ELSEVIER

Journal of Chromatography A, 847 (1999) 1–7

JOURNAL OF CHROMATOGRAPHY A

Identification of plasticizers in medical products by a combined direct thermodesorption–cooled injection system and gas chromatography–mass spectrometry

Hans Günther Wahl[a,*], Andreas Hoffmann[b], Hans-Ulrich Häring[a], Hartmut M. Liebich[a]

[a]*Medizinische Universitätsklinik Abt. IV, Zentrallabor, 72076 Tübingen, Germany*

[b]*Gerstel GmbH, 45473 Mülheim a.d. Ruhr, Germany*

Abstract

The combination of a new thermodesorption module with a cooled injection system now provides a powerful system for direct analysis of volatile trace compounds in gaseous, liquid and solid samples by gas chromatography–mass spectrometry (GC–MS). As a cooled injection system is used for the cryofocusing of the desorbed volatiles the GC–MS system still can be used for the regular analysis of liquid samples. Although plasticizers usually are analyzed by GC–MS after solvent extraction, contaminated solvents and glassware are very well known problems. Analysis of plasticizers in plastic materials by direct thermodesorption instead saves time and avoids cross contaminations. Many medical products are made of plasticized polyvinyl chloride. Extraction of the common plasticizer di(2-ethylhexyl) phthalate (DEHP) into blood will occur, and harmful effects of DEHP in the human body have been suggested. We therefore analyzed 21 different plastic devices which are used for various invasive techniques in medicine by direct thermodesorption GC-MS. In some of the plastics up to 30 different components were identified. By far the most common plasticizer found was DEHP, followed by diethyl and dibutyl phthalates.

Keywords: Thermodesorption; Cooled injection system; Injection methods; Plasticizers; Diethylhexyl phthalate; Phthalates; Poly(vinyl chloride)

1. Introduction

Polyvinylchloride (PVC) is the major durable plastic found in the building and construction trades, but also in the food and drug industries [1]. It has replaced the older rigid plastics in most medical applications. PVC is made flexible by interfusing various plasticizers containing phthalic acid esters such as di(2-ethylhexyl) phthalate (DEHP), which may constitute up to 40% of the finished plastic in medical products. In addition to the plasticizers antioxidants, catalysts, inhibitors and heat stabilizers are frequently added to the plastic [1]. The softer and more pliable the plastic, the more plasticizer present will readily leach into the liquids passing through it [2–6]. This is particularly true for lipid-containing fluids e.g. blood [5,6]. DEHP has been a priority pollutant for several years because of the large quantities produced and its widespread use and occurence in the environment [7]. There have been reports of extraction of DEHP from plastic intravenous infusion sets [2,4–6] into certain infusates and finally into the human body. Patients undergoing hemodialysis are exposed to DEHP via contact of blood with tubing containing DEHP [8,9]. There is great concern about the toxicity of DEHP [9–13] and

*Corresponding author.

0021-9673/99/$ – see front matter
PII: S0021-9673(99)00138-7

its metabolites [14–17], especially for risk groups such as patients on hemodialysis or critical ill patients, where DEHP has been detected in plasma [5,6,8]. Some of the proposed and shown effects are carcinogenity, peroxisome proliferation, mutagenic activity, infertility (toxic effect on Sertoli cells) and changes in lipid metabolism [10–13,15–17].

With the vast need of soft plastic articles for invasive techniques in medicine and the possible toxic effects of DEHP and its metabolites there has been a great effort to find alternatives: Pivipol, a phthalate plasticised PVC, coextruded with polyurethane (Bellco, Italy) shows less leachability of DEHP into blood of dialysis patients due to its inner polyurethane layer [18].

The standard analysis procedure for plastizicer would be solvent extraction and subsequent GC or GC–MS identification [3]. The major problem is the use of solvents which themselves are very often contaminated with plastizicers, especially DEHP. After sample extraction usually the enrichment of the analytes is required prior to the analysis. This is very time-consuming and with an increasing number of analyses this will cause a solvent waste problem.

