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Objekttyp: **Article**

Zeitschrift: **Mitteilungen aus Lebensmitteluntersuchungen und Hygiene = Travaux de chimie alimentaire et d'hygiène**

Band (Jahr): **96 (2005)**

Heft 5

PDF erstellt am: **09.08.2024**

Persistenter Link: https://doi.org/10.5169/seals-981958

Determination of carcinogenic aromatic amines in dyes, cosmetics, finger paints and inks for pens and tattoos with LC/MS

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Received 21 April 2005, accepted 1 September 2005

Introduction

Dyes are important if not to say indispensable in adding colour to our everyday life. They are used in a wide array of items and their production is an important economic factor. Aromatic amines represent widely used components in dye synthesis. Some of them, however, proved to be human carcinogens provoking bladder cancer in labourers of dye production plants. As a consequence, legal restrictions were enacted, banning the use of or setting limits for amines and dyes derived from them. Besides foodstuff, detailed regulations also exist for commodities, such as cosmetics, clothes, upholstery and toys. To our knowledge, Switzerland is the only country which has set limits for the release of aromatic amines in inks of writing utensils (1). These limits concern children who may write on their skin or suck on tips of the cartridges. The use of dyestuffs for tattoos has not been restricted so far. However, throughout Europe, implementing specific restrictions is regarded as urgent.

All restrictions concerning consumer goods as well as almost all analytical methods deal only with primary aromatic amines. This may be due to their scope (determination of amines after cleavage of azo dyes) or to the use of colorimetric methods (2–6). Even papers and norms, which deal with determining specific amines as impurities using GC/MS, HPLC or LC/MS mainly mention only them. Tertiary amines, such as michler's ketone (MK; tetramethyl-4,4'-diaminobenzophenone) and methane base (MB; 4,4'-methylenebis-(N,N'-dimethylaniline)) are important educts and intermediates for synthesising triphenylmethane dyes of which victoria blue (C.I. 44045), methyl violet (C.I. 42535) and crystal violet (C.I. 42555) are widely used in ballpoint pen inks. Victoria blue and food green 4 (C.I. 44090) are also allowed as cosmetic ingredients. Both MK and MB are regarded as potentially

carcinogenic (7). We are only aware of three papers which deal with the determination of MK: one investigated the migration of MK from food packaging cardboard (8), the other two determined MK in methyl violet respectively food dyes (9, 10). Auramine O, the imine homologue of MK, is another tertiary amine of toxicological concern. Although banned by the European printing industry on a voluntary basis, it is still used as a yellow dye for ballpoint pen inks in East Asia.

Up to now, sample preparation for checking migration of amines out of inks has been done with gastric juice simulant (diluted hydrochloric acid) presupposing oral contact as the main exposition pathway (11–13). These methods are tedious and eliminate MK during the following clean up process with solid phase extraction, which is essential when analysing with HPLC/DAD or GC/MS. In order to include tertiary amines, clean up procedures and detection methods have to be modified. A reevaluation done by the Federal Office of Public Health in Switzerland however showed, that in the case of ballpoint pens, skin contact is far more relevant. A determination of the total content using organic solvents would therefore better reflect the amount of amines absorbed via the skin from a liquid such as ink. Total extraction also applies to tattoo inks or cosmetics and to the supervision of an European directive which stipulates R45 labelling of technical products (e.g. dyes and inks) containing more than 1000 mg/kg of carcinogenic components (14).

The aim of our work was to develop an LC/MS method which can screen for over 30 aromatic amines in inks and dyes of pens and tattoos, be it with diluted acid or organic solvent as extractant and which can reliably quantify the four amines most often found.

Experimental

Materials and instruments

Analytical balance (AT 200, Mettler Toledo, Greifensee), ultrasonic bath (Branson 3510, Merck, Zürich), centrifuge (Heräus Biofuge Primo, BGB, Anwil), vortex (Genie, Bender & Hobein, Zürich), water bath with stirring units (Huber, Reinach).

Quaternary gradient HPLC system consisting of a low pressure mixing quaternary gradient pump (Surveyor MS), an autosampler with thermostatted column oven (Surveyor AS), a photo diode array detector (Surveyor UV6000LP fitted with 2 µl 10 mm flow cell), an ion trap MS^2 mass spectrometer (LCQ Duo) and a data station (Excalibur), all from Thermo Finnigan (Spectronex, Birsfelden).

Analytical column: Phenomenex Synergi Polar, 4 µm, 150×2 mm (Brechbühler, Schlieren); PVDF-syringe filters, 13 mm diameter, 0.2 µm pore size (Target; Morvay Analytik, Basel).

Chemicals

Methanol for LC/MS was from Riedel-de-Haën (Buchs), water for HPLC was from J.T. Baker (Stähelin, Basel), methanol p.a., formic acid p.a. and hydrochloric acid p.a. were from Merck (Dietikon).

