] synthesized a chiral surfactant based on (*R,R*)-tartaric acid for the use of enantioseparations in MEKC. Enantiomers having fused polyaromatic rings were separated easier than having only single aryl group, but overall enantioselectivity was not sufficient.

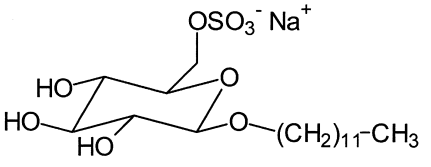
Other attempts to use chiral surfactants derived from tartaric acid have also appeared [66,67], where PTH-DL-amino acids and some drug enantiomers were successfully resolved.

3.5. Steroidal glucoside surfactants

Mechref and El Rassi introduced neutral steroidal



Sodium dodecyl β-D-glucopyranoside 4,6-hydrogen phosphate



Sodium dodecyl β-D-glucopyranoside 6-hydrogen sulfate

Fig. 7. Chemical structures of alkylglucoside chiral surfactants.

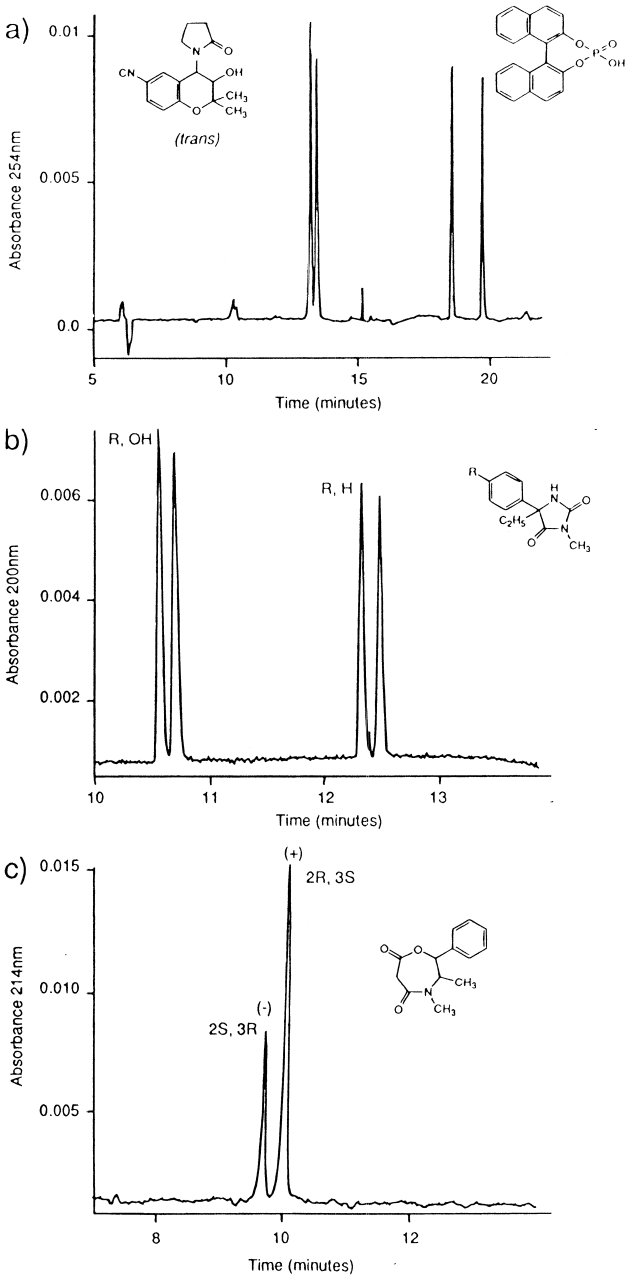


Fig. 8. Enantiomeric resolutions of (a) cromakalin and BNP, (b) mephenytoin and hydroxymephenytoin, and (c) 3,4-dimethyl,5,7-dioxo-2-phenyperhydro-1,4-oxazepine [59]. Separation solution, 45 m*M* dodecyl β-D-glucopyranoside 4,6-hydrogenphosphate in borate–phosphate buffer (pH 8); separation capillary, 57 cm (50 cm effective length)×50 μm I.D.; applied voltage, 20 kV; detection wavelength, 200 nm; temperature, 25°C.

glucoside surfactants [70], i.e., *N,N*-bis-(3-D-gluconamidopropyl)-cholamide (Big CHAP) and *N,N*-bis-(3-D-gluconamidopropyl)-deoxycholamide (Deoxy Big CHAP), which contain a cholic or deoxycholic acid moiety, respectively. By using a borate buffer under basic conditions, these surfactant micelles could be charged via borate complexation. Some binaphthyl enantiomers, Tröger's base, phenoxy acid herbicide and Dns-DL-amino acids were enantioseparated.

