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Study of some alcohol amounts in commercial alcoholic disinfectant solutions using gas chromatography with flame ionization detection

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RESEARCH ARTICLE

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ABSTRACT

A simple solvent extraction method was used to analyze alcohol-based hand rubs (ABHRs) using gas chromatography with a flame ionization detector. 79 samples including 68 liquid and 11-gelled ABHRs were analyzed in the Food and Drug Laboratories Research Center of Mashhad, Iran. 17 samples had methanol, 50 samples had the correct percentage of alcohol (60-80%), and 12 samples had the incorrect percentage of alcohol (<60%). The RSD% of methanol, ethanol, and isopropanol were as 2.28, 2.18, and 1.52, respectively. The relative recoveries for methanol, ethanol, and isopropanol were 102.5, 97.8, and 114, respectively. All experiments were repeated three times. The limit of detection and the limit of quantification for methanol, ethanol, and isopropanol were obtained as 0.22, 0.24, 0.10 (%) and 0.71, 0.82, 0.68 (%), respectively.

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1. Introduction

Hand rub products contain antiseptic(s), capable of stopping the existence or growth of microorganisms on the skin [1]. Among the many available hand rub productions, alcoholic products are the most popular. This is mainly because alcoholic products are more powerful and compatible, faster to be applied, and cause fewer skin problems [1,2]. Alcoholic hand rub contains mainly ethanol, isopropyl alcohol, or their combinations [3]. The use of alcohol for hand disinfection has received much attention in the community.

Methanol has been shown to cause irritation and inflamemation when applied to the skin [4]. Oral, pulmonary, or skin exposure to methanol can cause severe toxicity and death. Therefore, the manufacturer should avoid using methanol formulation of hand disinfectants. However, methanol can sometimes be found in hand sanitizers on the market and can cause poisoning, although, this rarely happen. Healthy subjects who were exposed to the methanol and the results showed that the rate of methanol's absorption through the skin into agents depends on its vapor, liquid, or solution state, exposure time, dose, concentration, and size of the contact area [5,6]. In diseased skin caused by methanol, such as descaling, and dermatitis [4,7], both the structure and barrier function are endangered; therefore, it allows methanol and other chemicals to be easily absorbed [8]. Due to the widespread and easy use of hand sanitizers, and the high toxicity of methanol, it is necessary to study the formulation very carefully [9]. Furthermore, global poison control systems can play an essential role in risk management [10].

It is essential to establish a regional or international network of toxins detection in all countries where they provide early warning signs measures to prevent the initial toxic threats of products immediately. The researchers should raise the necessary awareness among health professionals, who provide timely treatment [9]. The COVID-19 pandemic led to an increasing demand for alcoholic sanitizers [11]. Transmission of communicable diseases in society remains a significant concern [2], especially during the outbreak of severe acute coronavirus two syndrome (SARS-CoV-2; known as COVID-19) [3].

Using a hand rub has a vital role to reduce the rate of infection [2]. Hand washing with soap is usually better than alcoholic hand rubs, but both actions effectively reduce contamination by removing or destroying microorganisms [2,3].

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Table 1. Retention times of common impurities in technical-grade ethanol.

Compound	Retention time (min)	Limit of detection (LOD, %)	Limit of quantification (LOQ, %)
Methanol	2.27	0.22	0.71
Ethanol	2.47	0.24	0.82
Isopropanol	2.60	0.10	0.68
n-Butanol *	4.28	-	-

* Internal standard for gelled and liquid ABHRs.

