CYCLODEXTRINS IN CHROMATOGRAPHY. PART 1. LIQUID CHROMATOGRAPHIC METHODS.

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The objectives of the reviews are the collection, concise description, comparison and evaluation of the various chromatographic technologies using natural and modified cyclodextrins for the increase the seperation capacity of various chromatographic separation systems.

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Introduction

Chromatographic procedures were developed and successfully employed for the separation of a high number of organic and inorganic compounds present at trace level in complicated accompanying matrices. The capacity of chromatographic separation technologies can be increased by the modification of both the stationary and the mobile phase of the system. Because of their specific adsorption character cyclodextrins (CD) and cyclodextrin derivatives (CDs) have been frequently applied for the improvement of the separation parameters (mainly chiral separation capacity) of various chromatographic methods. The chiral separation capacity of cyclodextrins has been frequently exploited for the separation of enantiomers with markedly different biological activity employing CDs. CDs and CD derivatives can be equally used as additives of stationary phase or modifier of the mobile phase. The number of studies dealing with the application of CDs and CD derivatives for the increase of the separation capacity of chromatographic systems increased considerably. Because of their versatility CDs have found application in many special branch of chromatography such as liquid chromatography (LC), gas chromatography (GC), size exclusion chromatography (SEC), gel permeation chromatography (GPC), and electrically driven separation methods (CE, CZE), and ultra performance liquid chromatography (UPLC).

Application of cyclodextrins in liquid chromatographic techniques

Because of their versatility, reproducibility and sensitivity various HPLC methods have been frequently employed for the separation of optical and positional isomers in HPLC systems employing CDs in the mobile and/or stationary phases. The applications and development of new CD chiral stationary phases (CD-CSPs) have been recently reviewed and their use in capillary electrochromatography (CEC), open tubular CEC (OT-CEC, packed-bed CEC (P-CEC), pseudostationary CEC (PSP-CEC), monolithic CEC, and supercritical fluid chromatography (SFC), has been discussed more in detail.[1]

Another review has been published on the application of subs μm porous silica stationary phases in LC and CEC. The review established that these new materials are suitable for the rapid and efficace separation of a wide variety of analytes.[2]

The application of new chiral selectors in the enantiomeric separation using HPLC and CE technologies has also been reviewed and the importance of chiral discrimination in biological samples is emphasized[3]. Chemically bonded cationic β-cyclodextrin derivatives were synthesized and employed for the enantioseparation of racemic pharmaceutical compounds. Vinylene-functionalized cationic β-CDs were co-polymerized with vinylized silica in the presence of AIBN and conjugated monomers. It was established that this new stationary phase can be successfully employed in packed column supercritical fluid chromatography.[4]

The characteristics of the quercetin/hydroxypropyl-β-CD were investigated in detail using various physicochemical analytical method such as differential scanning calorimetry, Fourier transform infrared spectroscopy, X-ray powder diffractometry, scanning electron microscopy and HPLC. The measurements indicated that the inclusion complex formation increases considerably the water solubility of the end product.[5]

Silica gel layers impregnated with β-CD were employed for the enantiomeric separation of (±)-propanolol and (±)-atenolol. Silicagel layers were bulk-impregnated with β-CD. Analytes were enantioseparated in solvent systems of DMF-ethyl acetate-butanol (3:2:5, v/v) and butanol-acetic acid-ethyl acetate-ammonia (5:2:2:0.5, v/v), respectively. Analytes were detected with iodine.[6]

Countercurrent chromatography was employed for the isolation of bitter acids from hops (*Humulus lupulus L*). Analytical procedure applied two separate countercurrent methods. The first step used hexane and aqueous buffer and

resulted in a mixture of cis/trans diastereomers. Cis and trans diastereomers were separated in the second step using mobile phase containing β-CD. The successful separation of individual bitter acids from commercially available hop extracts was reported.[7]

