Chapter 2

Literature review

2.1 Analytical methods for determination of parabens

Various analytical techniques have been developed for determination of parabens in different matrices (including cosmetics, pharmaceuticals, foods, beverages, environmental samples, etc.) such as gas chromatography (GC) (Farajzadeh, Djozan, & Bakhtiyari, 2010; Han, Jia, Liu, Duan, & Chen, 2010; Yang, Tsai, Chen, Yang, & Lee, 2010), high performance liquid chromatography (HPLC) (Casoni, Kot-Wasik, Namieśnik, & Sârbu, 2009; Márquez-Sillero, Aguilera-Herrador, Cárdenas, & Valcárcel, 2010; Núñez, Turiel, Martin-Esteban, & Tadeo, 2010), ultra performance liquid chromatography (UPLC) (Pedrouzo, Borrull, Marcé, & Pocurull, 2009; Wu, Wang, Wang, & Ma, 2008), micellar electrokinetic chromatography (MEKC) (Šafra & Pospíšilová, 2008) and capillary electrophoresis (CE), as given in Table 2.1 (Bianco Prevot, Pramauro, Gallarate, Carlotti, & Orio, 2000; Blanco, Casais, Mejuto, & Cela, 2009; Chu, Wang, Zhang, & Ye, 2010). In order to prepare the parabens suitable for GC analysis, they require transformation into more volatile and thermally stable compounds. Therefore, gas chromatographic separation requires a prior derivatization of the compounds for increasing volatile property. The disadvantages of derivatization step for GC analysis are the requirement of the derivatizing reagent, reaction temperature and reaction time, so it has long analysis time and high operating cost. For example, Shanmugam et al. reported complete derivatization of parabens preservatives in the human breast cancerous tissue at a derivatization time of 30 minutes at 70 ^{o}C with 20 µL of MSTFA, *N*-Methyl-*N*-(trimethylsilyl) trifluoroacetamide, as derivatizing reagent (Shanmugam, Ramaswamy, Radhakrishnan, & Tao, 2010). Although, CE is often a more efficient separation method, this technique requires complicated operation and high operating cost. HPLC techniques, which are available in general laboratory, are therefore more commonly used for parabens determination. The determination of parabens using HPLC could be performed on various detection techniques such as ultraviolet, amperometric and mass spectrometric detections as shown in Table 2.1.

Table 2.1

Review of analytical methods of parabens

Year	Author	Analytes[a]	Samples	Method[b]-Detection[c]	Linearity ($mg\ L^{-1}$)	LOD ($mg\ L^{-1}$)
2007	Garcia-Jimenez	MP, EP, PP, BP	food, beverage and cosmetics	FIA- UV	MP: 0.08-60 EP: 0.38-80 PP: 1.01-80 BP: 2.52-80	MP: 0.03 EP: 0.13 PP: 0.35 BP: 0.85[d]
2009	Ballesta Claver	MP, EP, PP, BP	cosmetics	FIA-CL	MP: 0.15-50 EP: 0.15-55 PP: 0.15-18 BP: 0.15-20	MP: 0.003 EP: 0.005 PP: 0.004 BP: 0.008[e]
2008	Han, F.	MP, EP, PP	cosmetics	FIA-MEKC-UV	2.0-500	0.07-0.1[e]
2000	Driouich	MP, EP, *i*-PP, *n*-PP, *i*-BP, *n*-BP	pharmaceuticals	MEKC-UV	1.5-10	0.60-0.78[e]
2001	Mahuzier	MP, EP, PP, BP	pharmaceuticals	MEEKC-UV	500-1500	50[e]
2003	Huang	MP, EP, PP, BP	pharmaceuticals and cosmetics	MEKC-UV MEEKC-UV	5.0-100 5.0-100	0.04-0.77 0.13-1.49[e]

Table 2.1 (Continued)

Year	Author	Analytes[a]	Samples	Method[b]-Detection[c]	Linearity ($mg\ L^{-1}$)	LOD ($mg\ L^{-1}$)
2006	Hamoudova	MP, PP	pharmaceuticals	MEKC-UV	MP: 10-100 PP: 2.5-25	MP: 0.12 PP: 0.10[e]
2006	He	MP, EP, PP, BP	cosmetics	MEKC-UV	0.15-10	0.046-0.058[e]
2008	Safra	MP, PP	pharmaceuticals	MEKC-UV	MP: 2.0-40 PP: 1.0-20	MP: 0.38 PP: 0.53[d]
2001	Jinno	MP, EP, PP, BP	-	CEC-UV	25-200	-
2009	Blanco	MP, EP, PP, BP, BzP	surface and wastewaters	CE- UV	0.005-1	0.0018-0.0023[e]
2010	Chu	MP, EP, PP, BP	food samples	CE-AD	0.5-50	0.044-0.057[e]
2010	Farajzadeh	MP, EP, PP	food samples	GC-FID	0.02-30	0.005-0.015[e]
2010	Han, Y.	MP, EP, PP, BP	drinking water and beverage samples	GC-MS	0.002-0.1	0.0005-0.0029[e]
2010	Ramirez	MP, EP, PP, BP	air	GC-MS	0.01-20	0.01-0.3[e]
2010	Shanmugam	MP, EP, PP, BP	human breast cancerous tissue	GC-MS	0.05-0.3	-