All reference substances listed below were at least of analytical grade. Aniline [62-53-3], o-toluidine [95-53-4], benzidine [92-87-5], methane base (4,4'-methylenebis(N,N'-dimethylaniline)) [101-61-1], michler's ketone (tetramethylaminobenzophenone) [90-94-8], auramine O (4,4'-(imidocarbonyl)-bis-(N,N-dimethylaniline) monohydrochloride) [2465-27-2], 2,5-diaminoanisole as sulfate hydrate [66671-82-7], toluene-2,4-diamine [95-80-7], 4,4'-oxydianiline [101-80-4], 4,4'-methylenedianiline [101-77-9], p-toluidine [106-49-0], p-cresidine [120-71-8], o-dianisidine [119-90-4], o-tolidine [119-93-7], 4-chloro-o-toluidine [95-69-2], 5-chloro-o-toluidine [95-79-4], 4-aminobiphenyl [92-67-1], methylene-bis-(2-methylaniline) [838-88-0] all from Fluka (Buchs); 2-aminonaphthalene [91-59-8], 1-aminonaphthalene [134-32-7], 4-chloroaniline [106-47-8], 2,4-diaminoanisole [615-05-4] as sulfate hydrate, o-anisidine [90-04-0], p-anisidine [104-94-9], 4,4'-thiodianiline [139-65-1], p-phenylenediamine [106-50-3] as dihydrochloride, m-phenylenediamine [108-45-2], o-phenylenediamine [95-54-5], methylene-bis-(2,6-dimethylaniline) [4073-98-7], 1,5-diaminonaphthalene [2243-62-1] were all from Aldrich (Buchs); o-aminoazotoluene [97-56-3] was from Sigma (Buchs); 2,4,5-trimethylaniline [137-17-7] was from Riedel-de-Haën (Buchs), 3,3'-dichlorbenzidine [91-94-1] as dihydrochloride and 4,4'-methylene-bis-(2-chloroaniline) [101-14-4] were both from Pfaltz & Bauer (Brunschwig, Basel).

Procedures

Calibration and quality assurance

25 ml solutions of 50 mg of each aromatic amine in methanol were prepared. Standard calibration was performed with aniline, o-toluidine, benzidine, MB and MK. The solutions of these five amines are stable for at least one month if stored in the dark at 4 °C.

For determination of the total content 0.1 to 10 ng/µl (MB and benzidine) rsp. 0.25 to 25 ng/µl (aniline, o-toluidine, MK) calibration solutions were prepared by diluting with methanol. 1 µl was injected. For determining migration into gastric juice simulant, dilution must be performed with 0.07 M hydrochloric acid and 1 µl was injected.

Checks with a 1 ng/µl calibration solution were run at least after every 6th sample. The ratios of required values to actual values were used to correct for potential response factor drifts during the corresponding interval.

Sample preparation for total extraction

20 mg of dye, 100 mg of ballpoint pen ink, 1000 mg of fiber tip pen ink, tattoo ink, cosmetic or finger paint were weighed into a 50 ml Erlenmeyer flask. 20 ml of methanol were added and the solution vortexed thoroughly for one minute. The sample solution was then sonicated for 15 minutes in an ultrasonic bath at room temperature and filtered through a 0.2 µm PVDF HPLC filter into a HPLC glass vial. The first two milliliters were rejected. 1 µl of this solution was injected.

Sample preparation for migration tests with gastric juice simulant

Sample extraction was performed according to (13). The raw extract, however, was only filtered as described above without SPE clean-up or pH adjustment. 5 µl were injected for screening and 1 µl for quantitation.

Methods

HPLC parameters

HPLC analysis was performed with a gradient elution as described in table 1. Flow rate was 0.3 ml/min, run time was 27 minutes and column temperature was 20 °C.

Table 1
Gradient time table

time/min	*0.1 % HCOOH in water**	*0.1 % HCOOH in methanol**
0	100 %	0 %
3	100 %	0 %
14.9	10 %	90 %
21.9	10 %	90 %
22	100 %	0 %
27	100 %	0 %

*1 ml of formic acid are made up to 1 l with water or methanol

Spectra were recorded in the scan range of 220 nm to 600 nm, with a bandwidth and a resolution of 1 nm at a rate of 1 Hz. One discrete channel at 372 nm was recorded with a scan rate of 10 Hz and a bandwidth of 5 nm for cross-checking the quantitation of MK with DAD.

MS parameters

Quantitation was performed in the atmospheric pressure chemical ionisation (APCI) positive mode. Vaporizer temperature was set at 400 °C, heated transfer capillary temperature at 190 °C. Sheath gas flow was held at a rate of 38 arbitrary units, no auxiliary gas was used. Source voltage was set at 6 kV, source current was set at 5 µA and capillary voltage was set at 37 V. Scan filters and detection masses are listed in table 2. 2 to 5 parallel MS experiments (events) were performed in 13 time segments. For segments with 4 parallel scan events, at least 5 to 7 measuring points were still recorded – depending on peak width and concentration. For quantitative determinations, the number of parallel experiments was reduced to a maximum of 3.