The method of direct thermodesorption on the other hand is easy to perform and free of contamination as no solvents are introduced. With this technique it is possible to analyze samples over a wide boiling range, like volatiles in pharmaceuticals, fragrances in shampoos and laundry detergents or hydrocarbons in diesel filter paper [19]. We used this newly developed combined direct thermodesorption (TDS)–cooled injection system (CIS) with gas chromatography-mass spectrometry for the identification of plasticizers and other additives in plastic devices used for various invasive techniques in medicine.

2. Experimental

2.1. Samples

Plastic tubings which are used for various invasive techniques in medicine as well as storage containers in different sizes and of different brands, were collected from the local university hospital. Small portions of a few milligrams of the plastic under investigation were put in a blank glass tube for direct thermodesorption GC–MS analysis.

2.2. Instrumentation and operation principles

The system consisted of a thermodesorption system (TDS 2, Gerstel, Mülheim a.d.Ruhr, Germany, Fig. 1), a temperature programmable cooled injection system (CIS 3, Gerstel, Fig. 1) and a gas chromatograph with a mass-selective detector (HP 5890 series II, HP 5972, Hewlett-Packard, Waldbronn, Germany). Cryogenic cooling of the CIS-3 at −150°C was done with liquid nitrogen. A glass tube filled with the sample was inserted into the TDS 2 desorption chamber which was set at 20°C (liquid nitrogen from CIS-3) in order to prevent premature desorption. After purging with the carrier gas (helium) the tube was heated to the desired temperature and the volatiles were transferred in either split- or splitless-mode via a temperaturized transfer capillary into the precooled CIS for cryofocussing. After complete desorption the CIS is then heated up to the desired temperature to allow split or splitless transfer of the trapped volatiles to the analytical column. Fig. 1 shows a schematic drawing of the system employed with the individual components.

2.3. Analysis conditions

Initial temperature of the TDS was 20°C, which was kept for 1.2 min (purge time). Thermodesorption was achieved by raising the temperature of the desorption chamber up to 120°C at a rate of 60°C/min, kept for 10 min. The temperature of the transfer capillary was set at 200°C. During thermodesorption the temperature of the CIS was held at −150°C (liquid nitrogen) to cryofocus the components in solvent venting mode (split) for 11 min. After complete desorption the CIS was switched to splitless mode (1.1 min) and then heated to 280°C at a rate of 12°C/s with a final time of 5 min. After desorption the TDS was kept at 35°C (standby cooling) during the analysis before it was cooled down again to 20°C (initial temperature). A glass liner (I.D. 1.4 mm), partially filled with glass wool was used in the CIS.

A 60 m DB-5 column (I.D.=0.25 mm, d_f=0.25 μm; J&W Scientific, CA, USA) was used for the GC

