Monitoring the quality of ethanol-based hand sanitizers by low-cost near-infrared spectroscopy

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ABSTRACT

The use of near-infrared spectroscopy (NIRS) based on a low-cost portable instrument for monitoring the quality of the three major formulations of ethanol-based hand sanitizers used for prevention against CoVID-19 disease is described. The quality of the sanitizers was evaluated using two approaches. In the first, a qualitative method was developed to identify gross non-conformities, using NIR spectral data compression by principal components analysis and projection of the spectrum of the tested sample in the principal component space delimited by samples of sanitizers prepared in the laboratory. In the second, a quantitative method was designed to determine the active substance (ethanol) employing multivariate regression based on partial least squares. The results demonstrate that the first approach can be used to detect non-conformities in the sanitizer composition, mostly associated with incorrect ethanol content. The second explores the use of NIRS for determination of the ethanol content in the three formulations aiming the quality control of the sanitizer manufacturing process. The ethanol content can be determined with an absolute root mean square error of prediction (RMSEP) equal to 0.68% (m/m), 0.83% (m/m) and 1.0% (v/v) for the three formulations evaluated. The RMSEP was estimated as 1.3% (m/m) for the commercial products. The measurement protocol takes approximately 1 min and requires only about 120 μL of a sample. Besides, NIRS was employed to compare the rate of volatilization of the ethanol in the different formulations, an important parameter concerning the efficacy of ethanol-based sanitizers.

1. Introduction

Hand sanitizers are widely recommended to assist in the prevention of human contamination by micro-organisms such as bacteria and virus [1,2]. Several efficient formulations are commercialized. However, the most common contains ethanol as an active substance typically in concentrations close to 70% (m/m). The composition varies from samples containing only the alcohol and water to products containing small quantities of an emollient, such as glycerol, a fragrance, a colourant, or a gel-forming substance. The gel product, knowing as "alcohol gel", is the most common and recommended hand sanitizer by the health agencies, due safety and efficacy issues [1,2].

The coronavirus disease (CoVID-19) outbreak increased the worldwide consumption of ethanol-based hand sanitizers in an unprecedented way, as it becomes compulsory in all public and commercial places, and at homes [2]. Regulatory national health agencies, such as the Brazilian ANVISA (Brazilian National Agency of Sanitary Vigilance), took an emergency action to face the increasing demand for

sanitizers [3,4]. This measure includes the possibility of manufacturing and commercialize ethanol-based sanitizers by small companies without previous authorization from the regulatory agency. Naturally, the number of manufacturers increased substantially. Thus, the probability of frauds and non-conformities of commercial sanitizers also increased comparably.

The ANVISA describes the manufacturing procedures for three formulations attested for their sanitary efficacy [4]. The simple one (F1) is just a mixture of ethanol/water containing 70% (m/m) of ethanol. Another formulation (F2) contains ethanol at 80% (v/v) and small amounts of hydrogen peroxide and glycerol acting as emollient. The most commercialized formulation (F3) is also based on ethanol/water solution containing 70% (m/m) of the ethanol, using a gel-forming water-soluble polymer such as carbomer, after a pH adjustment between 5.0 and 7.0, using triethanolamine.

Furthermore, as a consequence of the flexibilization action and also due to the requirement for quality control of the ethanol-based sanitizers, fast, green and low-cost analytical methods become even more

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necessary. Near-infrared spectroscopy (NIRS) fulfil these characteristics [5], and was used to determine the amount of ethanol in several commercial products [6]. The ethanol content of beverages and spirits was successfully determined using NIRS [7–9]. The evaluation of fuel ethanol quality and the quantity of the alcohol additive found in gasoline were performed using NIRS [7,10–12]. In common, these works employ costly bench-type NIR spectrophotometers or instrument prototypes [13], and quantitative results were based on the use of multivariate regression methods.

The literature lacks in describing direct analytical methods for quality control of the composition of ethanol-based sanitizers. So far, only one communication very recently published on-line describes the determination of ethanol in hand sanitizers using infrared (IR) and near-infrared spectroscopy (NIRS) [14]. This communication attempted to determine the ethanol content of sanitizers neglecting the effect of interferents and employing costly NIRS instrumentation (above US$ 20,000), which restricts their extensive use by small companies and by inspection agencies. Besides, the use of NIRS was not fully explored for quality assessment of sanitizers, aiming to provide, for example, a fast qualitative screening of non-conformities, and information about the rate of volatilization of ethanol from different formulations.