Results and discussion

Chromatography and detection

Screening for over 30 substances made compromises between separation efficiency and sensitivity inevitable. Although many HPLC phases show a high reten-

Table 2
MS parameters for data acquisition and detection

Time min	*Scan Event Details: APCI(+)*	*Analytes*	*MH+*	*Detection masses*	*Rt min*
0.0–23.0	MS [90–390]	(full scan for spectra)			
0.0–2.6	MS [93.5–95.5]	aniline	94	93.7–94.3	2.1
0.0–2.6	MS2 [138.7–139.7]@30 [50–140]	2,5-diaminoanisole	139	107+108+124	1.5
		2,4-diaminoanisole	139	107+108+124	2.2
0.0–10.6	MS [107.8–124.5]	o-toluidine	108	107.8–108.4	4.2
		p-toluidine	108	107.8–108.4	4.4
		m-toluidine	108	107.8–108.4	4.6
		p-phenylenediamine	109	108.9–109.2	1.3
		m-phenylenediamine	109	108.9–109.2	1.5
		o-phenylenediamine	109	108.9–109.2	2.2
		2,4-xylidine	122	121.5–122.5	8.9
		2,6-xylidine	122	121.5–122.5	10.1
		2,4-diaminotoluene	123	122.5–123.5	2.1
		p-anisidine	124	123.5–124.5	3.8
		o-anisidine	124	123.5–124.5	4.4
2.6–4.6	MS [158.6–159.6]	1,5-diaminonaphthalene	159	158.6–159.6	3.8
2.6–4.6	MS2 [198.0–202.0]@35 [55–220]	4,4'-diaminodiphenylmethane	199	105.5–106.5	4.1
		4,4'-oxydianiline	201	107.5–108.5	3.1
4.6–6.0	MS2 [184.7–185.7]@40 [50.0–200.0]	benzidine	185	167.5–168.5	5.0
6.0–9.2	MS [127.5–130.5]	4-chloroaniline	128	127.7–128.7	7.8
	MS [137.8–138.8]	5-methyl-o-anisidine	138	137.5–138.5	8.6
9.2–10.6	MS2 [226.5–227.5]@45 [60–230]	4,4'-methylene-bis(2-methylaniline)	227	119.5–120.5	10.2
10.6–11.9	MS2 [212.5–213.5]@45 [60–230]	o-tolidine	213	195.5–196.5	11.2
10.6–11.9	MS2 [244.4–256.4]@45 [70–280]	o-dianisidine	245	229.7–230.7	11.1
		MB	255	239.7–240.7	11.3
10.6–11.9	MS [135.5–136.5]	2,4,5-trimethylaniline	136	135.5–136.5	11.5
11.9–13.5	MS2 [216.5–217.5]@45 [55–219]	4,4'-thiodianiline	217	123.5–124.5	12.8

Time min	*Scan Event Details: APCI(+)*	*Analytes*	*MH+*	*Detection masses*	*Rt min*
11.9–14.0	MS [137.8–145.5]	4-chloro-2-methylaniline	142	141.5–142.5	12.4
		5-chloro-2-methylaniline	142	141.5–142.5	13.9
		2-naphthylamine	144	143.7–144.7	12.3
		1-naphthylamine	144	143.7–144.7	12.3
13.5–15.0	MS [169.7–170.7]	4-aminodiphenyl	170	169.7–170.7	14.2
13.5–15.0	MS2 [254.7–255.7]@45 [70–260]	4,4'-methylenebis(2,6-dimethylaniline)	255	133.5–134.5	14.1
15.0–17.1	MS2 [197.5–198.5]@35 [50–200]	4-aminoazobenzene	198	94+105	16.4
15.0–17.1	MS2 [252.6–255.4]@45 [65–260]	3,3'-dichlorobenzidine	253	217+219	16.7
15.0–17.1	MS2 [266.6–269.4]@45 [70–270]	4,4'-methylenebis-(2-chloroaniline)	267	231+233	16.8
		auramine O	268	146.5–147.5	16.3
17.1–18.0	MS2 [225.7–226.7]@45 [60–230]	2-aminoazotoluene	226	91+120+121+133+209	17.4
18.0–23.0	MS2 [268.8–269.8]@45 [70–300]	MK	269	147.7–148.7	18.5

tion for polar molecules at pH 6, none of them proved to achieve satisfying retention for primary aromatic amines at pH values below 3, which on the other hand is needed for their sensitive detection by LC/MS. Substituting formic acid with the weak ion builder trifluoroacetic acid or raising the pH with ammonium formiate improved retention but sensitivity was decreased up to a factor of 20. This could not be amended with post column addition of formic acid. Best overall results were obtained with the phenylether linked stationary phase Synergi Polar. It not only best retained polar analytes, but also eluted MK, the amine with the highest retention time, before methyl and crystal violet which therefore could be kept out of the MS with a two-way valve. These cationic dyes are present in high concentrations in most blue or black ballpoint pen inks and would interfere with coeluting target compounds. As a disadvantage, this stationary phase showed bleeding in the middle of the run with base peaks m/z=195 and 209. Nevertheless, the determination of amines was still reliable.