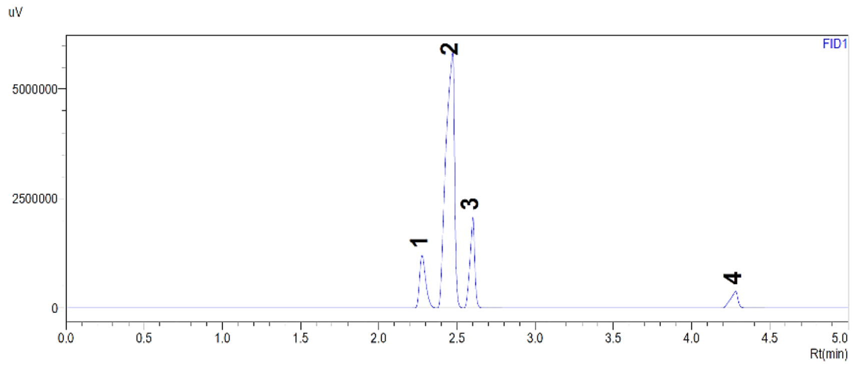

Figure 1. Chromatograms of the mixture of alcohol standards: (1) methanol (2.277 min), (2) ethanol (2.471 min), (3) isopropanol (2.602 min) and (4) *n*-butanol (4.282 min).

Educating the public about proper hand hygiene is a critical activity that can effectively reduce pathogenicity [11].

Various methods are used to quantify and measure alcohols that have long extraction stages or use expensive equipment such as the GC-MS or HS-GC-FID method [6,12]. The analysis of ABHRs can be further complicated by the addition of additives such as essential oils or other ingredients. Essential oils may be mixed in ABHR products in an attempt to mask body alcohol odors, so various methods for measuring alcohol have been suggested in articles, for example, the use of toxic solvents for the extraction of gelled ABHR [3].

Many methods are available for SPME- or HS-GC-FID for the analysis of alcohol-based hand rubs. A simple and fast analytical method, HS-SPME, is available using commercial fibers combined with gas chromatography by flame ionization detection (GC-FID) to extract and quantify ethanol in hand sanitizing gels [13]. Although commercial fibers have been used successfully in many fields, they still have disadvantages, such as fragility, lack of resistance to high temperatures and organic solvents, high cost, and short lifespan that limit their use.

However, in this process, a simple distillation method was used to extract and quantify the raw materials using GC-FID. In this study, seventy-nine hand rubs which commonly using in Iran were provided from local supermarkets and manufacturing plants. The contents of methanol, ethanol, and isopropanol were determined by GC-FID.

2. Experimental

2.1. Materials

Ethanol, methanol (HPLC grade), and isopropanol (Analytical grade), were obtained from Merck; the internal standard *n*-butanol (Analytical grade) was purchased from Merck (Table 1). A variety of 11 gelled and 68 liquid ABHRs were sampled from local supermarkets and manufacturing plants between June 2020 and March 2021.

2.2. Internal standard, standard and sample preparation

We used a simple distillation method to extract, qualify and quantify the raw materials. It is vided that the capacity of the distilling flask is sufficient (commonly two to four times the volume of the liquid to be heated). Usually, a mixture of 25 mL of gel and 25 mL of water is used and the distillation rate is such that clear distillates are produced. During all manipulations, precautions were taken to minimize the loss of alcohol to 10 mL by evaporation.

The liquid ABHRs were filtered with 0.45 µm polytetrafluoroethylene PTFE syringe filters. 2 mL filtrated ABHRs (Liquid sanitizer and prepared gel) spiked with 300 µL, *n*-butanol as an internal standard to 10 mL distilled water and analyzed directly via GC-FID with no prior treatment. Each sample was measured in triplicate, as mean±standard deviation.

To draw the calibration curve, we calculated the percentage concentration of analytes (w/w) in the calibration solutions, and then the calibration curve for each analyte was plotted as the ratio of the area of the analyte peak to the internal standard peak versus the analyte concentration to the internal standard concentration. Finally, we convert% (w/w) to %(v/v) using the density of alcohols and sample. Alcohol working solutions were used daily to prepare standard solutions.