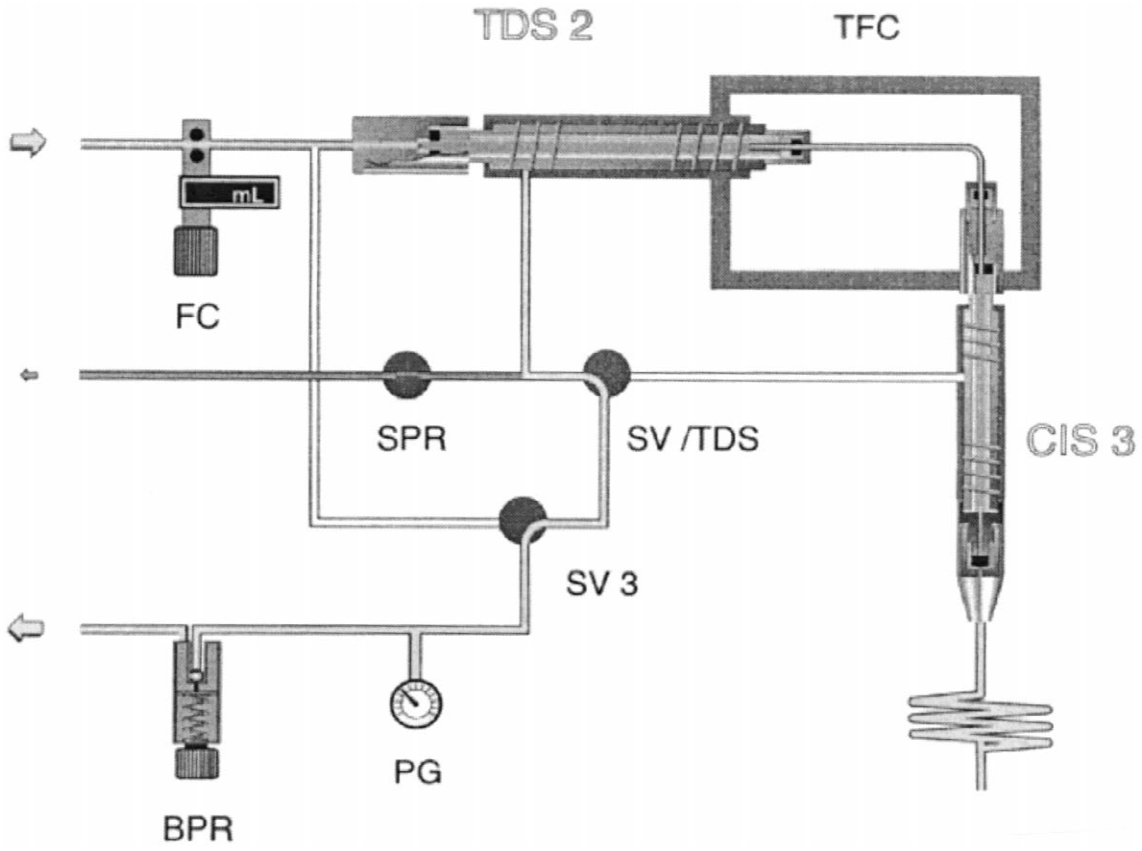

Fig. 1. Gerstel thermodesorption–cooled injection system. TDS 2=Thermodesorption system TFC=temperature controlled transfer capillary CIS 3=cooled injection system FC=mass-flow controller SPR=purge regulator; PG=pressure gauge; SV 3=split/splitless valve SV/TDS=3/2-way solenoid splitflow TDS/CIS; BPR=backpressure.

analysis under the following conditions: 50°C held for 1 min, heated to 300°C at a rate of 10°C/min and hold for 20 min; column head pressure was 120 kPa. The mass-selective detector was operated in full scan mode (electron-impact ionization, 10–350 amu). The MS transfer line was set at 310°C.

3. Results and discussion

For the qualitative comparison of different materials we used the same desorption time of 10 min in solvent venting mode where the analytes were trapped in the CIS (−150°C) while the excess gas passes through the split vent. The volatiles were then transferred splitless (1.1 min) to the GC column. The desorption temperature of 120°C was chosen in order to prevent polymer degradation. Although degradation of PVC occurs at 240°C it becomes elastic at 100°C and HCl cleavage starts at around 150°C. For the quantification of any particular component the analysis conditions would have to be optimized separately. Blank runs between the analyses showed no cross contaminations from the desorption chamber nor from the CIS under the here used conditions.

Depending on the nature of the plastic different plasticizers and additives were found. In some of the plastics up to 30 different components were found (Table 1) and identified with the help of MS libraries (NIST, Wiley PBM Library). By far the most common plasticizer found was DEHP, followed by diethyl and dibutyl phthalates.