In contrast to ball point pens and dyestuffs, no relevant interferences were encountered when analysing fibre tip pens, cosmetics, tattoo inks or finger paints.

Validation of the method

Validation data presented were obtained using ball point pen inks as this matrix proved to be the most difficult to handle.

Selectivity

In general, chromatographic separation combined with the detection of specific mass ranges guaranteed sufficient selectivity for unequivocal identification. However, while analysing more than one hundred ball point pen ink samples, we did occasionally encounter the following potential pitfalls:

N-methyl-aniline interferes with the mass identical o-toluidine. It is used or generated in the synthesis of several dyes or is present in rubber vial septa of inferior quality. It can be distinguished from o-touidine by its slightly shorter retention time and an additional mass peak at m/z=94.

High concentrations of methyl violet can hamper its chromatographic separation from MK, a problem aggravating with column age. Insufficient separation can lead to enhancement or quenching of the MK signal. Diluting sample solutions or rerunning HPLC with parameters optimised for MK determination may help.

1- and 2-aminonaphthalene are not separated with this method. However, we encountered only one positive sample. Verification of 1-aminonaphthalene was easily achieved by adjusting the gradient.

Special care has to be taken with ink samples containing ethyl violet (C.I. 42600). At first glance, the MS^2 signals of impurities of partly deethylated 4,4-' bis(diethylamino)-benzophenone, a homologue of MK, can be mistaken for MK: Scrutinising retention times and MS^2 spectra, however, reveals enough clues for positive identification (fig. 1).