Affinity capillary electrophoresis and mass spectrometry (ACA-MS) has been used for label-free solution-based affinity analysis. Drugs included in the investigations were: ibuprofen, s-fluorbiprofen, phenylbutazone, naproxen, folic acid, resveratrol, 4,4'-propane-1,3-diy) dibenzoic acid. The results of ACE-MS were compared with those obtained with direct infusion mass spectrometry (DIMS) and ACE with UV detection. It was established that the application of ACE-MS facilitate the simultaneous affinity analysis of multiple interactive pairsresulting in high-throughput screening of drug candidates.[8]

Estrogens in pork and chicken samples were determined by stir bar sorptive extraction (SBSE). Poly(dimethyl-siloxane) (PDMS)/β-CD)/divinylbenzene (DVB)-coated stir bar was prepared by the sol gel technique. Liquid desorption and HPLC followed by UV detection were employed for the separation and quantitative determination of the analytes. The limit of the detection was 0.21 – 1.6 μg L^{-1}, the dynamic range varied between 2 – 2000 μg L^{-1}. The relative standard deviation of the method was 6.0 – 9.7 %. It was stated that the method is simple, selective, sensitive, and can be successfully applied for the analysis of estrogens in pork and chicken samples.[9]

Thus, hydroxy-β-CD and gelatin were applied to increase the solubility of puerarin. The objectives of the measurements were to create puerarin nanoparticles which improves puerarin entrapment, efficacy, penetration and bioavailability. It was stated that puerarin nanoparticles are potentially applicable for the brain injury induced by ischemic-reperfusion.[10]

A new method combining in vivo microdialysis (MD) sampling, turbulent-flow chromatography (TFC) with LC/MS was developed and applied for the study of the pharmakokinetic of puqietinone. Separation was carried out on a fast LC column (4.6 mm x 50 mm x 1.8 μ). HP-β-CD was added to the system to increase the relative recovery of the analyte. The LOG value was 0.10 ng mL^{-1}. The method showed good linearity (R^2 = 0.9993) in the concentration range of 1.02 – 200.02 ng L^{-1}. It was established that the new method eliminates the influence of matrix effect. The efficacy of the technique was demonstrated by the application of the method for the pharmacokinetic study of the puqietinone in rats.[11]

The bioactive polyphenol resveratrol shows marked beneficial biological effects such as antioxidant, anti-inflammatory, anti-carcinogenic, and anti-aging activity. A considerable number of drug delivery sytems was developed to increase the poor bioavailability, the rapid metabolizing and excretion of resveratrol. The employments of various drug delivery systems such as nano and microformulations, liposomes, solid lipid nanoparticles, solid polymeric nanoparticles, solid lipid nanoparticles, liposheres, cyclodectrins. Polymeric microsheres, yeals cell carriers and calcium of zinc pectinate beads. The application of resveratrol in medicinal chemistry has been previously discussed.[12]

The inclusion complex of cefaclor with β-cyclodextrin was investigated by using thin-layer chromatography combined with densitometry and with proton nuclear magnetic resonance spectrometry.[13]

Cyclodextrins as mobile phase additives were successfully applied for the improvement of the separation of catechin components in tea. It was stated that the new method reduces the ratio of organic components in the mobile phase, improve resolution and retention factors. The best separation was obtained by employing a conventional C18 column and a mobile phase acetonitrile/water (12/88, v/v) containing 1.5 mM L^{-1} β–cyclodextrin. The flow rate was 1.0 mL min^{-1}. It was stated that the method can be applied for the separation and determination of other active compounds from natural plants.[14]

The application of SBECD (sulfobutyl ether β-CD) in RP-HPLC was investigated in detail. The method make possible the enantiomeric separation of fenoterol, idazoxan and its hydrolyzate, orciprenaline, terbutaline, tranylcypromine, 1-aminoindane, nefopam, and imazalil. It was further established that SBECD modifies the impurity profiles for the fermentation-derived drugs A40926, ramoplanin, teicoplanin and vancomycin. The measurements suggested that SBECD can be used for the modification of the separation character of C18 column being a viable alternative for the commercial chiral columns.[15]