Table 2.1 (Continued)

Year	Author	Analytes[a]	Samples	Method[b]-Detection[c]	Linearity ($mg\ L^{-1}$)	LOD ($mg\ L^{-1}$)
2010	Yang	MP, EP, *i*-PP, *n*-PP, *i*-BP, *n*-BP	cosmetics	GC-MS	10-1000	0.5-8.3[d]
2000	Labat	MP, EP, PP, BP	cosmetics	HPLC-UV	1.0-40	0.02-0.05
				CE-UV	5.0-200	016-0.21[e]
2003	Belgaied	PP, BP	pharmaceuticals	HPLC-UV	0.1-200	0.048-0.054[d]
2005	Saad	MP, PP	food samples	HPLC-UV	MP: 3.0-100	MP: 0.3
					PP: 1.0-75	PP: 0.1[e]
2005	Zhang	MP, EP, PP, BP	cosmetics and food samples	HPLC-CL	MP: 0.004-7	MP: 0.0019
					EP: 0.005-9	EP: 0.0027
					PP: 0.006-10	PP: 0.0039
					BP: 0.006-10	BP: 0.0053[e]
2006	Lee	MP, EP, PP, BP	cosmetics	LC-MS	0.02-2.0	0.0047-0.019[e]
2008	Gaona-Galdos	MP, PP	cosmetics	HPLC-UV	MP: 30-55	MP: 2.35
					PP: 8.0-18	PP: 0.57[d]
2008	Nunez	MP, EP, PP, BP, BzP	soils and sediments	LC-MS/MS	0.5-50	0.04-0.14[e]

Table 2.1 (Continued)

Year	Author	Analytes[a]	Samples	Method[b]-Detection[c]	Linearity ($mg\ L^{-1}$)	LOD ($mg\ L^{-1}$)
2008	Vidovic	MP	pharmaceuticals	HPLC-UV	100.4-300.8	0.1[d]
2009	González-Mariño	MP, EP, *i*-PP, *n*-PP, *i*-BP, *n*-BP, BzP	surface waters	LC-MS/MS	0.2-0.8	-
2009	Labbozzetta	MP, PP	pharmaceuticals	HPLC-UV	80-120	-
2010	Beltran	MP, EP, BP, BzP	river water	HPLC-UV	-	0.001[e]
2010	Márquez-Sillero	MP, EP, PP, BP	cosmetics	HPLC-C-CAD	MP: 5.3-400 EP: 4.6-400 PP: 3.0-400 BP: 2.0-400	MP: 2.1 EP: 1.5 PP: 0.7 BP: 0.5[e]
2010	Melo	MP, EP, PP, BP	cosmetics	HPLC-UV	MP: 0.2-2.5 EP: 0.15-2.5 PP: 0.05-2.5 BP: 0.03-2.5	-
2010	Nunez	MP, EP, *i*-PP, *n*-PP, *i*-BP, *n*-BP, BzP	soils and sediments	HPLC-UV	0.5-25	0.16-0.33[d]

Table 2.1 (Continued)

Year	Author	Analytes[a]	Samples	Method[b]-Detection[c]	Linearity ($mg\ L^{-1}$)	LOD ($mg\ L^{-1}$)
2010	Shabir	MP, EP, PP	pharmaceuticals	HPLC-UV	MP: 45-245 EP: 20-50 PP: 6-30	-
2010	Shabir	PP	pharmaceuticals	HPLC-UV	5.0-30	0.22[d]
2010	Zotou	MP, EP, PP, *i*-BP, *n*-BP	human saliva and toothpaste	HPLC-UV	0.3-50	0.1-0.2[e]
2008	Wu	MP, EP, PP, *i*-BP, *n*-BP	cosmetics	UPLC-UV	-	0.05-0.25[d]
2009	Pedrouzo	MP, EP, PP, BzP	surface waters	UPLC-MS/MS	3.0-5000	1.0[d]
2010	Manuela	MP	earthworm	UPLC-UV	0.1-10	0.045[e]

[a] MP: methyl paraben; EP: ethyl paraben; PP: propyl paraben; BP: butyl paraben; BzP: benzyl paraben

[b] FIA: flow injection analysis; MEKC: micellar electrokinetic chromatography; MEEKC: microemulsion electrokinetic chromatography; CEC: capillary electrochromatography; CE: capillary electrophoresis; GC: gas chromatography; HPLC: high-performance liquid chromatography

[c] UV: Ultraviolet detection; CL: Chemiluminescence detection; AD: Amperometric detection; FID: Flame ionization detection; MS: Mass spectrometry; C-CAD: Corona-charged aerosol detector

The limit of detection (LOD) is an estimation of 3σ[d] and 3S/N[e].