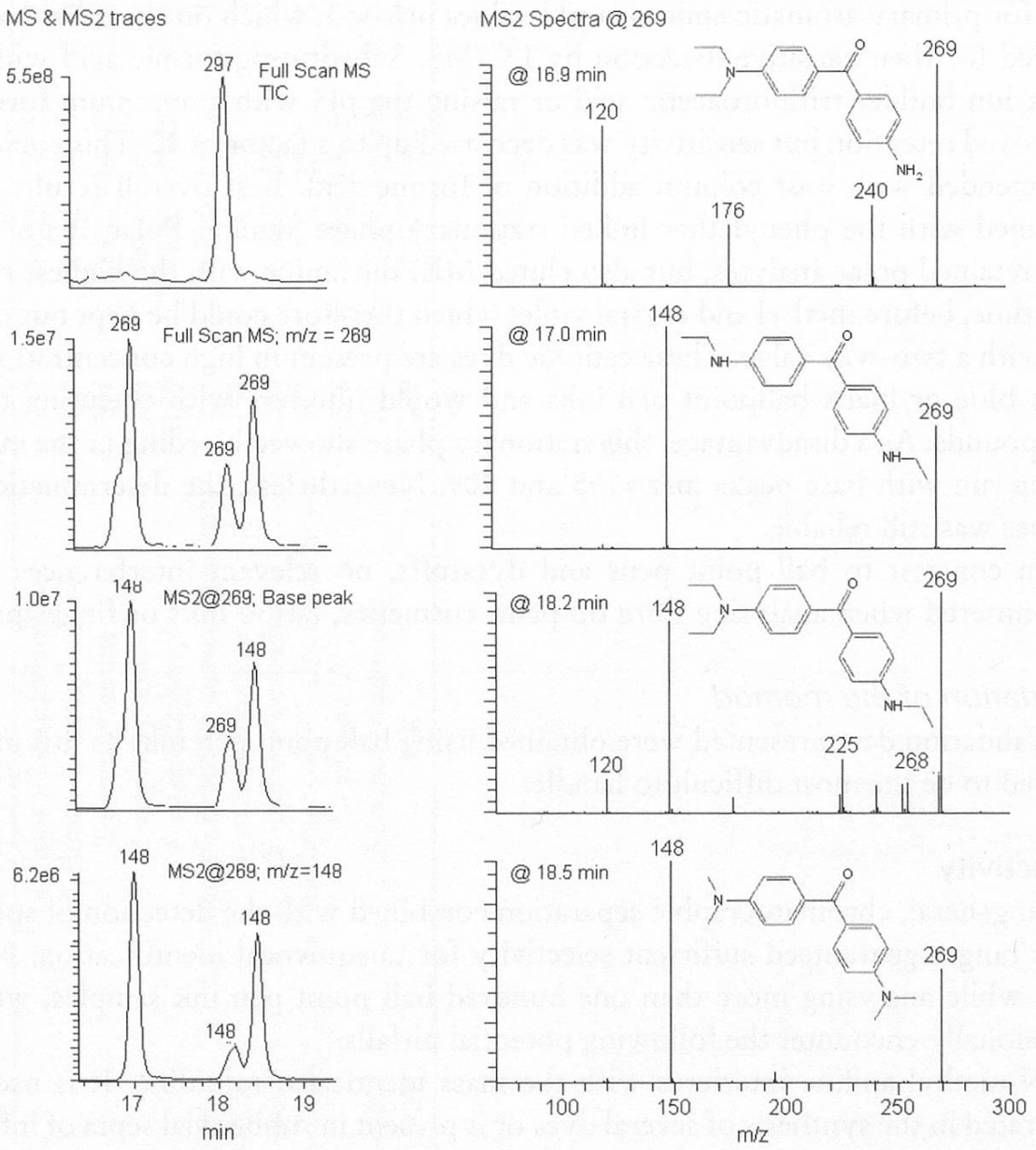

Figure 1 **MS and MS² traces as well as MS² spectra of partly deethylated michler's ethyl ketone and michler's ketone in a sample of ethyl violet**

Precision

The overall run to run precision of the analytical procedure was determined using a number of duplicate tests (15). Extraction with methanol gave a better precision than diluted hydrochloric acid for MK because ball point pen ink dissolves well in methanol but forms lumps in gastric juice simulant, where extraction of MK furthermore is incomplete (Table 3).

Table 3
Relative standard deviations of duplicate tests

Analyte	*detection mode*	*total content (methanol)*	*n*	*migration (0.07M HCl)*	*n*
michler's ketone	UV	4 %	37	12 %	52
michler's ketone	MS^2	7 %	32	11 %	51
michler's ketone	average	5 %	31	11 %	51
methane base	MS^2	12 %	26	11 %	46
aniline	MS			11 %	34
o-toluidine	MS			10 %	4

Recovery rates

Recovery rates for aniline, MB and MK were about 100 % (Table 4). This is remarkable when considering that, in cases of coeluting dye components, no isotope labelled internal standards were available for checking MK and MB quantitation.

Table 4
Recovery rates

	MB, MS^2	*MK, MS^2*	*MK, UV*	*aniline, MS*
Average recovery rate	98 %	112 %	106 %	107 %
Standard deviation	17 %	17 %	17 %	9 %
Rel. standard deviation	17 %	15 %	16 %	8 %
Number of determinations	n=21	n=94	n=91	n=10

Accuracy and ruggedness

No reference material was available for evaluating the accuracy of the method. As a substitute we compared results obtained with different HPLC columns using a phosphate buffer at pH 6 and UV detection with those obtained with the present method (table 5). Results of the 2 amines tested agreed very well.

Table 5
Accuracy obtained using different columns and detection modes

	*michlers ketone**		*aniline***
	methanol extracts	*HCl extracts*	*HCl extracts*
Average ratio in %	98 % (n=34)	99 % (n=20)	100 % (n=23)
Std deviation of the ratio	7 %	10 %	16 %

* chromatography on Inertsil ODS-3 (pH 6; UV 372 nm) vs. present method
** chromatography on Luna C8(2) (pH 6; UV 240 nm) vs. present method

Limits of detection (LOD)

Detection limits not only depended on the individual amine, but also on the given matrix and sample preparation method. On column amounts of standard solutions gave LOD's between 40 an 500 pg. LOD's for most compounds were

between 100 and 200 pg. Due to matrix effects, LOD's were 10 times higher in ball point pen inks than in other samples. LOD's using organic solvent extraction were 8 mg/kg ink for MB and MK respectively 20 mg/kg ink for o-toluidine and benzidine and 40 mg/kg ink for aniline. Most of the other amines had LOD's in ink between 20 and 40 mg/kg. The LOD's reflect compromises which have to be made when screening for over 30 amines. In cases where MK is not chosen as a target compound, samples do not have to be highly diluted which results in better LOD's. LOD's were generally about 20 times lower for migration testing.

Linearity

Calibration curves were linear from 250 pg to 25 ng for aniline, o-toluidine and MK and from 100 pg to 10 ng for benzidine and MB. For migration tests with diluted acid, however, a quadratic fit must be accepted for MK. This seems to be due to adsorption of small quantities of MK to the stationary phase when diluted acid is injected. Methanol solutions containing the same amounts of MK gave higher peaks with a linear fit. Adjusting pH before injection did not help because losses of both MK and MB occurred. In cases, where only MK has to be determined, the problem is best met by diluting samples and calibration solutions 1:1 with methanol before injection.