Nano-liquid chromatography (nano-LC) technology was developed for the enantioseparation of bioactive compounds. The monolithic column was synthesized using HP-β-CD as chiral selector and water-soluble comonomers. Analytes were separated employing aqueous mobile phases modified with methanol or acetonitrile and buffered with 0.1 % triethylamine-acetate. It was established that nomifensine and naproxen were baseline separate while praziquantel, metomidate and 5-methyl-5-phenyl-hydantoin was only partially resolved.[16]

A rapid and simple HPLC method was developed and successfully applied for the analysis of urocanic acid isomers extracted from human skin. Measurements were carried out on a β-CD column, the mobile phase was phosphate buffer-acetonitrile 15:85 v/v, the isocratic flow rate was 0.3 mL min^{-1}. Analytes were detected at 276 nm, the column temperature was 20^0C. It was established that the method separates urocanic acid isomers, it is rapid and can be employed for the quantification of urocanic acid isomers extracted from skin.[17]

The enantioselective separation capacity of CDs and cyclofructans (CFs) was compared. The basic compounds were derivatized using either dimethylphenyl or R-naphtylphenyl and their separation characteristics were investigated using normal phase HPLC method. The measurements indicated that both the structure of the cyclic oligosaccharide and the character of the derivatizing agent influence markedly the enantioselectivity of the separation system.[18]

The beneficial characteristics of natural CDs and their derivatives have been discussed in detail. It was emphasized that CDs are sussessfully applied in foods and food products, pharmaceutical preparations, agricultural practice and in a

wide variety of analytical procedures. It was further established that CDs are produced from a nenewable natural material (starch). Because of their encapsulation capacity they can be applied in the solution of many chemical problems, changing molecular solubility. Moreover, CDs and CD derivatives can enhance the stability of the included molecules. Because of their capacity to increase the solubility of environmental pollutants they can modify the departure of organic contaminants and heavy metal from soil, water and atmosphere.[19]

The influence of the drying method and drying carriers on the performance and physicochemical characteristics of spray-and spouted bed-dried phytopharmaceutical preparation of Bidens pilosa L. The efficacy of colloidal silicon dioxide, β-CD, maltodextrin dextrose equivalent (DE) 10, and microcrystalline cellulose on the drying process was investigated using the following parameters: particle size and morphology, total flavonoid content, solubility, flowability and water activity. Energetic efficiency, product recovery, elutriation and product accumulation were also determined.

The crystalline state of the powder was assessed by X-ray diffraction. The measurements indicated that the lowest flavonoid degradation (8.6 %) was achieved by using β-CD as drying carrier. The recoveries obtained by spray drying and spouted bed drying were 86.9 % and 72.9 %, respectively.[20]

A pharmacokinetic study was carried out for the comparison of the characteristics of two docetaxel parenteral formulations (SID530) and β-CD. The concentration of the active agent in whole blood and plasma was followed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). The measurements indicated that the behaviour of the two formulations were comparable. Maximum serum concentration, time to peak concentration, and area under the concentration-time curve were similar. It was concluded from the data that the drugs are bioequivalent in monkey. Experiments used cynomolgous monkey.[21]

The complex formation between CDs and the HIV inhibitor UC781 was studied in detail using RP-HPLC. CDs included in the experiments were: β-CD, HP-β-CD and methyl β-CD. Analytes were eluted isocratically with acetonitrile-water. It was established that the modification of β-CD also modified the complex formation.[22]

A novel magnetic nanoadsorbent (CMCD-APTS-MNPs) containing the superparamagnetic and molecular recognition properties was synthesized by grafting CM-β-CD on-3-aminopropyl-triethoxysile (APTS) modified FE304 nanoparticles. It was established that the new product can be employed for the rapid and selective separation of nucleosides and nucleotides in biological samples.[23]