The present work aims to improve the use of NIRS as a fast, green, and non-expensive technique to monitor comprehensively the quality of ethanol-based sanitizers. The study was conducted employing a low-cost portable NIR spectrophotometer (~US$ 1000), and a straightforward sample measurement protocol. The spectral data were analyzed using multivariate methods based on principal component analysis (PCA) and partial least square regression (PLSR) for qualitative, and quantitative purpose, respectively.

2. Experimental

2.1. Ethanol-based sanitizer samples

Samples of sanitizers (25 g for F1 and F3; 25 mL for F2) were prepared according to the three formulations preconized by ANVISA [4] described in Table 1 and worldwide adopted [1,2,15]. The content of ethanol in the stock solution was 92.15% (m/m), as determined using an automatic densimeter (Anton Parr, DMA 5000 M, Austria). Deionized water was used throughout. The ethanol content was varied from 40 to 85 % (m/m) for F1 and F3, and from 40 to 90 % (v/v) for F2. The quantities of additives were kept constant at the recommended amount by the regulatory agency. The number of samples prepared was 18, 17, and 18 for F1, F2, and F3 formulation, respectively. Additional samples of formulation F2 and F3 were produced changing the content of additives and used for interference evaluation. For F2 the quantity of glycerol (Polytecnica Química, Brazil, 98% (m/v)), and hydrogen peroxide (Dinamica, Brazil, 3% (m/v)) were changed. For F3 the quantity of glycerol, carbomer (3 V Sigma, USA, 98–100% (m/m)), and triethanolamine (Nitrogenius, Brazil, 85% (m/v)) were varied. The ethanol content was kept as recommended (Table 1).

Table 1

Composition of the three recommended ethanol-based sanitizers as specified by the Brazilian National Agency of Sanitary Vigilance (ANVISA).

Component	Formulation (ANVISA)		
	F1/% (m/m)	F2/% (v/v)	F3/% (m/m)
ethanol	70.0	80.0	70.0
water	30.0	14.4	29.5
carbomer	–	–	0.50
glycerol	–	1.4	–
hydrogen peroxide	–	4.2	–
triethanolamine	–	–	q.s.* pH = 5

* Quantum satis: quantity enough to. Typically 0.14 % (m/m).

Forty-one commercial samples of sanitizers were purchased in the local commerce of Viçosa, Minas Gerais state, Brazil. Two of these samples were formulated as ethanol/water solutions (F1). All others were formulated as a gel (F3). No commercial sample was found employing formulation F2. Thirty samples are formulated as a gel (F3) employing carbomer (a cross-linked polymer of acrylic acid) as a gel-forming agent, two samples employ *Astragalus gummifer* (a natural polysaccharide), and three uses hydroxypropyl methyl cellulose for the purpose. Other six gel samples make no mention of the gel-forming substance employed. Some labels products declare they contain a fragrance and/or moisturizing agents such as aloe vera and preservers in non-specified quantity, among several other additives. All gel-based and water/ethanol commercial samples specify a 70% (m/m) content of ethanol in their labels.

2.2. NIR spectrophotometer

The portable NIR – Generic Model (Young-Green, Hsinchu, Taiwan) based on the low-cost NanoNIR (Texas Instruments Inc., Dallas, Texas, USA) was employed. The instrument was previously evaluated for its signal-to-noise ratio for its monitoring spectral region (900–1700 nm) [16]. The best signal-to-noise ratio spectral region (960–1664 nm) was employed [16]. The instrument was held in place using a ring stand and a clamp, as shown in the Fig. S1. The optical measurement window was pointed down and kept at 6 mm above the ring stand platform. The instrument is connected to the controller microcomputer running a property software (Texas Instrument, DLP NIRscan Nano GUI v 2.2.0).

Spectra were obtained using the Hadamard multiplexed measurement protocol [13] aiming to improve the signal-to-noise ratio (SNR). The spectrophotometer operated with an automatic gain of the detector amplifier. The spectra were acquired as the average of 20 scans with 228 points obtained in the range 900–1700 nm. The total scan time per sample is 5.7 s. Only one average spectrum was acquired per measured sample.