Analysis of samples

During 2003 and 2004 we analysed tattoo and permanent make up inks (>250), eye shadows and mascara (30), coloured paper napkins (6), finger paints (14), fountain pen inks (15), felt and fibre tip pen inks (100), markers (30), dyes (85) and ball point pen inks (>200). The results concerning tattoo inks will be published elsewhere. We did not find any amines in samples other than permanent marker fluids on solvent basis or dyes and inks of ball point pens. Results for migration testing (fig. 2) in relation to total contents were comparable for aniline, o-toluidine and MB, whereas total contents of MK were two to five times higher. Migration results from a Swiss market survey in the year 2003 are shown in fig. 2.

All blue and almost all black ink samples contained MK in concentrations ranging from several hundred mg/kg up to two samples with 20000 mg/kg. These samples also contained 40000 mg/kg of auramine O. MK total contents of victoria blue, crystal violet and methyl violet dye stuffs ranged between about 1000 mg/kg up to 40000 mg/kg. MB concentrations were much lower both in black and blue inks and in the dyes mentioned, the highest concentration measured being 2300 mg/kg. O-toluidine was occasionally found in blue inks in concentrations below 100 mg/kg and was always accompanied by 1,3-di-o-tolylguanidine. Aniline was often found in black, green and red inks up to a concentration of 1400 mg/kg, and lesser so in blue inks. For black inks this was due to contaminated nigrosine dye stuff. In the case of red and green inks, aniline is either found in the presence of rhodamine B (C.I. 45170; red inks) respectively 1,3-diphenylguanidine (green inks). However, correlation is not fully understood for rhodamine B. Half of the permanent marker

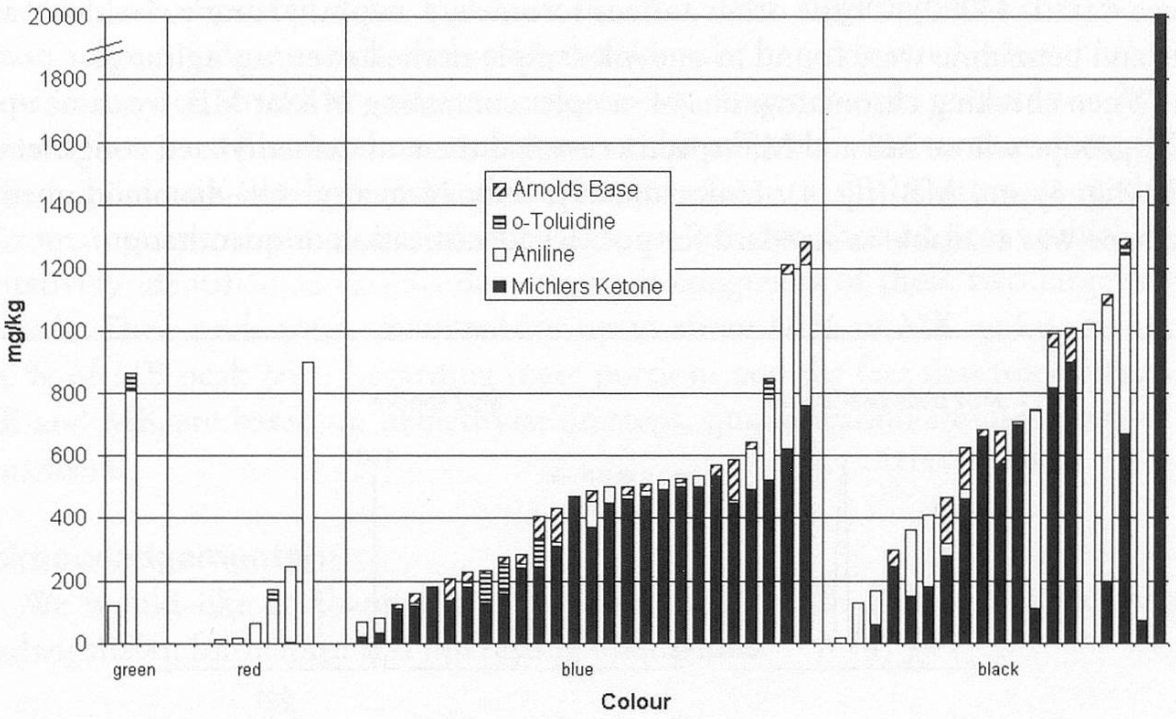

Figure 2 **Aromatic amine migration from ballpoint pen inks into gastric juice simulant from a Swiss market survey in the year 2003**