A molecularly imprinted polymer was prepared using ultrasonic irradiation, with attapulgitr as matrix, β-naphtol as template molecule, acryloyl-β-CD as functional monomer, and N,N-methylenebiacrylamide as cross-linking agent, respectively. The polymer was characterized by the traditional heat infrared spectroscopy and transmission electron microscopy. It was established that the new polymer has a better selectivity and the adsorption kinetic to estrol, estradiol, estrone and diethylstilbestrol. The limit of detection for these analytes were between 100 and 1000 ng g^{-1}. RSDs (n = 6) were lower then 5.1 %.[24]

A binary sorbent based on achiral liquid crystal 4-methoxy-4 -ethoxyazoxybenzene and macrocyclic heptakis(2,3,6-tri-O-acetyl)-β-CD (10.25 wt %) was prepared and the various physicochemical charactertistics of the product was investigated (mesomorphous, sorption, selectivity), and the excess thermodynamic function of sorption by the binary sorbent from gaseous phase was determined using 29 organic compounds as model compounds (n-alkanes, cycloalkanes, arenes, monoatomic alcohols, heterocycles, optical isomers of camphene, limonene, and butanediol-2,3). It was established that the binary sorbent showed high structural selectivity over a wide temperature range.[25]

Various physicochemical and thermodynamic methods were employed for the characterization of the bioactive hydroxy pentacyclic triterpenoic acids (HPTAs). The inclusion complex formation of gamma-CD with ursolic, oleanolic, and betulinic acids was investigated by differential scanning calorimetry and H-1 NMR spectroscopy. The apparent formation constants (K-f) were determined by RP-HPLC. Thermodynamic parameters Delta GA(0), Delta HA(0), and Delta SA(0) were measured in the temperature range 25 – 45^{0}C. The influence of gamma CD on the water solubility of HPTA was determined by phase-solubility measurements.[26]

A new chiral stationary phase was synthesized using surface initiated atom-transfer radical polymerization (ATRP). Poly(2-methyl-3-butyn-2-yl methacrylate-co-divinylbenzene) was grafted on silica surface via ATRP technology. Azide-modified β-CD was immobilized on the alkyne of the polymer layer used as chiral separation stationary phase. HPLC measurements were carried out of an column of 150 mm x 4.6 mm i.d. filled with the new stationary phase. The retention behaviour of aromatic and chiral compounds was investigated. The measurements indicated that the retention characteristics of the new stationary phase differ markedly from that of the original stationary phase.[27]

Two covalently bonded cationic β-CD chiral stationary phases (CSPs) were prepared and applied for the enantioselectivity of 12 racemic phamaceuticals and 6 carboxilic acids. The new phases were prepared by graft polymerization of 6(A)-(3-vinylimidazolium)-6-deoxyperphenylcarbamate-β-cyclodextrin chloride or 6(A)-N,N-allylmethylammonium-6-deoxyperphenylcarbamoyl-β-cyclodextrin. The results indicated that the enantiomeric separation capacity of CSPs was different, the separation capacity of CS containing imidazolium was markedly higher.[28]

A HPLC method was developed for the enantiomeric sepration of flavanol enantiomers (+)- and (-)-epicatechin and (-)-catechin in cocoa-based products. Isocratic elution was carried out with methanol ammonium acetate buffer. Analytes were detected by fluorescence. The measurements indicated that concentration of monomeric flavanols was the highes in each sample (68-91 %). The interday and intraday precision of the method varied between 1.46 – 3.22 % in cocoa based products. Recoveries ranged 82.2-102.1 % at

50 % spiking level, 83.7-102.0 % at 100 % spiking level, at 80.4-101.1 % at 200 % spiking level. Because of the favorable separation characteristics the method was proposed for the routine analysis of cocoa-based products.[29]

