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# Quantitative GC-MS Method for the Determination of Aniline, Chloroaniline and Toluidine Released from Inks of Ballpoint and Fiber-tip Pens

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## Introduction

In Switzerland legal restrictions limit the maximum release of aromatic amines from inks of pens designed for children (1). Recently, we presented a HPLC-method for the determination of such compounds (2). In this paper, we would like to show a further development of our former semi-quantitative gas chromatography-mass spectrometry (GC-MS) method, which was used to confirm the results of HPLC-analysis. GC-MS now allows precise quantification of aniline, chloroaniline and toluidine in inks of ballpoint pens.

## Method

### *Reagents and reference materials*

Methanol p.a. (Merck 1.06009), Hydrochloric acid 25 % p.a. (Merck 1.00316), sodium hydroxide p.a. (Merck 1.06545), toluene p.a. (Merck 1.08325), trifluoro acetic acid anhydride puriss. (TFAA) (Fluka 91719), deuterated aniline-d<sub>5</sub> 99 % (Cambridge Isotope Laboratories DLM-862) CAS-Nr. 4165-61-1, aniline > 99.5 % (Merck 1.01261) CAS-Nr. 62-53-3, o-chloroaniline 98 % (Aldrich C2,239-3) CAS-Nr. 95-51-2, m-chloroaniline 99 % (Aldrich C2,240-7) CAS-Nr. 108-42-9, p-chloroaniline 98 % (Aldrich C2,241-5) CAS-Nr. 106-47-8, o-toluidine purum (Fluka 89610) CAS-Nr. 95-53-4, m-toluidine puriss. (Fluka 89620) CAS-Nr. 108-44-1, p-toluidine puriss. (Fluka 89630) CAS-Nr. 106-49-0.

### *Sample preparation*

Extract samples with 0.07 M HCl as described in (2) and spike with aniline-d5 (final concentration for GC-MS injection 10 ng/ $\mu$ l). After conditioning with 10 ml methanol load a SPE cartridge (C8) with approx. 10 ml raw extract and rinse with 30 ml 0.07 M HCl. Adjust pH of the eluate to > 12 with 5 M NaOH. Shake with 2 x 7 ml of toluene and reject the lower water phase. Add 3 drops of TFAA in order to form amine perfluoroacyl derivatives and evaporate (40 °C) to minimal volume. Redissolve residue in a defined volume of toluene for subsequent GC-MS analysis.

### *Determination by GC-MS*

Identification and determination of amine perfluoroacyl derivatives were performed by GC-MS (Carlo Erba HRGC 5160, Fisons and GCQ, Finnigan MAT) under the following conditions: DB-5MS (J&W) fused silica column (30 m x 0.25 mm I.D., 0.25  $\mu$ m film) with a retention gap (0.5 m x 0.32 mm I.D., deactivated) used with on column injection of 1.0  $\mu$ l; temperature programme 90 °C (1 min.)-(5 °C/min.)-140 °C-(30 °C/min.)-200 °C (5 min.); carrier gas (helium) 60 kPa; Ionization mode: EI (trap offset 10), sec per scan: 0.5, mass range 50-230 amu.