Kinetic data were obtained employing the back-to-back scan facility available in the controlling software.

2.3. Sample cell and measurement protocol

The transflectance sample cell is depicted in the Fig. S2. It consists of a disk of Teflon® 5 mm height × 30 mm diameter. A shallow circular groove (15 mm diameter and 0.5 mm deep) was carved in one of the faces of the disk. The cell window is constituted of a 22 × 22 mm microscope glass slide, 0.10 mm thick.

Sample measurement is performed as follow. The cell groove is filled with about 120 μL of the sanitizer sample with the aid of a 1.0 mL plastic disposable syringe. The glass window is placed over the groove and gently pressed. The closed-cell is centrally placed under the measurement window of the NIR spectrophotometer (Fig. S1). The two radiation sources of the instrument illuminate the central groove of the cell, which is 1.0 mm distant from the optical window of the instrument. Guides fixed in the platform ensure the repeatability of cell positioning. The radiation from the instrument sources impinges on the cell, pass through the sample and is reflected in the entrance slit of the equipment, characterizing a transflectance measurement mode.

The reference signal for absorbance calculation was obtained every 20 min time interval, employing the empty closed-cell. Spectra files are named and stored in ASCII format.

2.4. Study of the volatilization rate

About 100 mg of F1 and F3 samples (containing ethanol as recommended by ANVISA) and two commercial samples were delivered to the open measurement cell. A reference for absorbance calculation was obtained using the empty open cell. The experiments were conducted at the temperature of (20 ± 1) °C. Spectra sets were obtained

using the functionality of the back-to-back scan of the spectro-photometer software during a 20 min in time intervals of 1 min, while the sample volatilizes. The number of scans for average was ten, allowing to reduce the acquisition time to 3.7 s.

2.5. Multivariate data analysis

Principal components analysis and partial least square regression [17] were performed using the Unscrambler 11.0 chemometric package (CAMO, Norway). The default pre-treatment of the spectral data set was performed sequentially by Savitizky-Golay smoothing (2°· polynomial, 9 points window) of the full spectrum, area normalization, and standard normal variate (SNV) of the spectral region between 960 and 1664 nm [17]. Data has been mean-centred before multivariate analysis.

3. Results and discussion

3.1. Spectral pre-treatment

Before starting the multivariate analysis, the best pre-treatment of the spectral data was established. Although the spectrum acquisition of a sample is very rapid and simple, it is difficult to maintain constant the sample quantity delivered into the measurement cell. As a consequence, its optical path changes as a function of the sample quantity and pressure imposed by the operator on the glass window. This fact generates a source of undesirable spectral variability. Fig. 1 shows three sets of five spectra each of F1 (ethanol, 70% (m/m)), F2 (ethanol 80% (v/v)) and F3 (ethanol, 70% (m/m)) sanitizers before (Fig. 1A) and after (Fig. 1B) transformation by smoothing, area normalization and standard normal variate [17]. The transformation is effective to correct the spectra set for unwanted sources of variability, keeping the original spectrum profile. Therefore, all data set was pre-treated this way before conducting the chemometric analysis.

In Fig. 1B is possible to observe that the F1 and F3 formulation samples containing the same recommended amount of ethanol (70% (m/m)) show very similar spectra (indistinguishable in Fig. 1B), despite F3 being formulated as a carbomer gel. F2 sample shows slightly different spectra, probably due to the addition of glycerol, whose molecule presents three O–H groups, absorbing strongly and overlapping the ethanol spectrum in the ethanol characteristic absorption spectral regions.
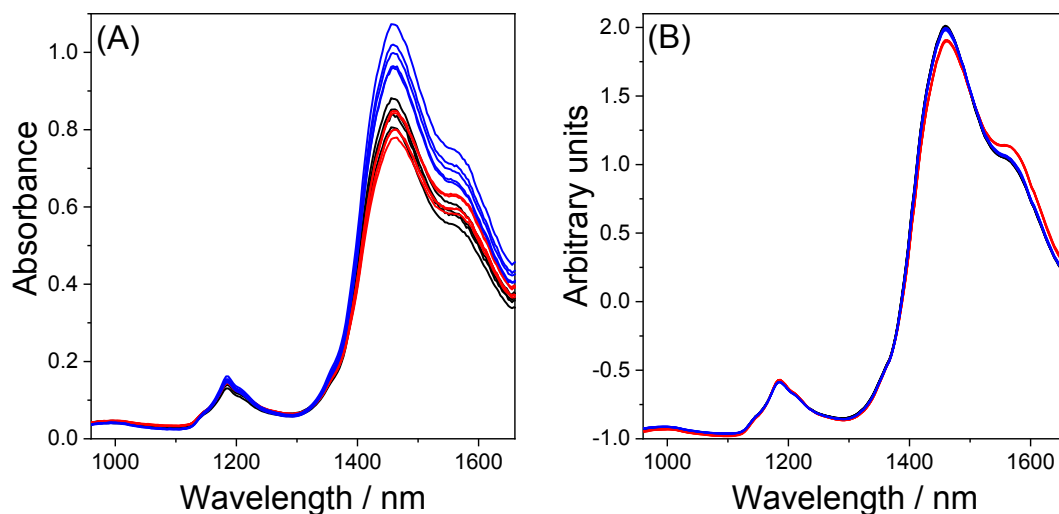