A silica adsorbent containing β-CD was developed for the preparative separation and purification of epicatechin gallate (EGCG) from green tea extracts. The measurements indicated that β-CD bonded silica sorbent possess excellent adsorption equilibrium capacity (over 55 %). Preparative separation of ECGC was achieved on a preparative column (220 mm x 15 mm i.d., particle size, 40 – 64). Analyte was eluted with methanol/acetonitrile/acetic acid. Sample was dissolved in acetonitrile and loaded at 0.8 mg g^{-1} sorbent.[30]

The enantioselectivity of nano-liquid chromatography and particulate capillary columns were compared using nonsteroidal anti-inflammatory drugs as model compounds (naproxen, ibuprofen, ketoprofen, fluorbiprofen, suprofen, indoprofen, cicloprofen, and carprofen). Measurements were carried out on achiral capillary columns and heptakis(2,3,6-tri-O-methyl)-β-cyclodextrin (TM-β-CD or hydroxypropyl-β-cyclodextrin (HP-β-CD) as chiral mobile phase additive (CMPA). Mobile phase consisted of water-ACN buffered with 50 mM sodium acetate at pH 3 containing 30 mM TM-β-CD (70:30, v/v). The column dimensions were 100 μm i.d.. The analyses proved that the retention capacity of monolithic column was lower then that of traditional columns. It was further established that the enantioselectivity of the systems depended markedly on the type of stationary phase and on the composition of the mobile phase.[31]

A review was prepared for the elucidation of the role of click chemistry in the family of cyclic olygosaccharides, including chromatography, biological applications, elaboration of superstructures, and metal detection.[32]

The separation and quantitative determination of resibufogenin and cinobufagin using RP-HPLC and gamma-cyclodextrin as mobile phase additive has been earlier reported. The factors influencing the retention have been studied in detail. The impact of the nature of cyclodextrin, the concentration of organic modifier in the mobile phase, the concentration of CD, the temperature of the separation was investigatated. It was established that both resibufogenin and and cinobufegin form inclusion complexes with CDs. The stability of the complex depends on the environmental conditions, and the stability of the inclusion complex decreases with inceasing temperature. It was further determined that the complex formation spontaneous, exothermic and enthalpy driven. The method has been successfully applied for the separation and quantitative determination in Chansu (Bufonis venenum) samples.[33]

Allyl-β-CD was prepared by treating β-CD with allylic bromine. A new type of molecularly imprinted polymers (MIPs) with selective adsorption for phtalate were synthesized using ally-β-CD and methachrylic acid (MAA) as binary funtional monomers. The product was characterized by scanning electron micrograph (SEM) and Fourier transform-infrared spectroscopy. Dipentyl phtalate (DPP) was employed as template. The allyl β-CD-MIPS was employed as selective sorbent for DPP and was employed for solid phase extraction, and its application as molecularly imprinted solid-phase extraction was proposed.[34]

A new polycarboxylate (MPC) superplasticizer was prepared by the copolymerization of acrylic acid, methallyl sulfonic acid, allyl poly(ethylene glycol)s and β-CD grafted maleic anhydride. The molecular characteristics of MPC was investigated by Fourier infrared spectroscopy and gel permeation chromatography. The impact of the concentration of β-CD on the application parameters of MPC was studied by the determination of cement paste fluidity, setting time, amount of adsorption of MPC on the cement particles. Differential scanning calorimetry and thermogravimetric measurements were also applied for the characterization of MPC. The measurements established that the initial fluidities and setting times of cement pastes increased with increasing number of β-CD side chains. It was assumed that the performance of MPC depended considerably on the solvation water film formed by the polyoxyethylene side chain and on the chelate formation between β-CD and the substructures of MPC.[35]

A novel HPLC method was developed and applied for the analysis of alpha-tocopherol in inclusion complexes formed by natural β-CD and 2-hydroxy-β-CD. The validation parameters of the method were: specificity, selectivity, linearity, precision, range and recovery.[36]