4. Enantiomer separation by MEKC with high-molecular-mass surfactants

Recently, the use of a high-molecular-mass surfactant (HMMS) or polymerized surfactant has been investigated as a pseudostationary phase in MEKC [71–73]. HMMS forms a micelle with one molecule, so that the enhanced stability and rigidity of the micelle can be obtained as well as easier control of the micellar size compared with a conventional low-molecular-mass surfactant (LMMS). Since the critical micelle concentration (CMC) of the HMMS micelle is essentially zero, the net micellar concentration is constant or independent of the concentration and composition of a buffer, pH, additives and temperature, and hence better reproducibility in the migration time can be expected in HMMS-MEKC than in LMMS-MEKC. In addition, HMMS is suitable to be adapted for on-line coupling of MEKC with mass spectrometry (MEKC–MS) because of the presence of no monomeric surfactant in the micellar solution.

Wang and Warner [74] first introduced a chiral HMMS for the enantioseparation by MEKC. They used poly(sodium *N*-undecylenyl-L-valinate) [poly(L-SUV)] as a chiral micelle, and binaphthol and laudanosine were enantioseparated. Dobashi et al. [52] showed the optical resolution of 3,5-dinitrobenzoylated amino acid isopropyl esters by MEKC with poly[sodium (10-undecenoyl)-L-valinate] as well as with SDVal, SDAla and SDThr.

As for the use of monomeric and polymeric chiral surfactants as pseudostationary phases for enantiomer separations in MEKC, a review article is available [75].

An achiral polymeric surfactant, butyl acrylate–butyl methacrylate–methacrylic acid copolymer (BBMA) sodium salt, was also employed for enantiomer separations in MEKC with CDs [76]. A better enantiomeric resolution of Dns-DL-amino acids was obtained by a β-CD–BBMA–MEKC system than an β-CD–SDS–MEKC system.

Billiot et al. [77] introduced polymerized dipeptide surfactants, which were derived from sodium *N*-undecylenyl-L-valine-L-leucine (L-SUVL), sodium *N*-undecylenyl-L-leucine-L-valine (L-SULV), sodium *N*-undecylenyl-L-leucine-L-leucine (L-SULL), sodium *N*-undecylenyl-L-valine-L-valine (L-SUVV). Among these, poly(L-SULV) showed the best enantioselectivity for the separation of 1,1′-bi-2-naphthol (BN) and BNP. Also the fast separation of BN and BNP was demonstrated by poly(L-SULV)–MEKC, as shown in Fig. 9.

Please refer to Table 3 for an overview of enantioseparations by MEKC with chiral surfactants.

5. Conclusions

A number of techniques for enantiomer separations by CE has been developed, including MEKC with chiral surfactants as well as CD modified capillary zone electrophoresis (CD-CZE) and CD-EKC. Studies on developing novel chiral surfactants adaptable to pseudostationary phases in MEKC are continuously progressed. Although it is not quite easy for an investigator to find out an appropriate mode of CE when one starts a specific enantioseparation, several chiral method development kits that are commercially available and/or this thematic issue and previous reviews would be helpful, as well as a book [78] including a wide range of CE techniques for chiral separations.

6. Abbreviations

Aba	α-Aminobutyric acid
Ala	Alanine
Asp	Aspartic acid
Ara	Arabinose
Arg	Arginine
BBMA	Butyl acrylate–butyl methac-