Most HPLC techniques for the determination of parabens have been reported the use of organic solvent as mobile phase incorporating to the conventional analytical column as shown in Table 2.2. In 2006, Lee et al. reported the use of C18 column, 250 mm length, 4.6 mm i.d. and methanol:water as mobile phase (Lee, Lin, Li, & Tsai, 2006). In 2008, Gaona-Galdos et al. reported the use of C18 column, 300 mm length, 3.9 mm i.d. and methanol:water as mobile phase (Gaona-Galdos, García, Aurora-Prado, Santoro, & Kedor-Hackmann, 2008). In 2010, Márquez-Sillero et al. reported the use of C18 column, 250 mm length, 4.6 mm i.d. and acetonitrile:water as mobile phase (Márquez-Sillero, et al., 2010). The conventional analytical columns in HPLC are expensive and long length column, thus the analysis time is quite long (Table 2.2). Moreover, the uses of organic mobile phases such as methanol and/or acetonitrile, etc., are toxicity.

In recent years, the use of micellar mobile phase in reverse phase high performance liquid chromatography (RPLC), instead of conventional organic mobile phases, has grown rapidly because of the biodegradability and lower toxicity of surfactants than the conventional organic mobile phases. This technique is termed micellar liquid chromatography (MLC) (Armstrong & Henry, 1980; Vlasenko, Loginova, & Iwashchenko, 2009). They have a few micellar liquid chromatographic methods for parabens analysis, as given in Table 2.3. (Noguera-Orti, Villanueva-Camanas, & Ramis-Ramos, 1999).

In 2005, Memon et al. developed the determination of parabens in cosmetics (shampoos, hand lotions, creams, and bath foam) and food samples (tomato ketchup, soya sauce, chicken spread, drinking syrup) by micellar liquid chromatography. The developed method consisted of Lichrosorb ODS, 250 mm length, 4.6 mm i.d., 5 µm column and aqueous 2% Brij-35 adjusted to pH 3.0 with phosphoric acid:propanol (80:20, v/v) as mobile phase at a flow rate of 1.0 mL min^{-1} and UV detection at 254 nm. The cosmetics and food samples were extracted by *n*-propanol before injected to the system. A linear calibration curve was obtained simultaneously for each component in the range of 5-150 mg L^{-1} and detection limits were within 0.025-0.050 mg L^{-1} (3S/N) (Memon, Bhanger, & Khuhawer, 2005).

In 2008, Kulikov et al. presented micellar liquid chromatographic method for the simultaneous analysis of cough-drop pharmaceutical formulations (syrups)

containing some active ingredients (paracetamol, caffeine, guaifenesin) and preservatives (methyl paraben, propyl paraben, sodium benzoate). The separation was effective by using the Kromasil C18 column, 150 mm length, 4.6 mm i.d., 5 µm and a mobile phase of 1-butanol:water (1:99, v/v), containing 0.04 mol L^{-1} sodium dodecyl sulfate and 0.1% (v/v) trichloroacetic acid at a flow rate of 1.0 mL min^{-1}, and UV detection at 260 nm for eluting all compounds. The syrups were extracted by mobile phase before injected into the chromatographic system. The calibration curves of methyl and propyl paraben were linear in the range of 5-94 and 2-42 mg L^{-1}, respectively. The detection limits of methyl and propyl paraben were 0.29 and 0.75 mg L^{-1} (3σ), respectively (Kulikov & Verushkin, 2008).

Although, Memon et al. (2005) and Kulikov et al. (2008) developed the chromatographic methods consisting of micellar mobile phase instead of conventional organic mobile phases, but both methods also used the conventional analytical columns which are expensive and long length columns. Thus, the analysis time is quite long and consumption of solvent used as mobile phase is also quite high (Table 2.3). The proposed methods of Memon and Kulikov were achieved in less than 30 and 25 minutes, respectively.

In 2003, Youngvises et al. reported the use of micellar mobile phase incorporating to a short column which normally used as guard column instead of expensive and common analytical column. The proposed method consisted of C18 column, 12.5 mm length, 4.6 mm i.d., 5 µm particle size and a mixture of aqueous sodium dodecyl sulfate solution (0.075 mol L^{-1}) and isopropanol (7.5 %v/v) as mobile phase with a flow rate of 0.7 ml min^{-1} and detection at 210 nm. The method was developed for the simultaneous separation and determination of lidocaine hydrochloride (LD HCl) and tolperisone hydrochloride (TP HCl) in various pharmaceutical preparations which achieved in less than 7.5 minutes and solvent consumption was 5.25 mL. Moreover, a green extractant, sodium dodecyl sulfate was used to extract the compounds in pharmaceutical preparations, instead of organic solvent (Youngvises, Liawruangrath, & Liawruangrath, 2003). Therefore, this method illustrated that it is not only an inexpensive method but also a greener analytical method (Armenta, Garrigues, & de la Guardia, 2008).

Most sample preparations for determination of parabens have been reported the used of extractant for extracted parabens from the samples (liquid-liquid extraction). Moreover, the sample clean-up for parabens analysis were solid phase extraction (Márquez-Sillero, et al., 2010), supercritical fluid extraction (Lee, et al., 2006) and stir bar sorptive extraction (Melo & Queiroz, 2010). The sample pretreatments for parabens analysis are shown in Table 2.2. The disadvantages of solid phase extraction, supercritical fluid extraction and stir bar sorptive extraction were high operating cost and long time sample preparation.