Fig. 2. Complete pre-treated spectral data set of sanitizers of formulation F1, F2 and F3. Ethanol content varying from 40 to 85 % (m/m) for F1 and F3, and 40–90% (v/v) for F2. The major spectral features associated with the water and alcohol content are indicated.

3.2. Qualitative evaluation of commercial sanitizers for frauds and non-conformities

Fig. 2 shows the pre-treated spectra data set of all three formulations. It can be inferred from the spectra profiles that the relevant information regarding the active substance (ethanol) of the hand sanitizers is located in the 1400–1600 nm spectral region where the absorption due to the first overtone of vibrational stretching mode of the O–H groups of the alcohol and water overlaps. The shoulder found at 1570 nm are clearly associated with the ethanol content, while the peak at 1458 nm shows increasing intensity as a function of the water content. The region of low-intensity absorption between 1200 and 1260 nm is attributed to the second overtone of C-H-stretching vibrational mode of the ethanol molecule or any other organic compound present in the sanitizer composition [18].

Fig. 1. Effect of the pre-treatment on the spectral data. (A) raw spectra of five replicates of samples of formulations F1 (black line), F2 (red line) and F3 (blue line). (B) transformed spectra; the spectrum sets of F1 and F3 are superimposed.
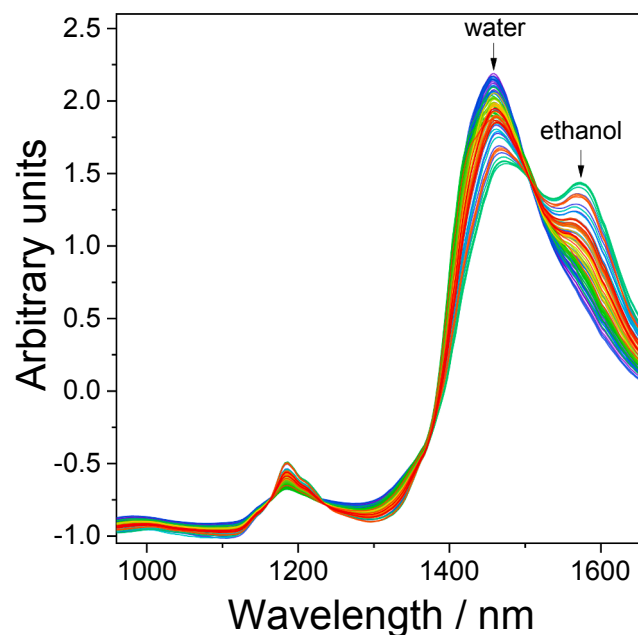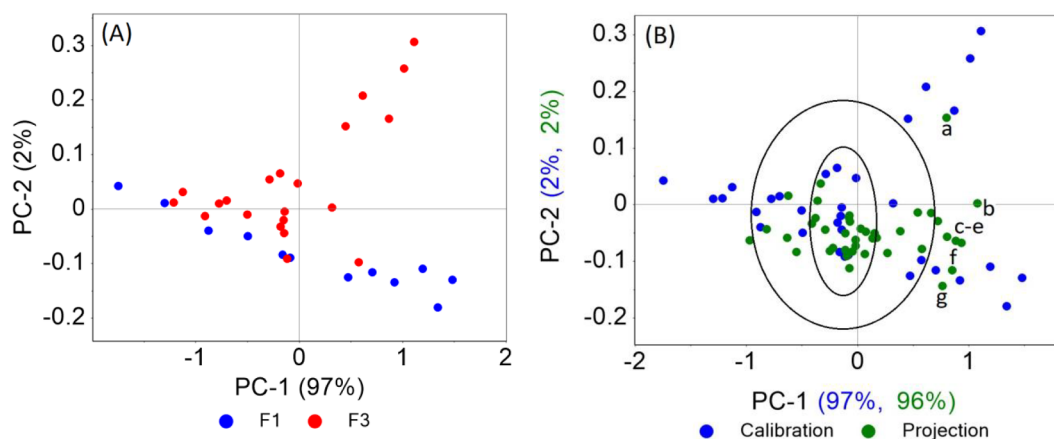
Fig. 3. (A) Score plot for the principal component analysis (PCA) model constructed using the samples of sanitizers prepared in the laboratory, according to formulation F1 (blue dots) and F3 (red dots). Ethanol content in the range 50–80 % (m/m). (B) Projected scores of the commercial sample set (green dots) in the PCA model of F1 and F3 sanitizer samples (blue dots). Refer to the text for more details.