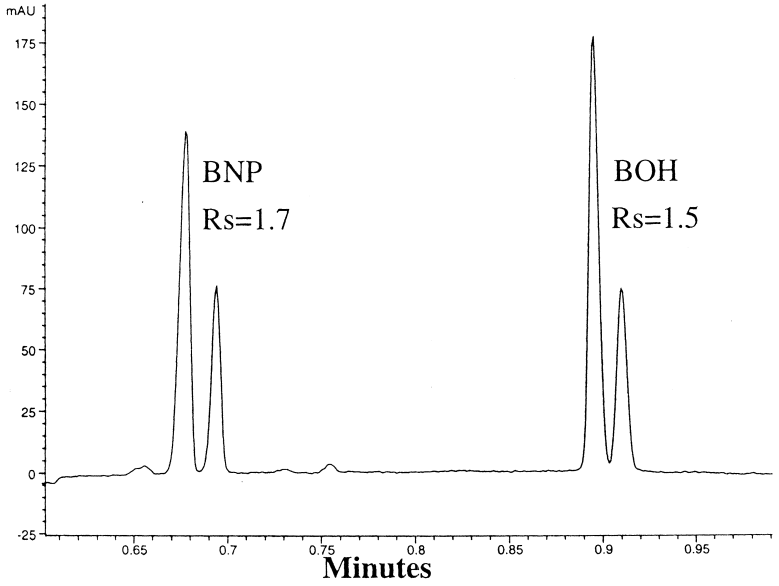


Fig. 9. A fast enantiomer separation of BNP and BN (indicated as BOH) by poly(L-SULV)–MEKC [77]. Separation solution, 1% (w/v) poly(L-SULV) in 100 m*M* Tris buffer (pH 10.5); separation capillary, 8.5 cm (effective length)×50 μm I.D.; applied voltage 30 kV; detection wavelength, 215 nm; temperature, 25°C.

	rylate–methacrylic acid co-polymer
Big CHAP	*N,N*-Bis-(3-D-gluconamidopropyl)-cholamide
BN	1,1′-Bi-2-naphthol
BNC	1,1′-Bi-2-naphthyl-2,2′-dicarboxylic acid
BNP	1,1′-Bi-2-naphthyl-2,2′-diyl hydrogenphosphate
Brij 30	Polyoxyethylene-4-dodecyl ether
Brij 35	Polyoxyethylene-23-dodecyl ether
Bz	Benzoyl
CBI-DL-amino acid	Naphthalene-2,3-dicarboxaldehyde-DL-amino acid
CD	Cyclodextrin
CD-CZE	Cyclodextrin modified capillary zone electrophoresis
CD-MEKC	Cyclodextrin modified micellar electrokinetic chromatography
CE	Capillary electrophoresis
CHES	2-(*N*-Cyclohexylamino)-ethanesulfonic acid
CMC	Critical micelle concentration
CPPA	Chlorophenoxypropionic acid
CZE	Capillary zone electrophoresis
DAsp	*N*-Dodecanoyl-L-aspartic acid
DDCP	*N*-Dodecoxycarbonylproline
DDCV	*N*-Dodecoxycarbonylvaline
Deoxy Big CHAP	*N,N*-Bis-(3-D-gluconamidopropyl)-deoxycholamide
DNB	3,5-Dinitrobenzoyl
Dns-DL-amino acid	Dansyl-DL-amino acid=5-dimethylaminonaphthalene-1-sulfonyl-DL-amino acid
DSer	*N*-Dodecanoyl-L-serine
DVal	*N*-dodecanoylvaline
EKC	Electrokinetic chromatography
Gal	Galactose
GC	Gas chromatography
Glc	Glucose
Glu	Glutamic acid
GRA	Glycyrrhizic acid
His	Histidine
HMMS	High-molecular-mass surfactant
HP-β-CD	Hydroxypropyl-β-cyclodextrin
HPLC	High-performance liquid chromatography