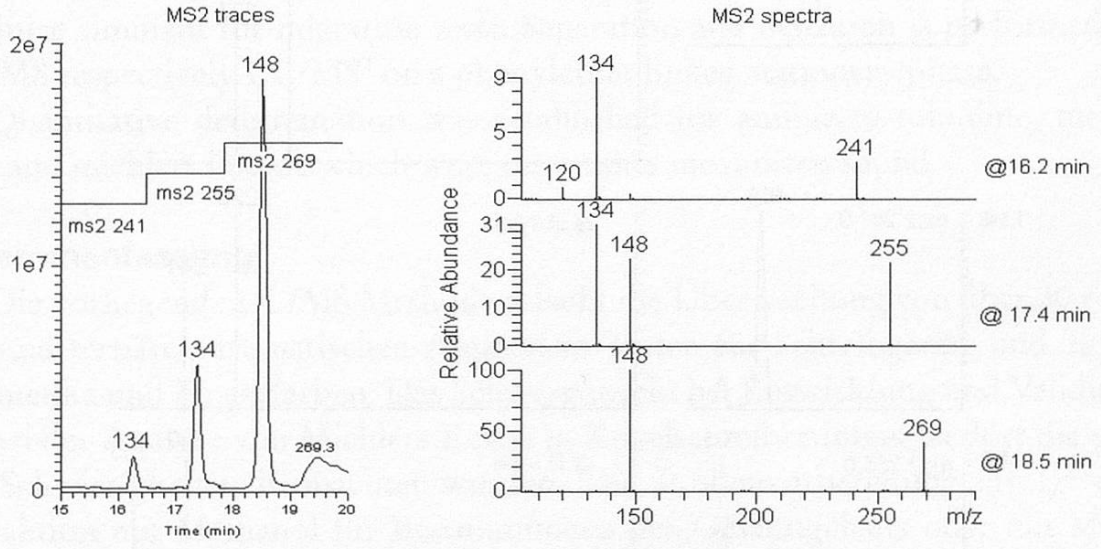

Figure 3 **Base peak of MS^2 traces and MS^2 spectra of michler's ketone (m/z=269 and demethylated congeners (m/z=241 and 255) in a sample of methyl violet.** The peak of m/z 241 consists of two isomers

fluids contained MK and/or MB respectively aniline in concentrations in the same order of magnitude as in ball point pen inks. No amines were detected in other

N-methylated triphenylmethane dyes, such as malachite green (C.I. 42040) or food green 4 (C.I. 44090). Of the other amines screened, 1-naphthylamine, 4-chloro-aniline and benzidine were found in one ink sample in the lower mg/kg range.

When checking chromatograms of samples containing MK or MB, we came upon peak groups whose MS and MS^2 spectra revealed them as demethylated congeners of MK (fig. 3) and MB (fig. 4). Unfortunately, only N-methyl-4,4'-diaminodiphenylmethane was available as standard for positive identification or quantitation.