A set of thirty-three spectra of F1 and F3 samples with ethanol content in the range 50–80 % (m/m) was submitted to a PCA. These formulations were selected because the commercial sample set contains only two products formulated as F1 and thirty-nine formulated as F3 (alcohol gel). The F3 set contains several samples with the recommended content of ethanol (70% (m/m)) and with variable contents % (m/m) of carbomer, triethanolamine and glycerol to simulate a few sources of variability in the composition of commercial products. Fig. 3A shows the score plot for the first and second principal components (PC) identified according to the type of formulation. The first PC captures 97% of data variance, and its scores are arranged in the direction of increasing ethanol content, from left to right in the Fig. 3A. The second PC captures an additional 2% variance, and together with the first PC certainly captures the relevant information present in the data set. The information is dominated by water/ethanol ratio content.

Fig. 3B shows the scores for the calibration and commercial samples projected in the PCA model constructed with the samples prepared in the laboratory. The scores of the commercial samples are distributed inside the PC space limited by the scores of the prepared samples. It means that, despite the composition variability of the commercial samples, their spectra do not differ significantly from those of the prepared samples set with F1 and F3 formulation. The smaller ellipse delimits the scores of the F3 and F1 samples presenting the correct ethanol content as recommended by ANVISA. The scores of twenty-five commercial samples are found inside this ellipse. These samples can be screened as in conformity with the recommended content of ethanol.

The larger ellipse was arbitrarily inserted to delimit the ethanol content tolerance between 62 and 75 % (m/m). This range was found to be capable of inactivating the coronavirus, causing CoVID-19 disease [15]. Commercial samples whose scores are located outside the large ellipse can be screened as non-conform or fraudulent products. For instance, commercial samples sold as alcohol gels labelled as "a", "b", "c-e", "f" and "g" in Fig. 3B, present a relatively high distance from the scores of the samples with correct composition. These samples can be screened as non-conforming samples. Gross frauds, exemplified by sample labelled as "a" in Fig. 3B, found very close to an F3 with only 52% (m/m) ethanol, can be easily identified.

Five samples were detected to have an ethanol content somewhat higher than the recommended. This samples may have a higher content of ethanol or may have employed glycerol as an additive. Three of those samples declare in their labels to contain glycerol in a non-specified quantity. In contrast, among the seven samples identified as non-conform, four declares not to contain glycerol. As this substance exert a positive interference on the content of ethanol detected by NIRS, it consists of additional evidence of fraud.

3.3. Quantitative determination of ethanol in sanitizers

Each of the three sets of samples prepared in the laboratory was split into two subsets. Besides the samples prepared according with the composition recommended by ANVISA, the calibration and validation sets included × additional F3 samples containing variable contents of the additives. One set was employed for PLSR model development aiming at the determination of the active substance (ethanol) in the sanitizers of the three formulations; the other was used for model validation. Table 2 shows the characteristics and summarize the calibration and validation results obtained. The three PLSR models employed only two PLS factors which together explain at least 98% of the spectral data and ethanol content variances. Loadings values reveal a strong correlation between the previously appointed spectral regions (Fig. 2) associated predominantly with the presence of water and ethanol in the sanitizer composition. The root mean square error of prediction (RMSEP) values obtained after model validation were improved when compared to those obtained previously by using NIRS and an instrument significantly more expensive [14].