Table 3
Overview of enantioseparations by MEKC with chiral surfactants

Solutes	Buffer components	Ref.
Dns-DL-Amino acids (Trp, Nle, Leu, Phe, Nva, Met)	STDC (pH 3.0)	[27]
Diltiazem, trimetoquinol, carboline derivatives, 1-naphthylethylamine, 2,2′-dihydroxy-1,1′-dinaphthyl	STDC (pH 7.0), STC (pH 9.0), SDC (pH 9.0), SC (pH 9.0)	[28]
Diltiazem and analogs	STC, STDC (pH 7.0)	[29]
Trimetoquinol and related compounds, diltiazem, tetrahydropapaveroline, 2,2′-dihydroxy-1,1′-dinaphthyl, 2,2,2-trifluoro-1-(9-anthryl)ethanol	STDC (pH 7.0)	[29]
Laudanosoline, norlaudanosoline, trimetoquinol, laudanosine	STDC (pH 7.0)	[30]
BN, BNP, biphenanthrene dihydroxide	SDC (pH 9.0) (with or without methanol)	[31]
BNC	STDC (pH 4.7)	[31]
Dns-DL-Amino acids (Thr, Nva, Trp, Glu, Asp), mephenytoin and metabolite,	TDC (pH 7.2) (with or without β-CD)	[32]
3-Hydroxy-1,4-benzodiazepins (oxazepam, temazepam, lorazepam, lormetazepam)	SC (pH 8.0)	[33]
Fenoldopam and derivative	TDC–β-CD (pH 7.2)	[32]
CBI-DL-Amino acids (His, Glu, Asp, Phe, Tyr, Arg), CBI-DL-baclofen, CBI-DL-phosphates, Dns-DL-amino acids (Arg, Ala, Pro), hydrolysis products of D-Phe^{7}-bradykinin	TDC–β-CD (pH 7)	[34]
Dns-DL-Amino acids (Thr, Leu, Trp, Nle, Nva)	TDC–β-CD (pH 7.8)	[35]
Phenylethylamines (diclofensine, nadolol, methylamphetamine, ephedrine, norephedrine, etc.)	STDC–HP-β-CD (pH 9.5) with or without propan-1-ol	[36]
BN, BNC, BNP	SDC (pH 8.0) (with or without α-CD)	[37]
Verapamil, norverapamil, gallopamil, BN, atenolol, BAYK8644	SC or SDC–Brij 30 (pH 8.1-8.3)	[38]
Verapamil, norverapamil, gallopamil	SDC–Brij 30 (pH 8.1-8.3) containing methanol	[39]
Bupivacaine, mepivacaine, prilocaine	STDC or STDC–Brij 35 (pH 3.13)	[40]
PCBs (84, 95, 176)	SC–urea (pH 10.0)	[41]
PTH-DL-Amino acids (Trp, Nle, Nva, Val, Aba, Ala)	Digitonin–SDS (pH 3)	[42]
PTH-DL-Amino acids (Nva, Val, Aba)	Digitonin–STDC–urea (pH 2.5)	[43]

Table 3 (*continued*)

Solutes	Buffer components	Ref.
Dns-DL-Amino acids (Ser, Thr, Val, Phe, Leu, Met)	Octyl-β-D-glucoside–GRA–SDS (pH 7.0)	[44]
PTH-DL-Amino acids (Trp, Nle, Nva, Met, Val, Aba, Ala, Ser, Thr)	β-Escin–SDS (pH 3.0)	[44]
DNB-DL-Amino acid isopropyl esters (Ala, Val, Leu, Phe)	SDVal (pH 7.0) containing methanol	[45]
DNB-DL-Amino acid isopropyl esters (Ala, Val, Leu, Phe), NB-DL-amino acids isopropyl esters (Ala, Val, Leu, Phe), Bz-DL-amino acid isopropyl esters (Ala, Val, Leu, Phe)	SDVal (pH 7.0)	[46]
PTH-DL-Amino acids (Aba, Val, Nva, Trp, Nle)	SDVal–SDS (pH 7)	[42]
PTH-DL-Amino acids (Nva, Met, Trp, Nle)	SDVal (pH 7)–methanol with or without urea	[47]
PTH-DL-Amino acids (Ser, Aba, Nva, Val, Trp, Nle), benzoin, warfarin	SDVal–SDS–urea (pH 9) containing methanol	[49]
PTH-DL-Amino acids (Aba, Met, Nva, Trp, Nle), benzoin	SDGlu–SDS–urea (pH 9) containing methanol	[43]
PTH-DL-Amino acids (Aba, Met, Val, Nva, Trp, Nle)	DSer–SDS–urea (pH 11) containing methanol or 2-propanol	[50]
PTH-DL-Amino acids (Aba, Val, Nva, Trp, Nle)	STGlu–SDS (pH 11) containing methanol with or without CHAPS	[51]
Atenolol, benzoin, bupivacaine ephedrine, homatropine, ketamine, metoprolol, *N*-methylpseudoephedrine, norephedrine, norphenylephrine, octopamine, pindolol, pseudoephedrine, terbutalin	DDCV (pH 8.8)	[53]
DNB-DL-Amino acid methyl esters (Ala, Aba, Leu)	DDCV (pH 7.8)	[54]
Piperidine-2,6-dione enantiomers (aminoglutethimide, glutethimide, thalitomide, etc.)	DDCV (pH 9.25), DDCP (pH 8.80)	[55]
PMP derivatized aldose enantiomers (Ara, Xyl, Gal, Glc)	DDCV (pH 7.0)	[56]
Dns-DL-Amino acids, BNP, mephenytoin, etc.	Dodecyl β-D-glucopyranoside 4,6-hydrogenphosphate (pH 8)	[59]
Hexobarbital, phenobarbital, fenoldopam	Dodecyl β-D-glucopyranoside 6-hydrogensulfate (pH 8)	[59]
Phenoxy acid herbicides (silvex, dichlorprop, mecoprop, CPPAs, 2-PPA)	Octyl-β-D-glucopyranoside (pH 6.5)	[61]
DL-Amino acid carbamates (Trp, Ile, Met, Val, Ala)	Nonyl-β-D-glucopyranoside (pH 10.5)	[62]