2.3. GC-FID analysis

Analyzing ABHRs were conducted using a Shimadzu GC 2010 plus equipped with a flame ionization detector with a split/split-less injector. The analytes were separated on ZB-624 capillary GC column (30 m × 0.32 mm, 1.80 µm) with ultrapure helium (99.999%) as carrier gas at a flow rate of 2 mL/min. The FID was operated at 250 °C with flow rates of 400 mL/min of air, 40 mL/min of hydrogen and 30 mL/min of helium. The initial oven temperature was 40 °C and held for 5 min. The temperature was increased to 200 °C at 10 °C/min and held for 5 min; giving a total run-time of 27 min. The inlet was operated in split mode (40:1) at 250 °C, and 1 µL of the sample was injected. The syringe was thoroughly washed with distilled water between injections.

3. Results and discussions

The retention times of the analytes and internal standard were determined by injection of five times neat methanol, ethanol, isopropanol, and *n*-butanol. Figure 1 shows a typical chromatogram obtained for the standard of the mixture of alcohols, and Figures 2 and 3 show liquid ABHRs and gel ABHRs, respectively.

Table 2. Percent content in alcohol-based hand rubs (liquid samples 1 to 68), and (gelled samples 69 to 79) *.

Sample	Methanol, % (v/v)	Ethanol, % (v/v)	Isopropyl alcohol, % (v/v)	Sample	Methanol, % (v/v)	Ethanol, % (v/v)	Isopropyl alcohol, % (v/v)
S_{1}	-	76.54	-	S_{41}	-	75.5	-
S_{2}	0.9	44	19.86	S_{42}	-	78	-
S_{3}	-	73.6	-	S_{43}	-	77.5	-
S_{4}	-	70.2	-	S_{44}	-	75	-
S_{5}	-	45	25	S_{45}	-	72	-
S_{6}	-	70	-	S_{46}	1.79	87.7	-
S_{7}	-	45.7	25.4	S_{47}	-	65.27	9.77
S_{8}	6.25	5.7	35.5	S_{48}	-	77.2	-
S_{9}	0.36	62.1	-	S_{49}	-	71.6	-
S_{10}	5.75	25.5	34	S_{50}	-	74.7	-
S_{11}	-	70	-	S_{51}	-	2.5	72.3
S_{12}	-	-	50.5	S_{52}	-	79.9	-
S_{13}	2.9	25.8	30	S_{53}	-	78.9	-
S_{14}	0.4	70	-	S_{54}	-	74.9	-
S_{15}	-	63.5	-	S_{55}	1.74	77.25	-
S_{16}	7.4	28.9	23.25	S_{56}	-	87.5	-
S_{17}	4.4	23.1	32.31	S_{57}	-	65.8	-
S_{18}	-	56.4	-	S_{58}	-	70	-
S_{19}	-	22	48	S_{59}	-	74.5	-
S_{20}	-	71	-	S_{60}	-	79	-
S_{21}	-	75.2	-	S_{61}	-	74	-
S_{22}	-	65.2	-	S_{62}	-	-	10.5
S_{23}	-	71	-	S_{63}	-	74.2	-
S_{24}	-	72	-	S_{64}	-	70	-
S_{25}	-	-	40	S_{65}	64.6	-	-
S_{26}	-	70	-	S_{66}	-	86.3	-
S_{27}	-	57.3	-	S_{67}	-	74.5	-
S_{28}	-	73	-	S_{68}	2	93.3	-
S_{29}	0.35	-	63.8	S_{69}	60	-	-
S_{30}	-	71	-	S_{70}	-	6.23	24
S_{31}	67.6	-	-	S_{71}	4.9	25.1	31.6
S_{32}	-	70	-	S_{72}	-	33	-
S_{33}	-	65.7	-	S_{73}	-	31	27.5
S_{34}	-	60	-	S_{74}	-	42.6	-
S_{35}	-	70	-	S_{75}	-	73	-
S_{36}	-	50.5	-	S_{76}	-	64	-
S_{37}	-	61.5	-	S_{77}	-	85.25	-
S_{38}	-	70	-	S_{78}	-	9.3	-
S_{39}	-	71.1	-	S_{79}	-	2.8	5.6
S_{40}	-	37.2	20.4				

* "-": No detected.

