High throughput analysis of anti-fungal parabens in personal-care products at 9 seconds per sample using LDTD-MS/MS

MP 237

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OVERVIEW

Purpose

- High throughput quantification of parabens in personal-care products.

Method

- Sample dilution in HCl (1N).
- Liquid-Liquid extraction.
- LDTD-MS/MS analysis

Quantification

- Linearity: $r^2 > 0.99$, over the calibration range (0.0125 to 0.500 g/kg)
- Accuracy ranging from 94.6 to 102.7%
- Precision ranging from 0.5 to 17.3%
- **Samples were analyzed with a run time of 9 seconds using LDTD-MS/MS system**

INTRODUCTION

Different varieties of cosmetics and personal-care products use parabens as an anti-fungal agent. There is controversy in the use of parabens, since adverse effects are not fully understood for concentrations typically used in body-care or cosmetics. Over the last several years, parabens have been targeted as a possible health hazard and consumers are seeking out paraben-free alternatives.

To evaluate the levels of paraben in cosmetic products, we developed a method using LDTD-MS/MS to quantify methyl, ethyl, propyl and butyl paraben in 9 seconds sample to sample. Sample pretreatment consists of a liquid-liquid extraction.

LDTD® Ionization Source:

The LDTD uses a Laser Diode to produce and control heat on the sample support **(Figure 1)** which is a 96 wells plate**.** The energy is then transferred through the sample holder to the dry sample which vaporizes prior to being carried by a gas in a corona discharge region. High efficiency protonation and strong resistance to ionic suppression characterize this type of ionization, and is the result of the absence of solvent and mobile phase. This allows for very high throughput capabilities of 9 seconds sample-to-sample analysis time, without carry over.

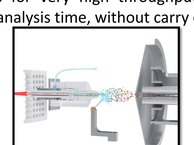

Figure 1 Schematic of the LDTD ionization source

METHOD

Personal-care products preparation

Samples are dissolved in HCl (1N) at 1 mg/mL. Solutions are then filtered on 0.2µm Nylon to remove suspension. Two different sample dilutions of filtered solutions were performed in HCl (1N) to obtain 200 µg/mL and 20 µg/mL. of cream.

Extraction Procedure

200 µL sample or calibration curve
400 µL Ethyl acetate.
Vortex
Phase separation
Transfer 5 µL of the upper layer in LazWell™ plate
Analyze after complete solvent evaporation

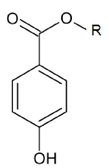

Figure 2 Paraben chemical structure
a) Methyl paraben: R = CH_3
b) Ethyl paraben: R = CH_2-CH_3
c) Propyl paraben: R = CH_2-CH_2-CH_3
d) Butyl paraben: R = CH_2-CH_2- CH_2-CH_3

Instrumentation

- LDTD model: S-960
- MS: Sciex 5500 QTRAP®

Figure 3 LDTD system on Sciex 5500 QTRAP®

LDTD Parameters

- Laser power pattern :
  - ➢ Increase laser power to 55 % in 3.0 s
  - ➢ Decrease laser power to 0 %
- Carrier gas flow : 3 L/min (Air)

MS Parameters

- APCI (-)
- MRM mode
- CE = -25
- Methyl Paraben: 151 → 92
- Ethyl Paraben: 165 → 92
- Propyl Paraben: 179 → 92
- Butyl Paraben: 193 → 92

RESULT

Linearity results

A calibration curve (0.0125-0.500 g/kg) has been prepared in HCl (1N) and analyzed in triplicate. Correlations were all over 0.9973. **Figure 4** presents a typical calibration curve for methyl paraben.

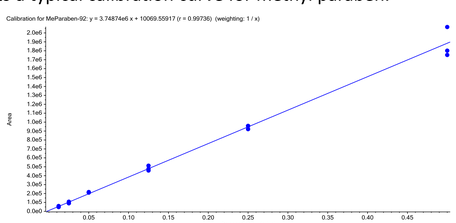

Figure 4 Typical Methyl paraben standard curve

Matrix effect

Sample containing parabens are evaluated with two different matrix dilutions (dilution 1: 20 µg/mL and dilution 2: 200 µg/mL). Samples concentrations are evaluated in the standard curve. The samples content in paraben are then evaluated using the paraben amount in the samples. **Table 3** shows the content of two parabens obtained from different sample dilutions. % of difference lower than 10 are obtained.

	Dilution 1	Dilution 2	%Diff
	g/kg	g/kg	%
Methyl paraben	0.3950	0.3577	9.9
Ethyl paraben	0.1325	0.1228	7.6

Table 3 Matrix effect evaluation

Precision/Accuracy results

Intra-run and inter-run precision/accuracy are calculated. Accuracy ranging from 94.6 to 102.7 % and precision ranging from 0.5 to 17.3 % were obtained. Results of Methyl paraben were reported in **Table 1** and **Table 2**. Similar results were obtained for other parabens.

Table 1
Intra-run precision and accuracy

	LLOQ	QC-Low	QC-Med	QC-High	ULOQ
Conc. (g/kg)	0,0125	0,0250	0,1250	0,25000	0,5000
N	3	3	3	3	3
Mean (g/kg)	0,0121	0,0238	0,1260	0,2493	0,4973
%RSD	15.4	10.5	6.0	2.4	9.0
%Nom	96.9	95.1	100.8	99.7	99.5

Table 2
Inter-run precision and accuracy

	QC-Low	QC-Med	QC-High
Conc. (g/kg)	0,0250	0,1250	0,2500
N	9	9	9
Mean (g/kg)	0,0254	0,1215	0,2450
%RSD	13.7	11.8	9.8
%Nom	101.6	97.2	98.0

Personal-care products analysis

Three samples are analyzed. No parabens are named in the tube's information for sample 1 and 3. Methyl, ethyl and propyl paraben are showed in the ingredients section for sample 2. Results were reported in **Table 4**. Low concentrations of methyl and ethyl paraben are detected in sample 1 (claim: no paraben). Paraben concentration limits within the industry : the maximum of individual paraben concentrations allowed in cosmetic formulas is 4 g/kg with a maximum of 8 g of total parabens per kg.

	Sample 1	Sample 2	Sample 3
	g/Kg	g/Kg	g/Kg
Methyl paraben	0.01875	0.3763	‹0.0125
Ethyl paraben	0.01855	0.1277	‹0.0125
Propyl paraben	‹0.0125	0.0316	‹0.0125
Butyl paraben	‹0.0125	‹0.0125	‹0.0125

Table 4- Personal-care sample product results

Figure 5 Sample 1

Figure 6 Sample 2

Figure 7 Sample 3

CONCLUSION

- **Methyl, Ethyl, Propyl and Butyl Paraben analysis in personal-care products can be performed in 9 seconds by LDTD-MS/MS.**
- **Good linearity, precision and accuracy are obtained. No matrix effect was observed.**
- **Ultra fast paraben quantification in different personal-care products can be easily achieved.**