In a few dialysis tubings we found cyclohexanone

Table 1
Identified volatiles

Compound	Retention time (min)	Compound	Retention time (min)
Cyclohexane	6.1	Butylated hydroxytoluene (BHT)	18.2
Toluene	7.1	Hexadecane	19.0
2,4-Dimethylheptane	8.0	Diethyl phthalate (DEP)	19.1
2,4-Dimethyl-1-heptene	8.3	Heptadecane	20.1
Styrene	9.1	4,4′-Dichloro-1,1′-biphenyl	20.6
Cyclohexanone	9.3	Octadecene	21.2
Decane	10.8	Octadecane	21.3
2-Ethylhexanoic acid (EHA)	12.5	Diisobutyl phthalate (DIBP)	22.2
Benzoic acid	13.4	Hexadecanoic acid	22.8
Dodecane	13.9	Dibutyl phthalate (DBP)	23.0
Caprolactam	14.7	Eicosane	23.3
Tetradecane	16.6	Butyl 2-ethylhexyl phthalate (BEP)	25.7
Dimethyl phthalate	17.4	Hexanedioic acid, bis (2-ethylhexyl) ester	26.9
Pentadecane	17.8	Di(2-ethylhexyl) phthalate (DEHP)	28.2
2,4-Bis(1,1-dimethylethyl)phenol	18.0		

(Fig. 2), a volatile we had found to be elevated in the urine of dialysis patients and other patients in our clinic [20,21]. The former unknown source of cyclohexanone in these patients might be due to the extraction from the tubing during dialysis or any other infusion. Fig. 3 shows a chromatogram of an infusion set with even more volatiles present and a compared to the plasticizers less amount of cyclohexanone.

Figs. 4 and 5 show chromatograms of syringes used for subcutaneous injections of insulin (Fig. 4) and for subcutaneous injections of heparin (Fig. 5). Although both syringes are quite stiff, look alike and can be used for both insulin and heparin injections the chromatograms reveal their different amounts of DEHP in relation to the other volatiles as well as the presence of different volatiles (butylated hydroxytoluene). Treatment with either one of the syringes probably would lead to different plasma and urine levels of the volatiles in the patients.

From the 21 different plastic articles analyzed (Table 2) phthalates were found mainly in soft

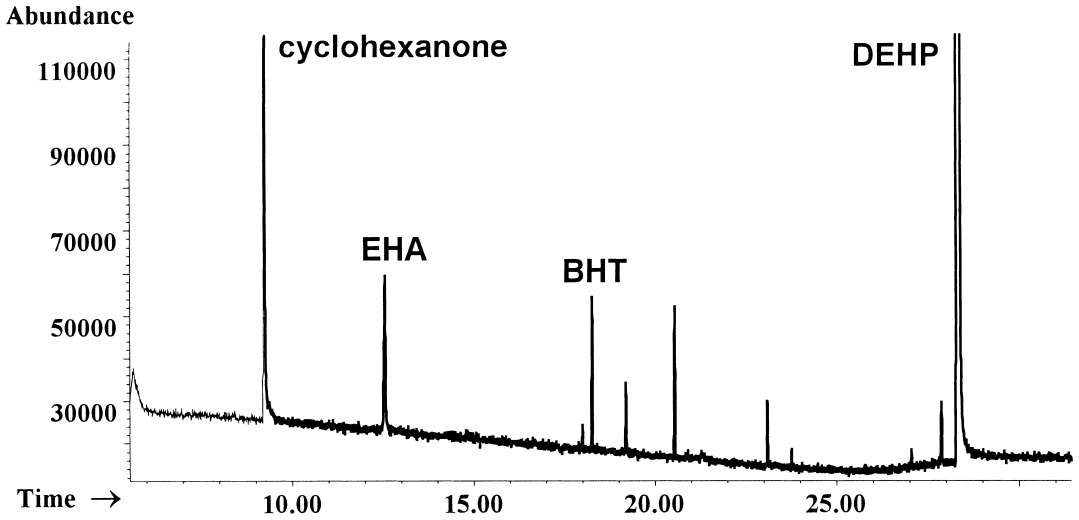

Fig. 2. Chromatogram of a dialysis tubing (GC–MS, scan 10–400 u). For peak identification, see Table 1. Time in min.