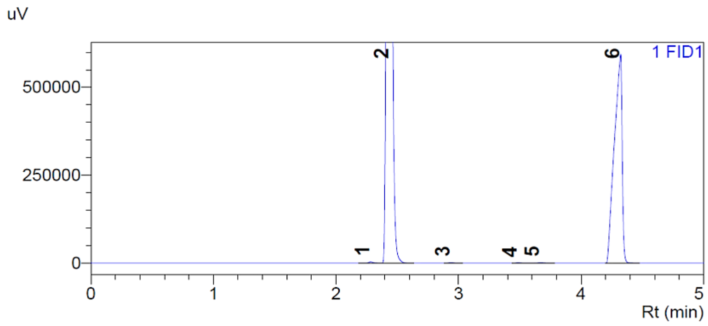

Figure 2. The compliant liquid ABHRs S_{9} (1) methanol (2.284 min), (2) ethanol (2.440 min), (3-5) impurity, and (6) *n*-butanol (4.322 min.

The COVID-19 pandemic has led to a growing demand for essential items [14], including hand rubs and surface disinfectants. This demand led to a crisis, and as a result, government regulators temporarily allowed the use of low-quality raw materials and substitutes for these disinfectants [15]. The collection reported here shows the percentage of disinfectants that use methanol in their formulation. The detection of ethanol in the sample is determined by comparing its retention time with the absolute ethanol of analytical grade [16]. A five-point calibration curve was derived for all alcohols listed in Table 1, achieving $r^2 > 0.9993$ with RSD ≤ 2.5%.

Methanol is very toxic and can even lead to death, and therefore, it should not be used in antiseptic formulations. However, it is sometimes used in some of these hand and surface disinfectants and causes poisoning, so government regulatory agencies are expected to monitor these products regularly [3]. Among the 79 samples tested, 21.25% had methanol and 60% were compliant with the Iranian Health interim guidelines (60-80) %v/v. As shown in Table 2, samples S_{31}, S65, and S_{69} have abnormally high methanol. On the other hand, some samples such as S_{2}, S_{8}, S_{9}, S_{10}, S_{13}, S_{14}, S_{16}, S_{17}, S_{29}, S_{46}, S_{55}, S_{68}, and S_{71} have methanol less than 10%. As shown in Table 2, the sample S_{68} has maximum ethanol (93.3%), and samples S_{1}, S_{3}, S_{4}, S_{6}, S_{9}, S_{11}, S_{14}, S_{15}, S_{20}, S_{21}-S_{24}, S_{26}, S_{28}, S_{30}, S_{32}-S_{35}, S_{37}-S_{39}, S_{41}-S_{50}, S_{52}-S_{61}, S_{63}, S_{64}, S_{66}-S_{68}, S_{76}, S_{76} and S_{77} have above 60% ethanol. Samples S_{8}, S_{51}, S_{78}, $S_{70,}$ and S_{79} have less than 10 % ethanol. Samples S_{12}, S_{25}, S_{31}, S_{63}, S_{65}, and S_{69} do not have ethanol, but samples S_{31}, S_{65}, S69 and S_{12}, S_{25}, S_{63} have methanol and isopropanol, respectively.

The alcohol contents (ethanol, isopropanol, or both of them) in the liquid ABHRs were 70-80% (v/v), and the gelled ABHRs varied between 60-80% (v/v) according to the Interim

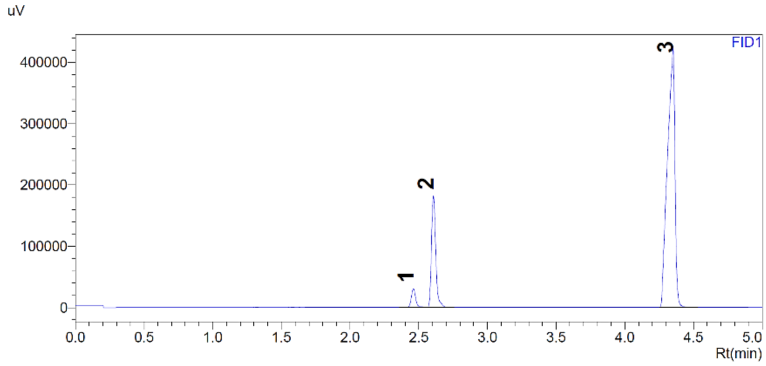

Figure 3. The compliant gel ABHRs S_{70} (1) ethanol (2.461 min), (2) isopropanol (2.607 min), and (3) *n*-butanol (4.351 min).