Table 3 (*continued*)

Solutes	Buffer components	Ref.
Phenoxy acid herbicides (Silvex, dichlorprop, mecoprop, etc.)	Octyl-β-D-maltopyranoside (pH 6.5)	[63]
Phenoxy acid herbicides (Silvex, dichlorprop, mecoprop, etc.)	Octyl-β-D-maltopyranoside (pH 6.5)	[64]
Dns-DL-Amino acids (Trp, Phe, Leu, Met, Val), bupivacaine, warfarin, BNP	Octyl-β-D-glucopyranoside, nonyl-β-D-glucopyranoside, octyl-β-D-maltopyranoside (pH 6.5)	[65]
PTH-DL-Aamino acids (Val, Ile, Trp)	Dodecyl β-D-glucopyranoside 6-hydrogensulfate (pH 7)	[67]
PTH-DL-Aamino acids (Val, Ile, Nle, Trp), BN	Hexadecyl β-D-glucopyranoside 6-hydrogensulfate (pH 7)	[67]
PTH-DL-Amino acids (Ala, Thr, Val, Ile, Trp), procaterol, indapamide, trimetoquinol, BN, BNP, ephedrine, norephedrine, etc.	2,3-Didodecyloxy-1,4-butylene disulfate (pH 7)	[66]
BN, laudanosine	Poly(L-SUV) (pH 9.0, 10.0)	[74]
Dns-DL-Amino acids (Phe, Thr, Asp)	BBMA–β-CD (pH 8.0) containing methanol	[76]
BNP, BN	Poly(L-SULV) (pH 10.5)	[77]

Ile	Isoleucine	SDAla	Sodium *N*-dodecanoyl-L-alaninate
Leu	Leucine		
LMMS	Low-molecular-mass surfactant	SDGlu	Sodium *N*-dodecanoyl-L-glutamate
MEKC	Micellar electrokinetic chromatography	SDThr	Sodium *N*-dodecanoyl-L-threoninate
Met	Methionine		
MS	Mass spectrometry	SDVal	Sodium *N*-dodecanoyl-L-valinate
NB	4-Nitrobenzoyl		
Nle	Norleucine	Ser	Serine
Nva	Norvaline	STC	Sodium taurocholate
PCB	Polychlorinated biphenyl	STDC	Sodium taurodeoxycholate
Phe	Phenylalanine	STGlu	Sodium *N*-tetradecanoyl-L-glutamate
PMP	1-Phenyl-3-methyl-5-pyrazolone	L-SULL	Sodium *N*-undecylenyl-L-leucine-L-leucine
Poly(L-SUV)	Poly(sodium *N*-undecylenyl-L-valinate)	L-SULV	Sodium *N*-undecylenyl-L-leucine-L-valine
PPA	2-Phenoxypropionic acid		
Pro	Proline	L-SUVL	Sodium *N*-undecylenyl-L-valine-L-leucine
PTH-DL-amino acid	Phenylthiohydantoin-DL-amino acid	L-SUVV	Sodium *N*-undecylenyl-L-valine-L-valine
SC	Sodium cholate		
SDC	Sodium deoxycholate	TDC	Taurodeoxycholic acid
SDS	Sodium dodecyl sulfate	Thr	Threonine

Trp	Tryptophan
Tyr	Tyrosine
Val	Valine
Xyl	Xylose

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