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Application News

Gas Chromatography

Quantitative determination of volatile impurities in ethanol used for hand sanitizers

No. SCA-180-036

▪ Introduction

Due to the worldwide outbreak of Covid-19 in 2019, the use of hand sanitizers increased. In Germany the sales of hand sanitizers spiked around 74.7 % in the first five months compared to the year before [1]. Even though the World Health Organization suggests to not disinfect the hands [2], but rather use water and soap, the demand of disinfectant in the private sector has been substantial. Since part of the hand sanitizer is absorbed by the skin, it is important to control potentially harmful substances present. The main ingredient in hand sanitizers is alcohols, specifically propanol or ethanol. These may contain volatile impurities that are regulated by the European Pharmacopeia. In this study ethanol was investigated according to the Pharmacopeia limits [3].

▪ Materials and methods

To determine the volatile impurities in ethanol, a gas chromatographic method was used. To be able to identify the target substances, each one was added to the examined ethanol. Subsequently the spiked reference solutions were compared to the ethanol test solution for quantification. Test and reference solutions were mixed following the instructions of the European Pharmacopeia. The examined substances along with additional information are listed in table 1. To ensure the reproducibility of the method, each sample was injected 6 times.

Designation	Added substance to ethanol	Additional information
Test solution a)	-	Pure ethanol
Test solution b)	4-Methylpentan-2-ol	Reference peak for total of other impurities (limit: 300 ppm V/V)
Reference solution a)	Methanol	Limit: 200 ppm V/V
Reference solution b)	Methanol	System suitability (resolution)
	Acetaldehyde	
Reference solution c)	1,1-Diethoxyethane	Acetaldehyde + 1,1-Diethoxyethane, expressed as acetaldehyde (limit: 10 ppm V/V)
Reference solution d)	Benzene	Limit: 2 ppm V/V

Table 1: examined substances

Analyses were performed using a GC-2030 gas chromatograph equipped with flame ionization detector (FID-2030). The necessary chromatographic separation for all target compounds was realized using a SH-Rtx-624 column (30 m length, 0.32 mm ID, 1.8 µm df; #221-75864-30). An overview of the method is listed in table 2.

Carrier gas	Helium
Injection temperature	200 °C
Injection mode	Split 1:20; 1 µL injection volume
Linear velocity	35.0 cm/sec
Column oven program	40 °C, 12 min, 10°C/min, 240 °C, 240 °C, 10 min (total time 42 min)
FID temperature	280 °C

Table 2: GC method parameters

- **Results**

In figure 1 the chromatogram of the tested ethanol (test solution a)) is shown. Since all target compounds elute before 18 minutes, the chromatogram was zoomed into this time range for better visibility.

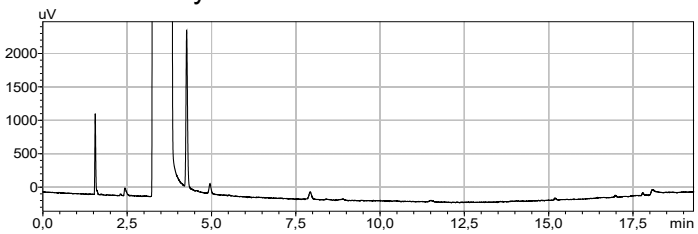

Figure 1: Chromatogram of the tested ethanol (test solution a))

The retention time and the calculated RSDs for each compound are listed in table 3. The calculation is based on the data obtained by reinjecting each reference solution six times.

Compound	Retention time [min]	%RSD [%]
Acetaldehyde	2.30	0.04
Methanol	2.42	0.02
Benzene	10.40	0.02
1,1-Diethoxyethane	15.16	0.01
4-Methylpentan-2-ol	15.18	0.01

Table 3: Retention times and %RSDs for each compound (n = 6)

To check the system suitability, the resolution between the acetaldehyde (1st peak) and the methanol peak (2nd peak) of reference solution b) is observed. The minimum acceptable value according to Pharmacopeia is higher than 1.5.

The achieved minimum resolution in this study was 1.54. In figure 2 the examined peaks are shown.