In this work, micellar liquid chromatography was developed incorporating with C18 guard column instead of expensive and common analytical column C18, and using surfactant as micellar mobile phase such as anionic surfactant (sodium dodecyl sulfate, SDS) and/or cationic surfactant (hexadecyltrimethylammonium bromide, CTAB) instead of conventional organic mobile phases due to their low toxicity. Therefore, the developed method is a green analytical method and friendly to environment.

2.1.1 Aims

i) To investigate the possibility of using C18 guard column as an analytical column in micellar liquid chromatography with UV detection and surfactant as mobile phase for determination of methyl paraben, ethyl paraben, propyl paraben and butyl paraben.

ii) To apply the developed method for parabens contents in cosmetics.

2.1.2 Scope of this part

In this work, the chromatographic behavior of parabens on C18 guard column was studied. Concentration of micellar mobile phase and flow rate were optimized by simplex optimization method. The use of surfactant as the extractant for sample clean-up and analytical features of this method were also studied. The developed method was applied for separation and detection of methyl paraben, ethyl paraben, propyl paraben and butyl paraben in cosmetics.

Table 2.2

Review of parabens determination in cosmetics by LC techniques

Author	Parabens	LC condition					Sample pretreatment[b]	Linearity (mg L^{-1})	LOD (mg L^{-1})	Analysis time (min)	Solvent consumption (mL)
		Column	Mobile phase	Flow (mL min^{-1})	Sample loop (µL)	Detection[a]					
Labat (2000)	MP EP PP BP	C18 (125x4.0 mm, 5 µm)	MeOH:1% CH_3COOH	1.0	20	UV (260 nm)	LLE (ether-1% CH_3COOH)	1.0-40 1.0-40 1.0-40 1.0-40	0.02 0.03 0.03 0.05[d]	20	20
Zhang (2005)	MP EP PP BP	C8 (150x4.6 mm, 5 µm)	MeOH:H_2O (60:40)	1.0	100	CL	LLE (MeOH)	0.004-7 0.005-9 0.006-10 0.006-10	0.0019 0.0027 0.0039 0.0053[d]	9	9
Lee (2006)	MP EP PP BP	C18 (250x4.6 mm, 5 µm)	MeOH:H_2O (gradient)	0.9 and 1.25	5	MS	SFE	0.01-1.0 0.02-2.0 0.02-2.0 0.02-2.0	0.0047 0.0135 0.0134 0.0193[d]	12	10.8-15

Table 2.2 (Continued)

Author	Parabens	LC condition					Sample pretreatment[b]	Linearity (mg L^{-1})	LOD (mg L^{-1})	Analysis time (min)	Solvent consumption (mL)
		Column	Mobile phase	Flow (mL min^{-1})	Sample loop (µL)	Detection[a]					
Gaona-Galdos (2008)	MP PP	C18 (300x3.9 mm, 10 µm)	MeOH:H_2O (gradient)	1.4	20	UV (220 nm)	LLE (MeOH:H_2O 50:50)	30-55 8.0-18	2.35 0.57[c]	14	19.6
Márquez-Sillero (2010)	MP EP PP BP	C18 (250x4.6 mm, 5 µm)	CH_3CN:H_2O (50:50)	0.5	20	C-CAD	SPE (carbon nanotubes)	5.3-400 4.6-400 3.0-400 2.0-400	2.1 1.5 0.7 0.5[d]	25	12.5
Melo (2010)	MP EP PP BP	C18 (125x4.0 mm, 5 µm)	MeOH:H_2O (70:30)	1.0	20	UV (250 nm)	SBSE	0.2-2.5 0.15-2.5 0.05-2.5 0.03-2.5	-	6.5	6.5

Table 2.2 (Continued)

Author	Parabens	LC condition					Sample pretreatment[b]	Linearity (mg L^{-1})	LOD (mg L^{-1})	Analysis time (min)	Solvent consumption (mL)
		Column	Mobile phase	Flow (mL min^{-1})	Sample loop (µL)	Detection[a]					
Zotou (2010)	MP EP PP *i*-BP *n*-BP	monolith (50x4.6 mm)	$CH_3CN:H_2O$ (gradient)	3.0	10	UV (254 nm)	SPE (RP-C18)	0.3-50 0.3-50 0.3-50 0.6-50 0.6-50	0.1 0.1 0.1 0.2 0.2[d]	15	45

[a] UV: Ultraviolet detection; CL: Chemiluminescence detection; MS: Mass spectrometry; C-CAD: Corona-charged aerosol detector

[b] LLE: liquid-liquid extraction; SFE: supercritical fluid extraction; SPE: solid phase extraction; SBSE: stir bar sorptive extraction

The limit of detection (LOD) is an estimation of 3σ[c] and 3S/N[d].