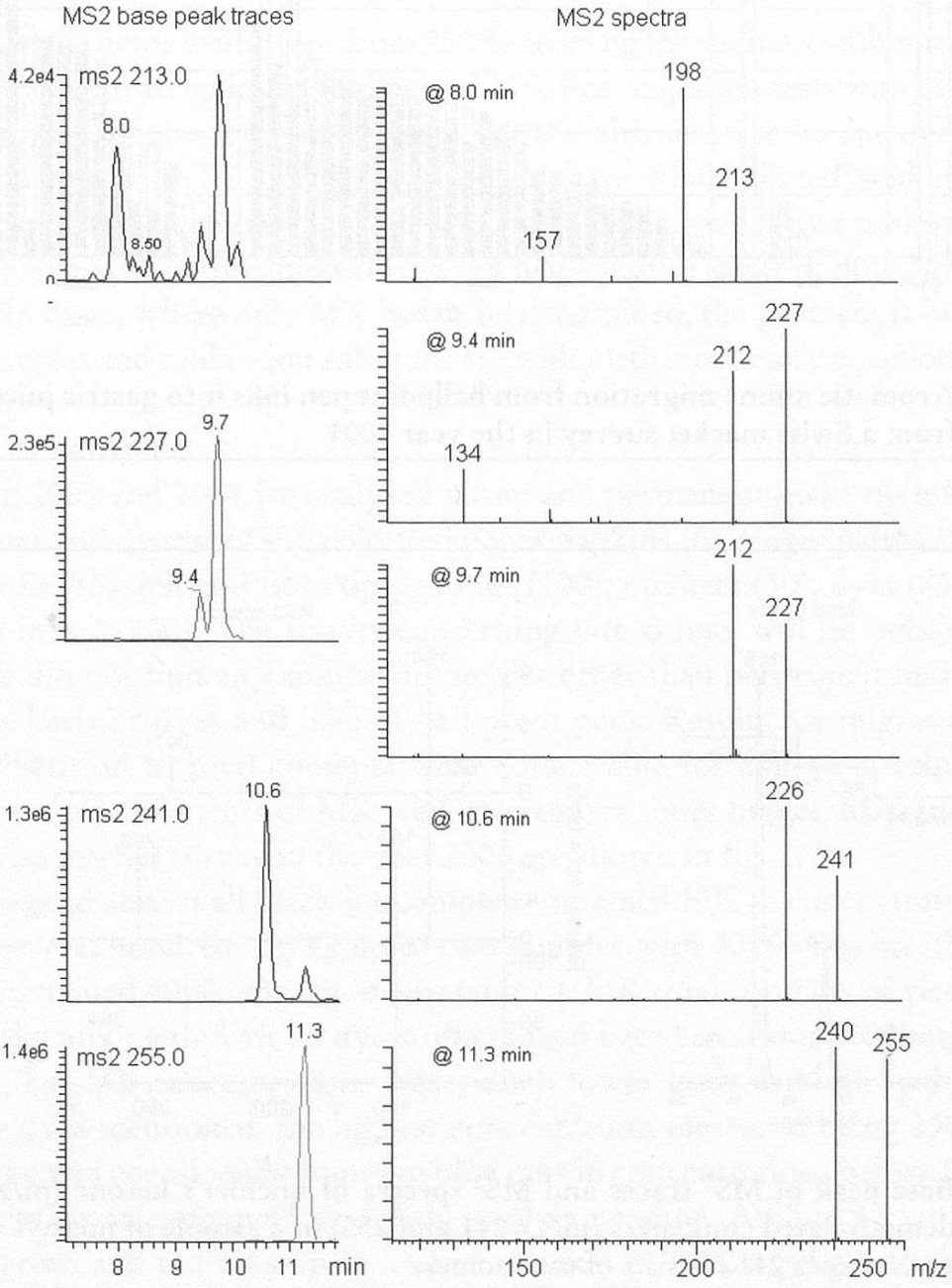

Figure 4 **Base peak of MS^2 traces and MS^2 spectra of methane base (m/z=255) and demethylated congeners (m/z=213, 227 and 241) in a sample of methyl violet.** For m/z=227 two isomers are detected

Conclusions

The method proved to be applicable for inks, dyes, finger paints, cosmetics and tattoo inks. Migration tests with acid should only be performed when problems considering oral intake are relevant respectively where sample preparation is prescribed that way. Results show that some of the most relevant contaminants (MK, MB) respectively additives (auramine O) were missed with the previous methods. Chromatograms of samples containing MK or MB also showed peaks which were tentatively identified as various demethylated congeners of these two target compounds. Their peak areas amounted for up to about 60 % of MK and up to about 300 % of MB peak area. Regarding these portions and the fact that toxic effects of MB and MK are based on demethylation steps, quantification should consider all congeners.

Acknowledgements

We would like to thank Dr. U. Wilhelm and Dr. B. Polzin of Dokumental Ludwigshafen for helpful and interesting discussions.

Summary

An LC/MS method is presented which can screen for over 30 primary and tertiary aromatic amines in all kinds of inks for pens and tattoos, cosmetics and finger paints. Emphasis is laid on the analysis of michler's ketone in ballpoint pen inks and dyes as these proved to be the most difficult matrices to handle. Sample preparation is done by extraction either with methanol for determining the content or with gastric juice simulant for migration tests. Separation and detection is performed with LC/MS respectively LC/MS^2 on a phenylether linked stationery phase.

Quantitative determination was established for aniline, o-toluidine, methane base and michlers ketone which were the amines most often found.

Zusammenfassung

Die vorliegende LC/MS Methode erlaubt die Überwachung von über 30 primären und tertiären aromatischen Aminen in Tinten für Schreibgeräte und Tattoos, Kosmetika und Fingerfarben. Das Schwergewicht bei Entwicklung und Validierung lag bei der Analyse von Michlers Keton in Kugelschreibertinten, da dort die grössten Schwierigkeiten beobachtet wurden. Die Probenvorbereitung erfolgt durch Extraktion mit Methanol für Bestimmungen des Gesamtgehalts oder mit Magensaftsimulans zur Bestimmung der Migration. Die auf einer Phenylether-Umkehrphase aufgetrennten Substanzen werden mittels LC/MS respektive LC/MS^2 quantifiziert.

Die Methode wurde erfolgreich für die quantitative Bestimmung der meist gefundenen Amine Anilin, o-Toluidin, Michlers Keton und Methan Base verwendet.

Résumé

La méthode présentée permet de détecter plus de 30 amines aromatiques primaires et tertiaires dans les encres pour écrire et pour tatouages, les cosmétiques et les peintures à doigts. Le développement et la validation de l'analyse de la cétone de Michler dans les encres de stylos à bille ont présentés les plus grandes difficultés. La préparation des échantillons se fait par extraction avec du méthanol pour le dosage ou avec du simulant du suc gastrique pour la détermination de la migration. La séparation des substances est faite par HPLC sur une phase stationnaire inverse du type éther phényle et la quantification s'effectue par LC/MS et LC/MS^2.

La méthode a été utilisée avec succès pour la determination d'amines fréquemment trouvées dans les encres, telles l'aniline, l'o-toluidine, la cétone de Michler et methane base.

Key words

Aromatic amines, Writing utensils, Ballpoint pen inks, Tattoo inks, Cosmetics, HPLC, LC/MS

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