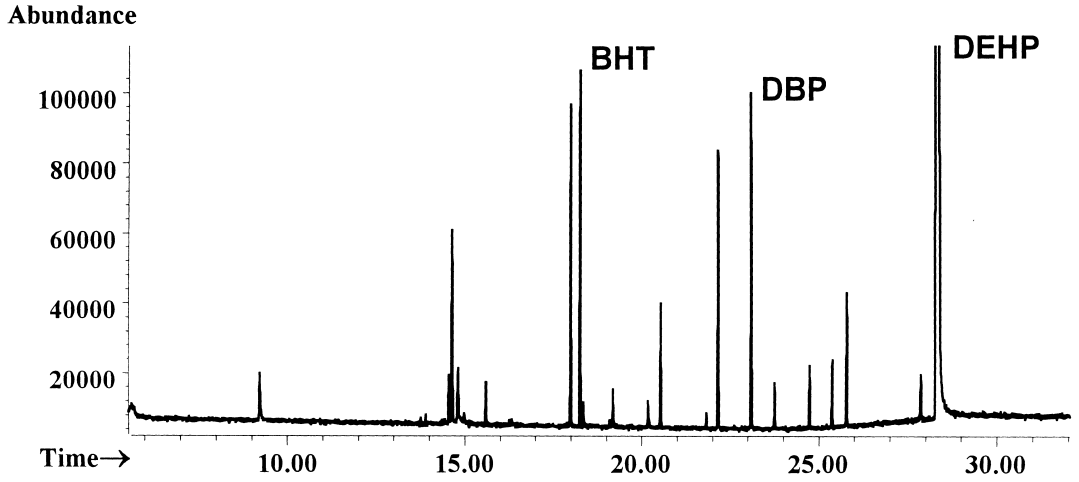

Fig. 3. Chromatogram of an infusion set (GC–MS, scan 10–400 u). For peak identification see Table 1. Time in min.

pliable PVC plastics used for invasive applications. Pipette tips and rigid plastic containers used for urine collection or storage of other liquids, often made of polypropylene, did not contain DEHP. Instead a variety of alkanes, alkenes and BHT were found in large amounts and to a lesser extent DEP and DBP.

This qualitative analysis can be very helpful in identifying possible sources of volatiles found in human plasma and urine as has been shown in the case of cyclohexanone. For further studies of plasticizers uptake and human metabolism the amount of plasticizer found in infusions has to be quantified. If this concept of direct TDS–CIS could be applied to the quantification of plasticizers is under current investigation.

The combined direct TDS–CIS could also be very helpful in the chemical risk assessment in plastic processing due to polymer compound and/or addi-