A novel RP-HPLC method was applied for the separation of five catechin compounds in tea. It was established that cyclodextrin additive in the mobile phase decreased considerably the use of toxic and inflammable organic solvents without reducing resolution and separation efficacy. Analytes were separated on a traditional C18 column using isocratic separation mode. Mobile phase consisted of acetonitrile/water (12/88, v/v) containing 1.5 mM L^{-1} β-CD. The flow rate was 1.0 mL min^{-1}. It was stated that the method is eco-friendly, and can be applied for the separation and determination of other bioactive compounds from natural plants.[37]

The 1:1 inclusion complex of quercetin with β-CD was prepared by rotational electromagnetic stirring and rotating evaporation. The inclusion complex was characterized by differential scanning calorimetry, and fourier-transform infrared spectroscopy. The water solubility of the inclusion complex was investigated by HPLC. It was concluded from the results that the formation of inclusion complex increased markedly the water solubility.[38]

In vivo microdialysis sampling (MD) and turbulent-flow chromatography (TFC) followed by liquid chromatography-mass spectrometry was employed for the measurement of puqietinone after intravenous administration to rat. Separations were carried out on a column of 4.6 mm x 50 mm, particle size: 1.8 μm. Puqietine, is a lipophilic alkaloid from Fritillaria paqiensis. It was found that the method employing MD combined with TFC-LC/MS is suitable for invivo monitoring experiments.[39]

Chiral liquid chromatography was employed for the enantiomeric separation of ibuprofen in pharmaceutical formulations and the overlapping chromatographic profiles were evaluated by partial least squares regression (unfolded-partial least-squares regression, U-PLC). It was stated that

the method can be successfully applied for the analysis of ibuprofen. The analytes were partially separated on a permethyl-β-CD chiral column and the chromatograms were detected between 198 – 241 nm. U-PLC was employed for the evaluation of the chromatograms. It was found that the R-(-)-enantiomer can be determined in tablet formulations at the level of 0.5 mg limits in the presence of 99.9 % of the S-(+)-enantiomer.[40]

Hydroxypropyl-β-CD additive was employed in the HPLC analysis of isoflavone glycosides (calycosine-7-O-β-d-glucoside and formononetin-7-O-β-d-glucoside) and aglycones (calycosin and formononetin). The influence of validation parameters on the retention was investigated in detail. It was established that β-CD reduces considerably the retention of flavone aglycones. It was further assumed that the interaction between analytes and CD results in formation of 1:1 complexes influencing the retention of the analytes. It was further stated that the method can be successfully applied for the separation and quantitative determination of isoflavone glycosides and aglycones in Radix Astragali samples.[41]

The isomerization of perindopril was also determined by HPLC. The isomerization rate constants and Gibbs activation energies of isomerization were directly calculated from the chromatographic peak parameters. The relationships between peak shape and chromatographic conditions (flow-rate, temperature, pH, organic modifier, and the concentration of β-CD were investigated.[42]

Three new β-CD-based chiral stationary phase were synthesized and their separation chatacteristics were determined and compared with each other. The derivatives included in the investigation were: β-cyclodextrin, (R,S)-2-hydroxypropyl-β-cyclodextrin and permethyl-β-CD based The retention behavior of various analytes such as coumarins, dansyl amino acids and propionic acid derivatives was investigated. The measurements indicated that the CD derivatives showed considerably different retention behaviour, the differences in the retention markedly depended on the mode of preparation of the chiral stationary phase (CSP). The best enantiomeric separations were obtained on the stationary phase containing permethylated β-CD. The stationary phases consisted of 0.1 % aqueous triethylammonium phosphate (pH 3.5) and MeOH in different ratios.[43]