### *Calibration and quality control*

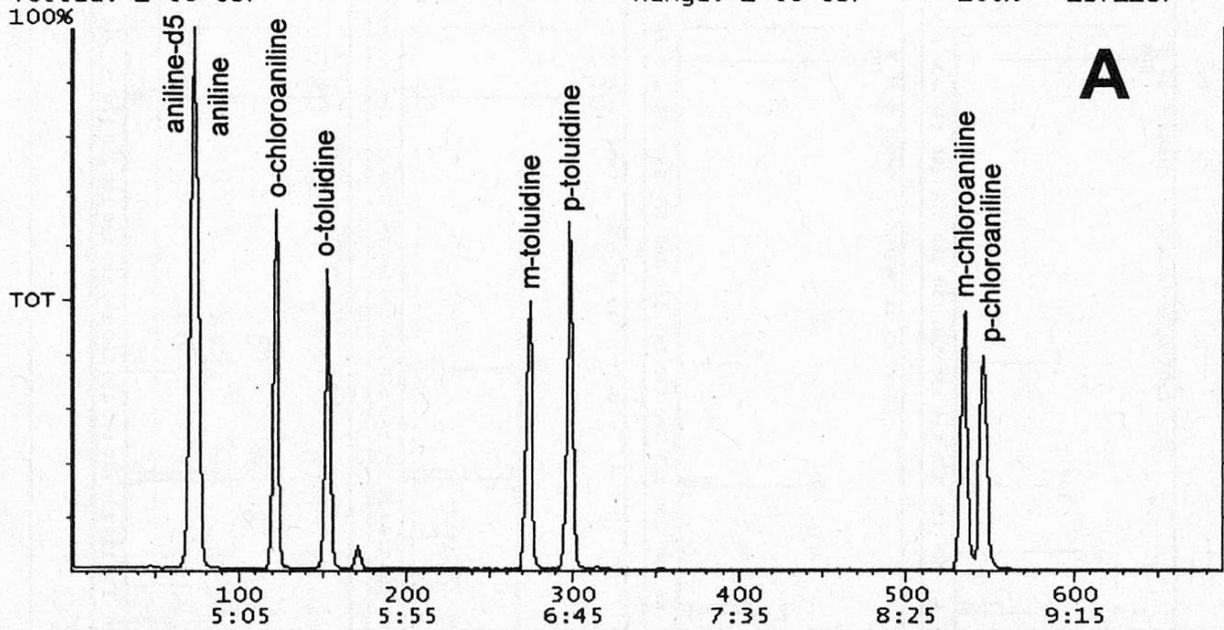
Internal standard calibration was performed with a constant concentration of 10 ng/ $\mu$ l aniline-d5 (quantification mass 194 amu) in each calibration solution (0.5 ml toluene and 2  $\mu$ l TFAA). Aniline (quan. mass 189), o-chloroaniline (quan. mass 188), m-chloroaniline, p-chloroaniline (both quan. mass 223), o-toluidine, m-toluidine and p-toluidine (quan. mass 203) were used for calibration in amounts ranging from 0.2 ng to 10 ng (correlation coefficients  $r > 0.998$ ). Corrections of quantitation were based on the internal aniline-d5 standard. Recovery rates of the standards were between 95 % and 110 %. Reproducibility of four ink sample replicates expressed as mean relative standard deviation of each compound was between 1 and 8 %. The calculated limits of detection ( $s/n > 3$ ) were for all compounds 0.2 mg/kg dry weight of ink in the worst case.

## **Results and Discussion**

### *Gas chromatography and mass spectra of amine derivatives*

The applied GC-MS method allowed the separation of all aromatic amine perfluoroacyl derivatives of interest by retention time in calibration mixtures (fig. 1a) as well as in real ink samples (fig. 1b). With the specific mass traces it was also possible to distinguish between the coeluting deuterated ( $m/z$  194) and unlabelled ( $m/z$  189) anilines (not shown here). The use of deuterated aniline as an internal standard solved our former problems with fluctuations of sensitivity of the mass detector (ion trap) in real ink samples especially. Such effects can now be eliminated making precise quantification possible.

Chromatogram Plot C:\GCQ\DATA\MN\AMIN98\KUGEL304 11/09/98 15:29:29  
 Comment: AMCAL2 5.0 ng 1u1 OC  
 Scan No: 1 Retention Time: 4:15 RIC: 9516 Mass Range: 50 - 92  
 Plotted: 1 to 687 Range: 1 to 687 100% = 1271187



Chromatogram Plot C:\GCQ\DATA\MN\AMIN98\KUGEL310 11/10/98 10:43:18  
 Comment: EX980632 1u1 OC  
 Scan No: 1 Retention Time: 4:15 RIC: 23891 Mass Range: 50 - 109  
 Plotted: 1 to 687 Range: 1 to 687 100% = 3919000