The repeatability of the ethanol content determined by using the PLSR models, was assessed by five replicate measurement of three samples, one of each formulation, including the sample loading procedure. The mean and standard deviation found for the determination of the ethanol content in these samples were: (68.35 ± 0.06) % (m/m), (76.9 ± 0.2) % (v/v), and (68.9 ± 0.3) % (m/m) for the F1, F2, and F3 formulation, respectively.

A joint regression model, including the spectra of prepared samples

Table 2
Summary of the performance of the NIRS-based PLSR models constructed for the determination of ethanol in different hand sanitizers formulations.

Model characteristics	Formulation			
	F1	F2	F3	F1 + F3
ethanol range/% (m/m)	40–85	40–90.5*	40–85	40–85
calibration samples	8(1)	9	10(1)	18(2)
validation samples	9	8	7	16
number of PLS factors	2	2	2	3
RMSECV/% (m/m)[†]	0.45	1.4	0.66	0.71
RMSEP/% (m/m)[‡]	0.68	1.0	0.94	0.96
R² calibration[§]	0.9989	0.9952	0.9979	0.9961
R² validation[§]	0.9972	0.9941	0.9952	0.9940

* Ethanol range/% (v/v); [†]root mean square error of full cross-validation; [‡]root mean square error of prediction (validation); [§]coefficient of determination. The numbers between parenthesis refer to the outliers removed from the original set due high residual and/or leverage [17].

of F1 and F3 formulations, was also evaluated. These formulations specify the ethanol content in % (m/m). To make a joint model is reasonable, considering the results showing in Fig. 1B, where the spectra similarity between the F3 and F1 formulation containing the same amount of ethanol is evidenced. The difference is the presence of the gel-forming carbomer 0.5% (m/m) in F3. The calibration and validation results can be seen in Table 2.

The join model required three PLS factors. Interesting, the joint model can predict the ethanol content of the two formulations with an acceptable RMSEP of 0.96% (m/m) found after model validation. It means that the gel-forming additive when present in regular quantity does not impart a significative effect on the determination of the ethanol content by NIRS and PLSR. In the Fig. S3 it is possible to observe the calibration and validation performance of this model.

3.4. Interferences

The determination of ethanol content in the three formulations may suffer interference of other additives and/or the change in the content of substances such as glycerol, hydrogen peroxide and carbomer already present in formulations F2 and F3 as recommended by ANVISA. The variety of composition found in the commercial alcohol gel samples is astonishing. Thirty-seven additives were reported in the labels of the commercial products used in this study. The most common are glycerol, denatonium benzoate (denaturant), aloe barbadenis, aminomethyl propanol, propylene glycol, and fragrances. Though the manufacturers mention the composition, they do not mention the quantities of the additives. Nevertheless, they refer to substances that must be present in small quantities in the sanitizer formulation [2]. Therefore, they should not affect significantly the determination of the ethanol content using the PLSR models developed in this work.

Several samples of formulations F2 and F3, mostly containing ethanol close to 70% (m/m) or 80% (v/v), were prepared with different amounts of additives in order to verify the effect of concomitants on the determination of ethanol. For F2, the quantity of glycerol and hydrogen peroxide was doubled, halved and not added. For F3, the amount of carbomer, and triethanolamine was also halved and doubled, with consequent change of the final pH of the gel from 5 to 7. In the present case, the amount of triethanolamine (85% (m/v)) changed from 2 to 7 drops (0.043–0.15 g) in 25 g, added to alkalinize the water–ethanol-carbomer mixture to form the gel. Also, glycerol was included in different quantities in the formulation F3, as several commercial products mention the addition of this emollient substance, even though ANVISA does not recommend its use in the manufacture of alcohol gel.

The ethanol content of the prepared samples was predicted using the previously validated model for each formulation. The results are shown in Table 3.

As can be observed, glycerol can be identified as the most interfering concomitant. Overall, the interference caused by variable quantities of additives in formulations F2 and F3 is tolerable with a mean absolute error of 1.4% (v/v) and 1.3% (m/m).