Table 2.3

Review of parabens determination in cosmetics by MLC techniques

Author	Parabens	LC condition					Sample pretreatment[b]	Linearity (mg L^{-1})	LOD (mg L^{-1})	Analysis time (min)	Solvent consumption (mL)
		Column	Mobile phase	Flow (mL min^{-1})	Sample loop (µL)	Detection[a]					
Noguera-Orti (1999)	MP EP PP BP	C18 (octadecyl silica column)	0.1 M SDS (pH 3.0): n-propanol (97.5:2.5)	-	-	UV (254 nm)	LLE (n-propanol)	-	0.03-0.3[d]	-	-
Memon (2005)	MP EP PP BP	C8 (250x4.6 mm, 5 µm)	2% Brij-35 (pH 3.0): propanol (80:20)	1.0	5	UV (254 nm)	LLE (n-propanol)	5-150 5-150 5-150 10-150	0.025 0.025 0.025 0.050[d]	25	25
Kulikov (2007)	MP PP	C18 (150x4.6 mm, 5 µm)	0.04 M SDS :1-butanol (99:1)	1.0	25	UV (260 nm)	LLE (SDS:1-butanol)	5-94 2-42	0.29 0.75[c]	25	25

[a] UV: Ultraviolet detection; [b] LLE: liquid-liquid extraction; The limit of detection (LOD) is an estimation of 3σ[c] and 3S/N[d].

2.2 Analytical methods for determination of perchlorate

Many reports have been reported the inhibition of perchlorate with the thyroid gland's ability to produce thyroid hormones (Charnley, 2008; James-Walke, Williams, Taylor, & McMillen, 2006). Therefore, the effective and sensitive method for determination of perchlorate in environmental samples such as drinking water, groundwater and soil is required. From the literature survey, the analytical methods can be classified in two groups based on detection technique. The first one is screening methods and another one is confirmatory methods that used the mass spectrometric detection, as shown in Table 2.4.

2.2.1 Screening methods

The screening methods for perchlorate analysis are spectrophotometric method (Burns & Tungkananuruk, 1987; Nabar & Ramachandran, 1959), electrochemical method (ion selective electrode, ISE) (Segui, et al., 2006) and chromatographic method; i.e. ion chromatography (Tian, Dasgupta, & Anderson, 2003) and capillary electrophoresis, as given in Table 2.4 (Breadmore, Haddad, & Fritz, 2001; Haumann, Boden, Mainka, & Jegle, 2000).

In 1987, Burns et al. presented spectrophotometric determination of perchlorate. Perchlorate (0-30 µg) can be determined spectrophotometrically at 639 nm after its adsorptive extraction with Brilliant Green on microcrystalline benzophenone at pH 6.5 after dissolution of the solid phase in benzene (Burns & Tungkananuruk, 1987).

In 2006, Segui et al. proposed the development of miniaturised perchlorate-selective electrodes in thick-film technology. It was found that a range of perchlorate was concentration from 1×10^{-4} to 1×10^{-1} mol L^{-1} with a detection limit of 5×10^{-5} mol L^{-1} (Segui, et al., 2006).

Perchlorate is oxyhalide anion. Therefore, ion chromatography coupled with conductivity detection (CD) is a commonly used for perchlorate analysis. In 2003, Tian et al. developed an IC/CD method coupled with automated on-line preconcentration and preelution for determination of trace perchlorate in high-

salinity water samples. Because CD responds to any species with sufficient conductivity, the lack in specificity will result in a need for confirmatory testing. Severe signal suppression is seen for samples that contain common anions, particularly sulfate and chloride at much higher concentrations than perchlorate. The effects of common anions can be reduced by using conductivity suppression and sample preconcentration techniques. Therefore, a simple and automated system which reported by Tian can improve the problems. Since, the sample is preconcentrated, and less strongly held ions preeluted before the analyte is transferred to the principal separation system, as shown in Figure 2.1. A recovery of 92% was obtained for perchlorate at 25 ppb in the test matrix containing 2000 mg L^{-1} each of SO_4^{2-}, Cl^-, and CO_3^{2-}. However, the disadvantages of this method are complicate and high operating cost.