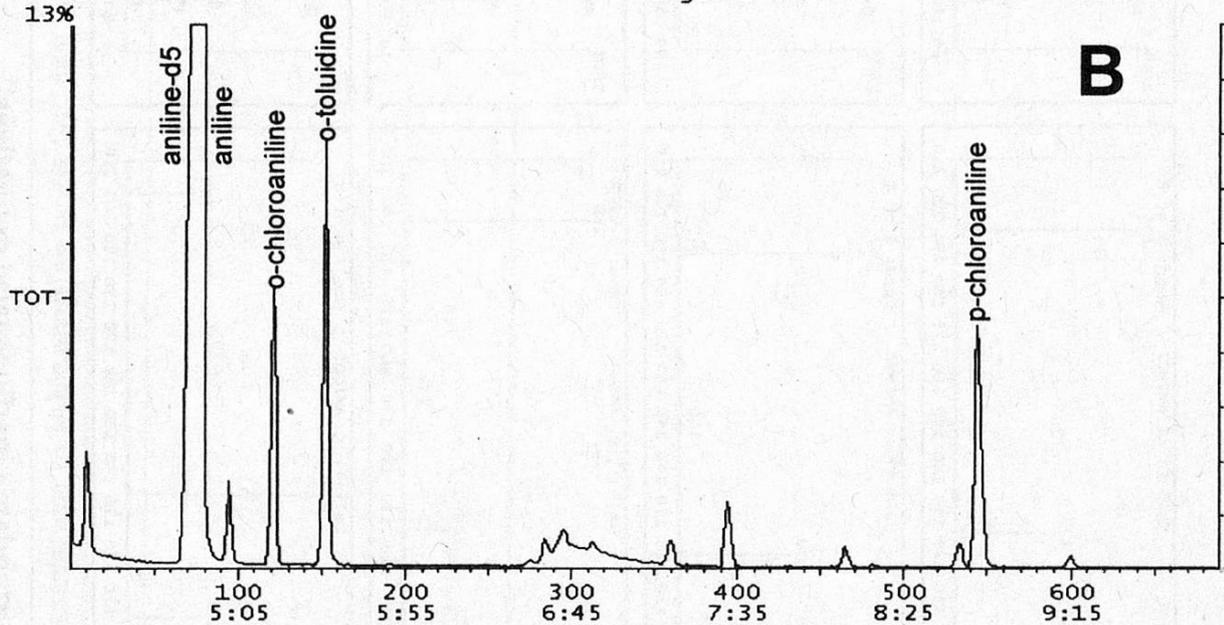


Figure 1 GC-MS run of amine (perfluoroacyl derivative) standard mixture (A) and ink sample (B)

Additionally, we were able to identify each compound according to their specific mass spectra (fig. 2). Eventhough spectra were similar a reliable differentiation between the m- and p-isomers of chloroaniline with differing carcinogenic potentials could be done: The perfluoroacyl derivative of the carcinogenic p-chloroaniline (3) shows an inverse signal ratio of m/z 126 and m/z 154 as well as lacking a signal of m/z 111 compared to the noncarcinogenic m-isomer.