Liquid chromatography-tandem mass spectrometry has been employed for the enantioselective separation of hexabromocyclododecane (HBCD) in fish. Analytes were microextracted with a supramolecular solvent (SUPRAS) made of reversed aggregates of decanoic acid. The enantiomers of α-, β-, and γ-HBCD were separated on a chiral stationary phase. Quantitative limit for the determination of indicidual HBCD enentiomers in hake, cod, sole, panga, whiting and sea bass were 0.5 - 3.4 ng g^{-1}; 0.9-2.5 ng g^{-1}; 0.6 – 1.4 ng g^{-1}; 1.0 – 5.6 ng g^{-1}; 0.8 – 1.03; 0.5 - 3.05 ng g^{-1}; respectively. Recoveries ranged 87 – 114 %, the relative standard deviation was between 1–10 %.[44]

The chiral recognition and quantification of propanolol entiomers was achieved by surface enhanced Raman scattering (SERS) combined with multivariate regression analysis. The factors influencing chiral recognition such as nature and concentration of chiral auxiliary, selector – selectand ratio, pH, interaction time, etc. were investigated in detail. It was stated that the SERS method is simple, fast, and accurate and can be employed for the enantiomer analysis of propanolol without the use of tedious and expensive chiral separation technique. It was further established that the data obtained by SERS correlated well with the data obtained by chiral high-performance liquid chromatography.[44]

A poly(dimethyl)siloxane) (PDMS)/β-cyclodextrin (β-CD)/divinylbenzene(DVB)-coated stir bar was prepared for the stir bar extraction of four extrogens from animal-derived foods. Stir bar was prepared by the sol gel technology for the stir-bar sorptive extraction (SBSE). Analytes were preconcentrated by liquid desorption (LD) followed with HPLC. Estrogens were detected by UV. LOD of the method was 0.21 – 1.6 μg L^{-1}, the relative standard deviations varied between 6.0 % and 9.7 %. It was stated that the method was simple, sensitive and was successfully applied for the determination of estrogens in pork and chicken samples.[45]

The current topics and trends in the chiral separation technologies were previously discussed in detail. The application of HPLC, micellar electrokinetic chromatography, counter-current chromatography, capillary-zone-electrophoresis, moving bed chromatography, tandem mass spectrometry, ultra-high pressure chromatography was mentioned. The advantages and disadvantages of the methods mentioned above has also been disussed thoroughly.[46]

The retention behaviour of major isoflavonoids in *Radix Puerariae lobatae* and *Radix Puerariae thomsonii* was analysed by HPLC using CDs as mobile phase modifiers. The flavonoids included into the measurements were puerarin, daidzin, daidzein and genistein. Analytes were separated on a C18 column using isocratic elution. The influence of various chromatographic conditions on the retention such as the nature of the CD, the concentration of HP-β-CD, the amount of methanol in the mobile phase was studied in detail. The best separation was achieved with the mobile phase consisting methanol/water 25:75 containing 5 mM HP-β-cyclodextrin. It was established that the method can be sussessfully applied for the investigation of traditional Chinese herbs.[47]

The pharmacokinetics of Rhizoma Curcumae oil-pure drug (RCO-PD) and its β-cyclodextrin inclusion complex (RCO-β-CD) were determined in pigs after oral administration. The concentration of the active ingredients in the plasma were measured by HPLC using UV detection.

The measurements indicated that the pharmacokinetics of the two preparations shower marked differences, the bioavailability of the RCO-β-CD being higher than that of RCO-PD.[48]

The impact of temperature, ultrasonication, and chiral mobile phase composition on the separation of various analytes has been vigorously investigated. A new technology separated amino acids using CSP (chiral stationary phase) with CMPA (chiral mobile phase additive procedure). Mobile phase additive participating in the experiments were β-CD, γ-CD, and HP-β-CD. Separations were carried out at 25 and 50^0C, with and without sonication.