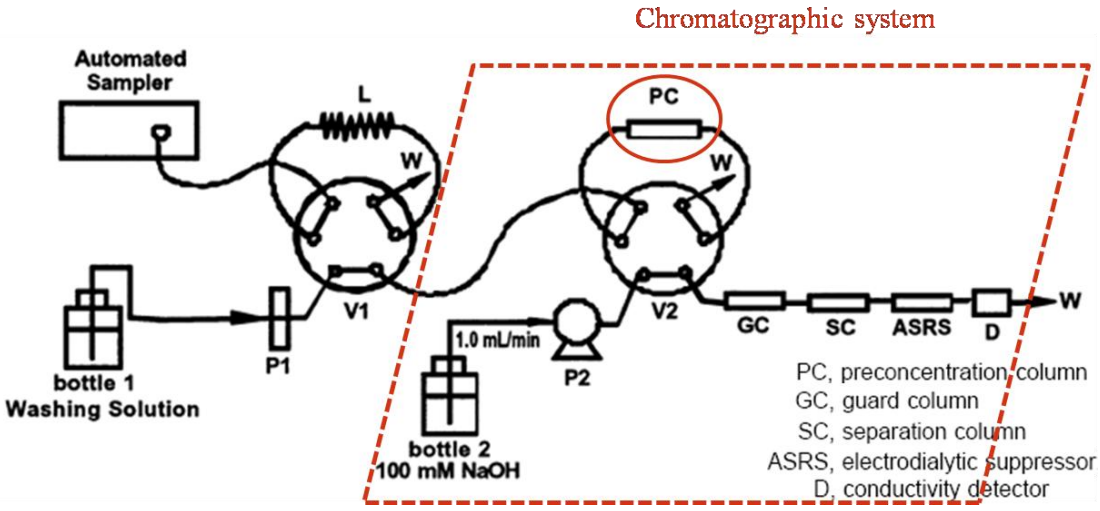

Figure 2.1 Schematic diagram of IC/CD method
(100 mM NaOH as eluent at 1.0 mL min^{-1} and AS16, 4 x 250 mm, as analytical column) (Tian, et al., 2003)

Because of CD responds to any species with sufficient conductivity, thus it has the lack in specificity that will result in a need for confirmatory testing (Jackson, Gokhale, Streib, Rohrer, & Pohl, 2000; Tian, et al., 2003; Winkler, Minteer, & Willey, 2004).

2.2.2 Confirmatory methods

For confirmatory methods review, it can be divided to two groups, which are the first group is the analysis of direct form of perchlorate and another one is the analysis of ion-pairing formation of perchlorate. The first group was carried out by using solid phase extractions for sample pretreatment (Li & George, 2005; Tian, et al., 2003). They are typically used to remove of major common anions and minimize ion suppression caused by the matrix because of the direct analysis of perchlorate. The second groups were carried out by using ion-pairing extraction and post column ion-pairing complexation (Dasgupta & Martinelango, 2007; Magnuson, Urbansky, & Kelty, 2000; Martinelango, Tian, & Dasgupta, 2006; Soukup-Hein, Remsburg, Dasgupta, & Armstrong, 2007). These methods can improve the sensitivity and selectivity of the determination of perchlorate by using electrospray ionization mass spectrometry (ESI-MS). The descriptions are followed and summarized in Table 2.5.

2.2.2.1 Direct form

Due to ion suppression is a well-documented problem associated with ESI, which may adversely affect the accuracy and precision of perchlorate determination, the direct analysis of perchlorate by using electrospray ionization (ESI) MS and MS/MS have been improved the sensitivity and selectivity by common anions removing (Magnuson, et al., 2000). In 2005, Li et al. proposed a reversed phase LC-ESI-MS/MS method for the analysis of perchlorate in drinking water and source water, by incorporating the use of Dionex OnGuard cartridges. The three cartridges in barium, silver, and hydrogen forms in series were used to pretreat the samples which were eliminated potentially high concentrations of common anions prior to analysis, as shown in Figure 2.2. The Ba cartridges were used to remove sulfate (SO_4^{2-}) and phosphate (PO_4^{3-}). The Ag cartridges were used to remove chloride (Cl^-). The H cartridges were used to remove carbonate (CO_3^{2-}) and excess metal ions. These cartridges have been evaluated before use and did not retain perchlorate (Li & George, 2005). However, one disadvantage of pretreating samples with these cartridges is that it increases the analytical cost.

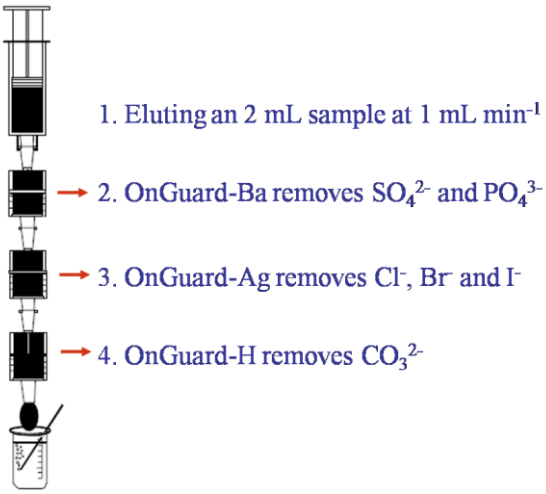

Figure 2.2 Dionex barium, silver and hydrogen OnGuard cartridges in series (Li & George, 2005)

The one problem associated with ESI is ion suppression. For example, small anions with masses below the mass cutoff of the mass spectrometer (specifically ion traps) cannot be detected and generate reside in the region of high chemical noise, which reduced sensitivity compared to larger ions in some mass spectrometers (Henriksen, Juhler, Svensmark, & Cech, 2005; Soukup-Hein, et al., 2007). Furthermore, the direct observation of perchlorate may be limited by the presence of interfering species at the *m*/*z* of the most abundant ion, *m*/*z* 99, i.e., by hydrated bromide $Br(H_2O)^-$ and $H^{34}SO_4^-$ (Magnuson, et al., 2000; Martinelango, et al., 2005). Li also presented $H^{34}S^{16}O_4^-$, $H^{32}S^{18}O^{16}O_3^-$ and $H_2P^{18}O^{16}O_3^-$ that could cause the spectral interferences (*m/z* 99) (Li & George, 2005). Therefore, the use of an ion-pairing reagent to form a complex with perchlorate can improve many problems, using mass spectrometric detection.