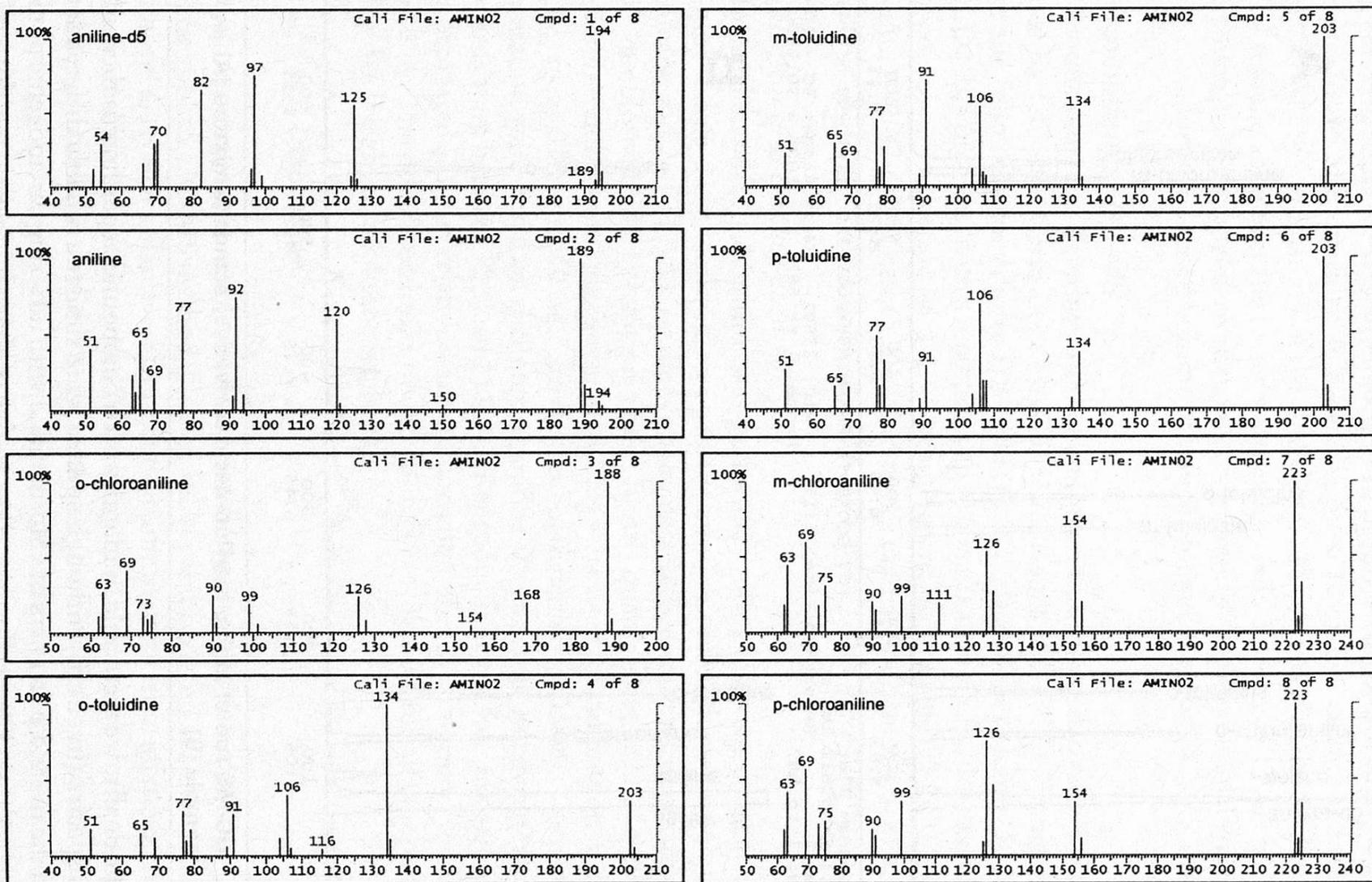


Figure 2 MS spectra of amine standards (perfluoroacetyl derivatives)

**Table 1**  
**Comparison of amine determination in ink samples with GC-MS and HPLC**

	<i>sample</i>	1	2	3	4	5	6	7	8	9	10	<i>correlation</i>
aniline	HPLC	74.5	31.1	567.8	275.6	100.5	64.1	819.9	127.2	99.4	715.0	0.9896
mg/kg dwt	GCMS	80.8	33.3	781.9	272.9	87.0	36.7	885.2	109.3	68.5	826.0	
	ratio %	109	107	138	99	87	57	108	86	69	115	
o-toluidine	HPLC	< 0.7	12.2	44.5	105.9	< 0.7	19.8	65.2	< 0.7	< 0.7	130.0	0.9871
mg/kg dwt	GCMS	< 0.2	9.9	38.7	116.3	< 0.2	9.9	45.3	< 0.2	< 0.2	130.0	
	ratio %		81	87	110		50	70			100	

ratio % = ratio of HPLC to GCMS in percent

dwt = dry weight

## *Comparison of amine determination with GC-MS and HPLC*

Results obtained for aniline and toluidine in inks of ballpoint pens showed good agreement with our HPLC-method (table 1). Ratios (%) of HPLC to GC-MS determination were in an acceptable range with the exception of sample 6. The same was true for p-chloroaniline found in sample 3 and 7 (ratios 107–126 %, not shown in table 1). The two methods are highly correlated for both, aniline and toluidine ( $r > 0.98$ ). Therefore, GC-MS is an excellent alternative method for the determination and confirmation of volatile aromatic amine derivatives in ink samples.

### **Summary**

A GC-MS method concerning the identification and quantitative determination of free aniline, chloroanilines and toluidines in inks of ballpoint and fiber-tip pens is presented. Fluctuations of sensitivity of the mass detector are compensated by using deuterated aniline as an internal standard. O-, m- and p-isomers having different carcinogenic potentials can be discriminated by specific masses of their perfluoroacetyl derivatives. Results obtained for aniline and toluidine in ink samples show good agreement with our HPLC-method.

### **Zusammenfassung**

Es wird eine GC-MS-Methode vorgestellt, mit der freies Anilin, Chloraniline und Toluidine in Kugelschreibertinten sowie in Filz- und Faserstiftflüssigkeiten identifiziert und quantitativ bestimmt werden können. Mit Hilfe von deuteriertem Anilin als internen Standard werden Empfindlichkeitsschwankungen des Massendetektors kompensiert. Aufgrund der spezifischen Massenspektren der Perfluoroacetyl-derivate ist es möglich o-, m- und p-Isomere, welche eine unterschiedliche Kanzerogenität aufweisen, zu unterscheiden. Die Resultate von Anilin und Toluidin in Tintenproben zeigen eine gute Übereinstimmung mit unserer HPLC-Methode.

### **Résumé**

La méthode GC-MS présentée permet d'identifier et de déterminer l'aniline, les chloroanilines et toluidines libres présentes dans les encres de stylos à bille et de stylos-feutre. A l'aide d'un standard interne d'aniline marqué au deutérium on peut compenser les fluctuations de sensibilité du détecteur de masse. Les spectres de masse spécifiques des dérivés de perfluoroacetyl permettent de différencier les isomères o, m et p, qui ont un potentiel cancérogène différent. Les résultats obtenus avec l'aniline et la toluidine dans les échantillons d'encre montrent une bonne corrélation avec notre méthode de chromatographie en phase liquide.

### **Key words**

Aromatic amines, GC-MS, Ink, Ballpoint pen, Fiber-tip pen

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