Health Iran Guidelines. However, isopropanol is fully effective against viruses with lipid envelopes [17]. Therefore, combining these alcohols could potentially have a synergistic effect (Table 2) [9]. Generally, alcohol concentrations between 60 and 95% (v/v) have good antibacterial properties. The current formulations of hand sanitizer suggested by the World Health Organization are either 80% (v/v) of ethanol or 75% (v/v) isopropanol [3]. According to USP 37, rubbing alcohol contains not less than 68.5% and not more than 71.5 % by volume of dehydrated alcohol, the remainder consisting of water and denaturants, with or without color additives and perfume oils [18].

Samples S_2, S_5, S_7, S_8, S_{10}, S_{12}, S_{16}, S_{17}, S_{19}, S_{29}-S_{40}, S_{47}, S_{51}, S_{62}, S_{70}, S_{71}, and S_{73}-S_{79} have isopropanol. From these samples except S_{12}, S_{62}, the others have a combination of alcohols could potentially have a synergistic effect. In this work, thirteen samples (S_8, S_{12}, S_{13}, S_{16}, S_{17}, S_{18}, S_{27}, S_{36}, S_{62}, S_{73}, S_{74}, $S_{70,}$ S78 and S_{79}) have less alcohol than allowed by the Interim Health Iran guidelines (Letter Number: 665/113367), alcohol content 60-80 % (v/v) dependent on color additive, perfume oil, *etc.* is different [19].

4. Conclusion

With the advent of the Covid-19 epidemic, the Food and Drug Laboratories Research Center of Iran issued instructions for the formulation of hand rubs and surface disinfectants to address high-quality ethanol deficiency. Thus, trade-in disinfectant production proliferated, and many factories with a high capacity of ethanol purification became operational. Due to different brands of alcohol-based disinfectants in the market, it was necessary for regulatory laboratories to monitor these products continuously therefore, most brands on the market were tested for the presence of methanol or the appropriate level of other alcohols to make sure they are not harmful to consumers. The 79 samples analyzed, 17 samples had methanol, 50 samples had the correct percentage of alcohol 60-80 %(v/v), and 12 samples did not have methanol, but had the incorrect percentage of alcohol (<60%). The percentage RSD of methanol, ethanol, and isopropanol was obtained as 2.28, 2.18, and 1.52, respectively. Relative recoveries were obtained for methanol, ethanol, and isopropanol 102.5, 97.8, and 114(%), respectively.

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Disclosure statement

Conflict of interest: The authors declare that they have no conflict of interest.
Ethical approval: This study was confirmed by the ethics committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1399.537).
Sample availability: Sample of the compounds are available from the author.

CRediT authorship contribution statement

Conceptualization: Masoumeh Darbanian; Methodology: Masoumeh Darbanian; Software: Masoumeh Darbanian; Validation: Masoumeh Darbanian, Vafa Baradaran Rahimi; Formal Analysis: Masoumeh Darbanian, Vafa Baradaran Rahimi; Investigation: Masoumeh Darbanian, Vafa Baradaran Rahimi; Resources: Masoumeh Darbanian; Data Curation: Masoumeh Darbanian; Writing - Original Draft: Masoumeh Darbanian; Writing - Review and Editing: Azizollah Nezhadali; Visualization: Azizollah Nezhadali; Funding acquisition: Masoumeh Darbanian; Supervision: Azizollah Nezhadali; Project Administration: Azizollah Nezhadali.

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