2.2.2.2 Ion-interaction (ion-pairing) formation

The improvement of the selectivity and sensitivity for perchlorate analysis is based on the complexation of perchlorate with ion-interaction (ion-pairing) reagents. By observation of a complex at mass > 300 units higher than that of perchlorate, the classical chemical noise region was avoided.

In 2000, Magnuson et al. described the analysis of perchlorate in water by ion-pairing extraction (liquid-liquid extraction) followed by flow injection electrospray mass spectrometry (ESI/MS), as shown in Figure 2.3. Cationic surfactants, mostly alkyltrimethylammonium salts (decyltrimethylammonium bromide, C10), are used to ion-pair aqueous perchlorate, forming extractable ion pairs. The cationic surfactant associates with the perchlorate ion to form a complex detectable by ESI/MS. The selectivity of the extraction and the mass spectrometric detection increases confidence in the identification of perchlorate. The method detection limit of this method for perchlorate based on $3.14\sigma_{n-1}$ of seven replicate injections was 100 ng L^{-1} (Magnuson, et al., 2000). The disadvantages of ion-pairing extraction are reagent consumption and waste generation.

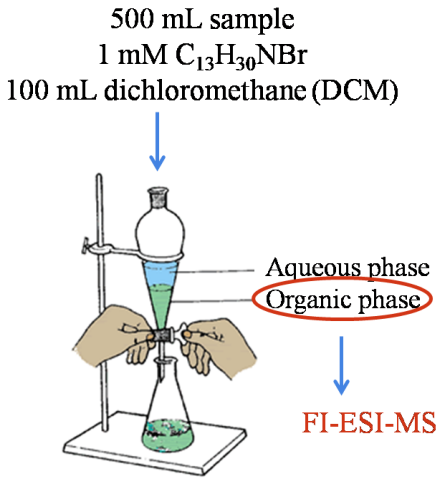

Figure 2.3 Ion-pairing extraction method (Magnuson, et al., 2000)

Some researchers proposed the sensitive and unambiguous methods, post column ion-pairing complexation, for measuring perchlorate using long chain dipositive cationic agent (D^{2+}), as shown in Figure 2.4. Perchlorate is, thus, detected as $DClO_4^+$ in the positive ion mode at an *m/z* value between 300 and 500 (depending on the D^{2+}).

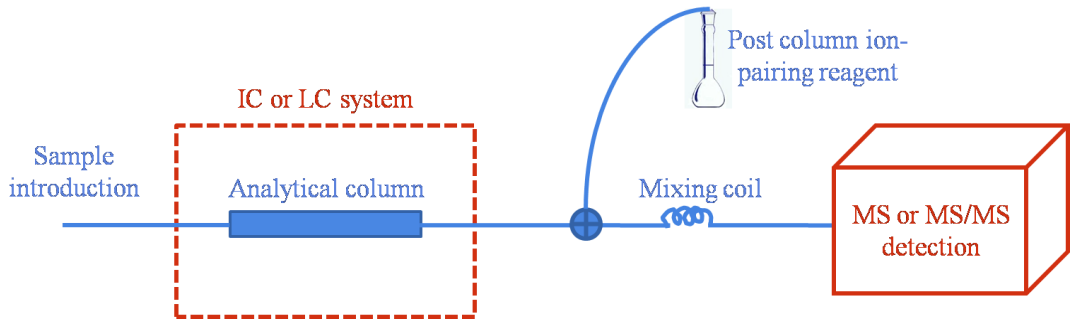

Figure 2.4 Post column ion-pairing complexation
(Martinelango, et al., 2006; Soukup-Hein, et al., 2007)

Compared to higher-*m*/*z* ions, low-*m*/*z* ions are often not as efficiently transferred by ESI due to mass discrimination. Furthermore, background noise tends to be higher at low *m*/*z*. One potential way to convert a low mass analyte to a higher-mass measurand is to form an adduct with a reagent of appreciable mass. If a cationic reagent is used, it must be multiply charged so that one or more net positive charges remain. Any such reagent ion should ideally be dipositive to maximize the *m*/*z* value; namely, the reaction of interest should be equation (2.1).

$$D^{2+} + ClO_4^- \rightarrow DClO_4^+ \qquad \text{.....(2.1)}$$

An optimum reagent ion should bind perchlorate with high affinity and selectivity. If such a positively charged perchlorate adduct can be efficiently generated, sensitivity benefits will also result: positive ions are, in general, more easily detected in ESI-MS.

In 2006, Martinelango et al. reported the results on the perchlorate content of seawater samples. They also reported the iodide and perchlorate concentrations of 11 different species of seaweed growing in the same general region off the coast of Northeastern Maine in USA. The seaweed extracts and the Maine seawater samples, after appropriate dilutions, were analyzed by IC-MS/MS method in the positive ion mode. The separation of perchlorate from matrix was performed using AG16 column. Then 1,12-bis(trimethylammonium)dodecane difluoride (DF_2) reagent (0.2 mmol L^{-1} in water) was introduced through the syringe

pump at a flow rate of 5 μL min^{-1} before entering the MS. The system are shown in Figure 2.4 (Martinelango, et al., 2006).