It was found that the ultrasound decreased at each temperature the elution time and enantioselectivity.[49]

HPLC has also been employed for the enantiomeric separation of nonproteinogenic amino acids. The methods applied up-till now have been resently listed and critically evaluated.[50]

The inclusion of the antibacterial agent thymol on β-cyclodextrin-grafted organic cotton was obtained. It was established that the incorporation of monoterpene thymol into β-cyclodextrin-grafted organic cotton increased considerably the efficacy and durability of the end product. Grafting was carried out using citric acid as crosslinker in the presence of sodium hypophosphite by fixing at 150^0C for 10 min. The efficacy of grafting procedure was verified by visible and FTIR spectroscopy of β-cyclodextrin, β-cyclodextrin-grafted fabric, ungrafted thymol and thymol-loaded fabric. Samples were extracted with ethanol and the concentration of thymol was determined by HPLC. It was established that the inclusion of antibacterial agent into grafted fabric showed marked enhanced antibacterial efficacy even after 10 cycles of washing. The investigations indicated that the grafting of CD on fabric, and inclusion of thymol into their cavity produced a durable antibacterial textile[51].

Surface molecular imprinting technology was employed for the preparation of a highly selective sorbent. Solid-phase extraction followed by HPLC (SPE-HPLC) was employed for the determination of norfloxacin in complicated accompanying matrices. Molecularly imprinted polymer (MIP) was obtained by applying NOF as the template, β-cyclodextrin-methyl-methacrylate (β-CD-MMA) and acrylamide (AM). MIP extracted NOF selectively. The recoveries of the method was high (over 85.7 %). Because of the good validation parameters the method was proposed for the analysis of NOF in fish samples and for the preconcentration of quinolones in real samples[52].

Reversed-phase liquid chromatography was employed for the analysis of resibufogenin and cinobufagin. The separation efficacy of the method was enhanced by adding gamma cyclodextrin to the mobile phase. The parameters influencing the validation parameters were investigated in detail (nature of cyclodextrins and organic modifiers, temperature of column). It was established that the stability of complexes decreased with increasing temperature. The method has been applied for the measurements of resibufogenin and cinobufagin in Chansu (Bufonis venenum) samples.[53]

Thin-layer chromatographic method was applied for the separation and detection of degraded polysaccharides. The hydrolytic oligosaccharides from galactomannan or glucomannan together with pentasaccharide, tetrasaccharide, trisaccharide, and disaccharide were detected in the hydrolyzate.[54]

Abbreviations

ACE-MS	affinity capillary electrophoresis mass spectrometry
ACN	acetonitrile
CD-CSPs	cyclodextrin chiral stationary phases
CEC	capillary electrochromatography
CZE	capillary zone electrophoresis
DIMS	direct infusion mass spectrometry
EKC	electrokinetic chromatography
Es-GC-MS	enantioselective GC-MS
GCxGC	comprehensive two dimensional gas chromatography
GC/MS	gas chromatography/mass spectrometry
HCA	hierarchical cluster analysis
H-DAS-β-CD	Heptakis(2,3-di-O-acetyl-6-O-sulfo)-β-CD
H-DMS-β-CD	Heptakis(2,3-di-O-methyl-6-sulfo)-β-CD
HP-β-CD	hydroxypropyl-β-CD
HRE	heat reflux extraction
HSA	human serum albumin
HS-SPME	headspace solid phase microextraction
LOD	limit of detection
LOQ	limit of quantitation
MAE	microwave-assisted extraction
MD	in vivo microdialysis sampling
MDGC	heart-cut multidimensional gas cromatography
MDMA	3,4-methylenedioxy-methamphetamine
NAIM	saccharide-naphthimidazole derivatives
OT-CEC	open tubular CEC
PCA	principal component analysis
p-CEC	packed-bed CEC
psp-CEC	pseudostationary CEC
QSMR	quantitative structure-mobility relationship
SBE-β-CD	sulfobutylether-β-cyclodextrin
SFC	supercritical fluid chromatography
TAS	Total analysis system
TFC	turbulent-flow chromatography
USE	ultrasonic extraction

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