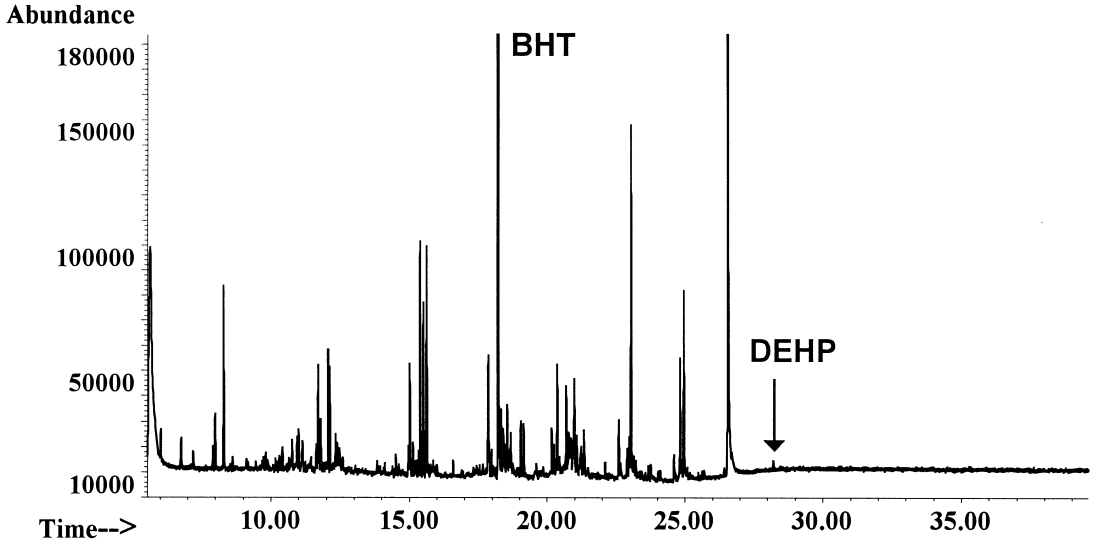

Fig. 4. Chromatogram of a syringe used for subcutaneous insulin injections (GC–MS, scan 10–400 u). For peak identification see Table 1. Time in min.

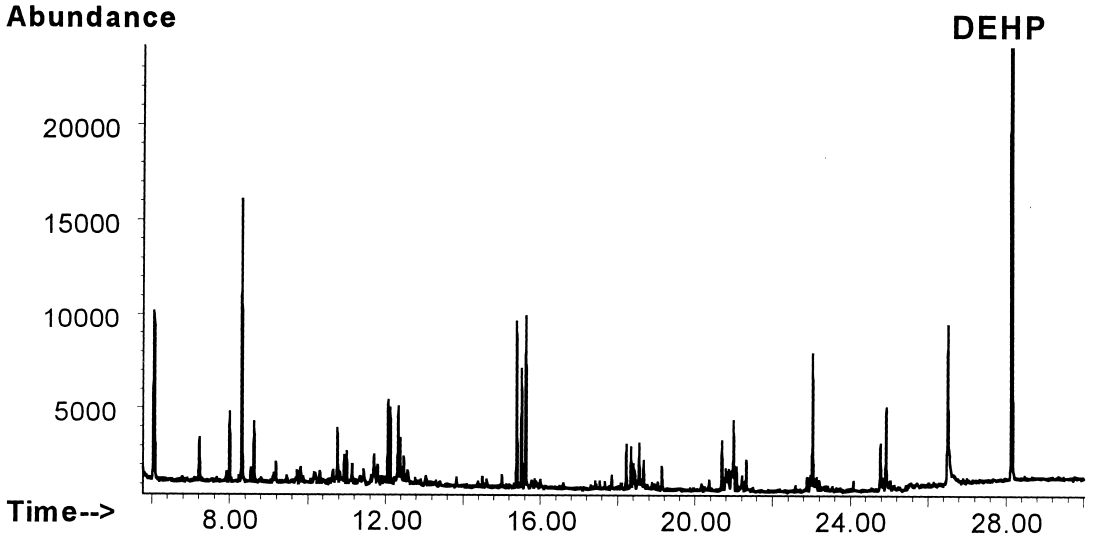

Fig. 5. Chromatogram of a syringe used for subcutaneous heparin injections (GC–MS, scan 10–400 u). For peak identification see Table 1. Time in min.

tives degradation. The temperature of the TDS module would only have to be set to the processing temperature under investigation or to the degradation temperature of the particular polymer. The analysis also could be used for the detection of DEHP or other plasticizers in food wrapping or in the food itself. For the analysis of food one only would have to modify the TDS–CIS combination (e.g. glass liners with adsorbent) due to the higher water content in food.

Table 2
Phthalates identified in medical plastic articles[a]

Plastic article	DEP	DIBP	DBP	BEP	DEHP
Eppendorf pipette tips	x		(x)		
Eppendorf cup	(x)		(x)		
Urine container 100 ml	(x)		(x)		
Urine container 500 ml	(x)		(x)		
Urine container 2500 ml	(x)		(x)		
Urine bag 1500 ml	(x)		(x)		x
Syringe 60 ml	(x)		(x)		(x)
Insulin syringe	(x)		(x)		
Heparin syringe	(x)		(x)		x
Microfilter 40 μl	x		x	(x)	x
Serum monovette	(x)		(x)		
Butterfly	x			x	x
Luerlock obturator	(x)		(x)		x
Infusion tubings	(x)	x	x	x	xx
Infusion bag	(x)		x	(x)	xx
Blood storage bag					xx
Blood infusion tubings	(x)		(x)	x	xx
Intestinal tubings	x		x		x
Dialysis tubings	(x)		(x)		xx

[a] (x)<1%, x<20% and xx>85% of total volatiles.