In 2007, Soukup-Hein et al. proposed a general and sensitive method of detecting singly charged anions by LC-ESI-MS as positive ions. This method utilizes a dicationic reagent, which was synthesized according to Anderson et al. (Anderson, Ding, Ellern, & Armstrong, 2004), to form a complex with the anion that retains an overall positive charge for analysis by MS. The introduction of the dicationic solution in methanol at concentration of 0.04 mmol L^{-1} was located between the column and mass spectrometer, as shown in Figure 2.4 (Soukup-Hein, et al., 2007).

In 2007, Dasgupta et al. measured perchlorate and other hydrophobic ions with a dicationic agent (D^{2+}) to form a positively charged ion pair ($DClO_4^+$). All the dicationic reagents contain a straight aliphatic hydrocarbon chain and tetraalkylammonium end groups with the general structure $Me_3N^+ - (CH_2)_n - NMe_3^+$; n is a number of methyl group. Compound I (n=12) was synthesized and used in previous work (Martinelango, et al., 2005). Compounds II (n=10) and III (n= 6) were both purchased as the dibromide. The on-line preconcentration and preelution method developed by Tian was used for separation (Figure 2.1) (Tian, et al., 2003). Then the dicationic agent was introduced as a postcolumn reagent (PCR) and was monitored in the positive ion mode (Figure 2.4). The results showed that, ion-pairing reagent (Compounds III), 1,6-bis(trimethylammonium)hexane dibromide, can improve the sensitivity and selectivity of single-quadrupole MS methods (Dasgupta & Martinelango, 2007). However, these methods, post column ion-pairing complexation, are quit complicated and are not robustness. Perchlorate is required the clearly separation on chromatographic column prior to formation with ion-paring reagent following detection with mass spectrometer.

In this work, the use of on-column ion-pairing formation in liquid chromatography-electrospray ion trap mass spectrometry (LC-ESI-MS/MS) for determination of perchlorate in environmental samples was therefore developed.

Table 2.4

Review of analytical methods of perchlorate in environmental samples

Type	Year	Author	Samples	Method	Detection	Linearity ($\mu g\ L^{-1}$)	LOD ($\mu g\ L^{-1}$)
Screening method	1959	Nabar	-	Spectrophotometric method	Visible (600 nm)	-	-
	2000	Haumann	drinking water	CE	indirect UV (220 nm)	-	0.8[b]
	2003	Tian	high-salinity water	IC	CD	1-400	0.770[b]
	2006	Segui	water and soil	Electrochemical method (ISE)	-	0.99-990 x 10^4	0.49 x 10^4
Confirmatory method	2004	Winkler	water and soil	LC	MS/MS	0.05-1.0	0.02[b]
	2006	Li	drinking water and groundwater	LC	MS/MS	0.05-10	0.007[a]
	2007	Dasgupta	tab water and groundwater	IC	MS/MS	0.2-10	0.022[b]

The limit of detection (LOD) is based on 3.14σ[a] and $3S/N$[b].

Table 2.5

Review of the analysis of direct form and ion-pairing formation of perchlorate

Type	Year	Author	Sample	Sample preparation	Method[a]-Detection[b]	Linearity ($\mu g\ L^{-1}$)	LOD ($\mu g\ L^{-1}$)
Direct form	2003	Tian	high-salinity water	On-line preconcentration	IC-CD	1-400	0.770[d]
	2005	Li	water	Solid phase extraction (Ba, Ag, H cartridges)	LC-MS/MS	0.02-10	0.009[c]
Ion-pairing formation	2000	Magnuson	drinking water and tab water	Ion-pairing extraction	FI-MS	1-100	0.100[c]
	2006	Martinelango	seawater	Post column ion-pairing complexation	IC-MS/MS	-	0.070[d]
	2007	Soukup-Hein	tab water	Post column ion-pairing complexation	LC-MS/MS	-	0.010[d]
	2007	Dasgupta	tab water, groundwater, milk and seaweed	Post column ion-pairing complexation	IC-MS	0.2-10	0.022[d]

[a] IC: ion chromatography; LC: liquid chromatography; FI: flow injection

[b] CD: conductivity detection; MS: Mass spectrometry

The limit of detection (LOD) is based on 3.14σ[c] and 3S/N[d].

2.2.3 Aims

i) To develop and investigate on-column ion-pairing formation for confirmatory of perchlorate using liquid chromatography with mass spectrometric detection (LC-MS/MS).

ii) To apply the proposed method for determination of perchlorate in environmental samples.

2.2.4 Scope of this part

In this work, a confirmatory and quantitative LC-MS/MS method was developed for perchlorate analysis. Chlorine isotopic ratio and oxygen-labeled sodium perchlorate ($NaCl^{18}O_4$) as internal standard were used for the improvement of specification and sensitivity. Ion-pairing reagent and sample clean-up method were optimized. The proposed method was applied to determine perchlorate in environmental samples such as drinking water, tap water, ground water and soil samples.