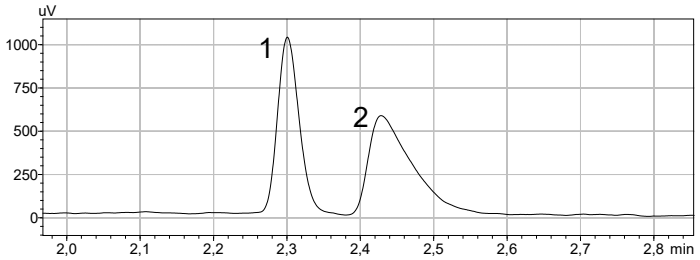

Figure 2: Resolution between acetaldehyde (1) and methanol (2) in reference solution b)

To meet the limit of methanol content in ethanol, according to the Pharmacopeia, the peak area of methanol in test solution a) should be not more than half the respective area found in reference solution a). The average area of the methanol peak in test solution a) is 452 and in reference solution a) is 34787, with RSDs of 3,20 % and 7.84 %, respectively. So the methanol content is below the tolerated limit of 17393.5.

To determine the sum of contents of acetaldehyde and 1,1-Diethoxyethane in parts per million the following equation is used:

$$\frac{10 * A_E}{A_T - A_E} + \frac{30 * C_E}{C_T - C_E} * \frac{44{,}05}{118{,}2}$$

The first term is calculated by using the area of the acetaldehyde peak in test solution a) (A_E) and reference solution b) (A_T). C_E and C_T are the area of the 1,1-Diethoxyethane peak in the chromatogram obtained with test solution a) and reference solution c), respectively. The last term is composed of the molecular mass of acetaldehyde (44.05 g/mol) and 1,1-Diethoxyethane (118.2 g/mol). Using the average of the measured areas, the result is an acetaldehyde and 1,1-Diethoxyethane impurity of 0.361 ppm. Since the maximum allowed content is 100 ppm according to the European Pharmacopeia and the measured value is far below, this impurity is negligible.

In order to evaluate the benzene content, the following equation is used:

$$\frac{2 * B_E}{B_T - B_E}$$

B_E and B_T are the area of the benzene peak in the chromatogram obtained with test solution a) and reference solution d), respectively. In the chromatogram of test solution a) there was no benzene peak detected (fig. 3). Therefore, it can be concluded that the benzene content is under the limit of detection and the allowed limit of 2 ppm.

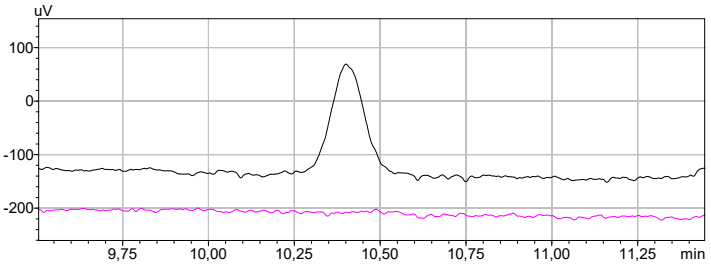

Figure 3: excerpt of the chromatograms of test solution a) (pink) and reference solution d) (black)

To estimate the total of other impurities the area of all peaks in test solution a), excluding the area of the ethanol peak, was calculated. The results in table 4 showed that the total impurities peak area was smaller than the area of the 4-Methylpentan-2-ol peak in test solution b).

Area obtained of	Average area [UA]
All peaks of test solution a)	17941
The peak due to 4-Methylpentan-2-ol	153375

Table 4: Estimation of other impurities

Even including the peaks with an area smaller than 3 % of the area of the 4-Methylpentan-2-ol peak, which could be disregarded according to the Pharmacopeia, the area of all peaks of test solution a) is substantially smaller than the area of the 4-Methylpentan-2-ol peak. Therefore it can be concluded that the examined ethanol had a high grade of purity.

▪ Conclusion

Potentially harmful volatile impurities in alcohols used for disinfectant production are subject of control according to European Pharmacopeia regulation. The use of a GC-2030 with FID-2030 detector ensures reliable quantitation of the target substances, fulfilling system suitability demands given by the Pharmacopeia.

▪ Literature

[1] https://de.statista.com/outlook/18060000/137/handdesinfektionmittel/deutschland 2020/06/16

[2] https://www.who.int/gpsc/clean_hands_protection/en/ 2020/07/27

[3] European Pharmacopoeia (Ph. Eur.) 10th Edition, chapter “Ethanol (96 per cent)” 01/2015:1317, released in July 2019

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