4. Conclusions

The combined direct TDS–CIS permits a high desorption flow, since the CIS focuses the analytes in the glass inlet liner, while the excess gas passes through the split vent. This causes fast analysis times. Large sample concentration ranges can be accommodated by choosing the appropriate split or splitless mode for desorption and sample transfer. DEHP was found mainly in soft pliable PVC plastics used for invasive applications, dialysis tubings and blood storage bags, but not in rigid plastic containers nor in most syringes.

The thermodesorption method for the direct analysis of plasticizers described here is a convenient way to identify plasticizers and other volatiles of medical plastic tubing, syringes, etc. without the problem of contamination and the excess use of solvents. The method also could be applied for quantification of

volatiles in solids (e.g. plastic, food) and this is under current investigation.

References

[1] W. Tötsch, Nachr. Chem. Tech. Lab. 40 (1992) 715.
[2] V.A. Noah, M. Godin, J. Intraven. Nurs. 17 (1994) 210.
[3] B.D. Page, G.M. Lacroix, Food Addit. Contam. 12 (1995) 129.
[4] M.S. Sharman, W.A. Read, L. Castle, J. Gilbert, Food Addit. Contam. 11 (1994) 375.
[5] L.M. Flaminio, R. Bergia, L. De Angelis et al., Int. J. Artif. Organs 11 (1988) 428.
[6] L.M. Flaminio, L. De Angelis, M. Ferazza, M. Marinovich, G. Galli, C.L. Galli, Int. J. Artif. Organs 11 (1988) 435.
[7] T.J. Wams, Sci. Total. Environ. 66 (1987) 1.
[8] L. Nassberger, A. Arbin, J. Ostelius, Nephron 45 (1987) 286.
[9] G.M. Pollack, J.F. Buchanan, R.L. Slaughter, R.K. Kohli, D.D. Shen, Toxicol. Appl. Pharmacol. 79 (1985) 257.
[10] E. Berman, M. Schlicht, V.C. Moser, R.C. MacPhail, J. Toxicol. Environ. Health 45 (1995) 127.
[11] M.G. Narotsky, R.J. Kavlock, J. Toxicol. Environ. Health 45 (1995) 145.
[12] A.M. Cimini, A. Sulli, S. Stefanini et al., Cell Mol. Biol. Noisy. le. grand. 40 (1994) 1063.
[13] J.F. Crocker, S.H. Safe, P. Acott, J. Toxicol. Environ. Health 23 (1988) 433.
[14] D.W. Arneson, G.O. Kuhn, C.W. Jameson, J. Appl. Toxicol. 15 (1995) 1.
[15] P.J. Deisinger, R.J. Boatman, D. Guest, Xenobiotica 24 (1994) 429.
[16] N.J. Loftus, B.H. Woollen, G.T. Steel, M.F. Wilks, L. Castle, Food Chem. Toxicol. 32 (1994) 1.
[17] H.A. Dirven, P.H. van den Broek, F.J. Jongeneelen, Int. Arch. Occup. Environ. Health 64 (1993) 555.
[18] B. Branger, M. Garreau, G. Baudinand, J.C. Gris, Int. J. Artif. Organs. 13 (10) (1990) 697.
[19] A. Hoffmann, R. Bremer, in: P. Sandra (Ed.), Proceedings of the 16th International Symposium on Capillary Chromatography, Riva del Garda, Hüthig, Heidelberg, 1994, p. 1165.
[20] H.M. Liebich, J. Chromatogr. 112 (1975) 551.
[21] H.M. Liebich, O. Al-Babbili, J. Chromatogr. 112 (1975) 539.