The ethanol content of the thirty-nine commercial alcohol gel and two water/ethanol samples was estimated using the F1 + F3 joint PLSR model. The ethanol content of commercial samples varied from 56 to 77% (m/m). Fig. 4 shows the frequency distribution of the ethanol content of the samples. The seven samples previously identified by PCA as non-conform show ethanol content from 56 to 62% (m/m), confirming the results obtained by projection on the PCA model.

3.5. Determination of the ethanol content of commercial samples

As previously mentioned, positive interference caused by the glycerol can be anticipated, as its molecule present three O–H groups and its spectrum overlaps that of ethanol almost along the entire NIR spectral region employed in this work. This fact can explain the higher ethanol content (77% (m/m)) obtained for only one sample whose label

Table 3
Results for the interference of selected concomitants on the determination of ethanol in sanitizers by NIRS.

| Sample	Component/% (m/m)				Ethanol content/% (m/m)		Absolute error/% (m/m)
	H_2O_2	glycerol	water	carbomer	found	expected	
1*	4.16	2.90	13.94	–	81.38	79.00	2.38
2*	4.16	0.73	16.11	–	77.78	79.00	−1.22
3*	4.16	0.00	16.84	–	76.50	79.00	−2.50
4*	8.32	1.45	11.23	–	79.04	79.00	0.04
5*	2.08	1.45	17.47	–	78.88	79.00	−0.12
6*	0.00	1.45	19.55	–	77.12	79.00	−1.88
7	–	–	32.48	0.50	67.17	67.28	−0.11
8	–	–	29.83	0.50	69.86	69.72	0.14
9	–	–	29.81	0.50	69.94	69.75	0.19
10	–	–	29.30	1.00	68.43	69.75	−1.32
11	–	–	29.80	0.50	70.33	69.76	0.57
12	–	–	51.81	0.50	46.88	49.48	−2.60
13	–	–	35.26	0.50	63.25	64.73	−1.48
14	–	–	29.83	0.50	69.21	69.74	−0.53
15	–	–	24.36	0.50	75.19	74.77	0.42
16	–	0.49	29.30	0.50	69.52	69.76	−0.24
17	–	0.97	28.75	0.50	69.58	69.83	−0.25
18	–	2.00	27.65	0.50	77.56	69.90	7.66

* Ethanol content in % (v/v).
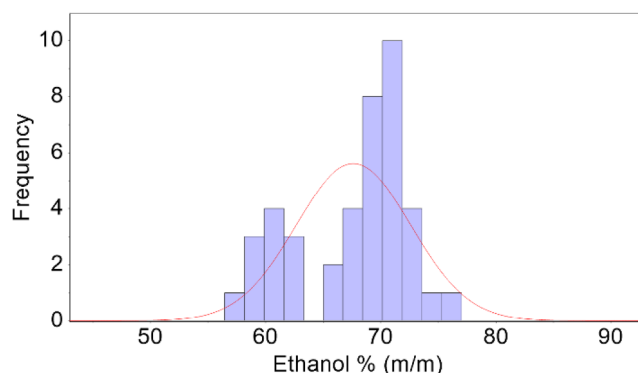
Fig. 4. Frequency of ethanol content of the commercial sample set, as determined by NIRS.

declares to contain glycerol. However, the confidence interval (called in the Unscrambler as "deviation" [17]) of this result shows that the sample must be classified as a prediction outlier. This fact reveals that the multivariate regression model can detect commercial samples whose composition are significantly different of the recommended by the regulatory agency.

On the other hand, as the quantity this substance added in the gel formulations must not exceed 1% (m/m) [2], the interference can be considered negligible. Therefore, is possible that this sample may also have a higher ethanol content.

Considering that the efficiency of the gel sanitizer to inactivate the SARS – Cov-2 virus is ensured for ethanol content in the range 62–71 % (m/m) [15] the global error caused by concomitants present in the commercial formulations should not jeopardize the use of NIRS for the determination of the ethanol content in commercial products, ensuring their quality and efficacy. The expected error would be ± 1.3% (m/m) for F1 and F3 formulation.

3.6. Volatilization study

The time interval the active substance, ethanol in the present case, remains in contact with the hands during sanitization is a relevant factor regarding the sanitizer efficiency [2,15]. Ethanol is volatile at room temperature, and it is lost during the sanitization procedure.
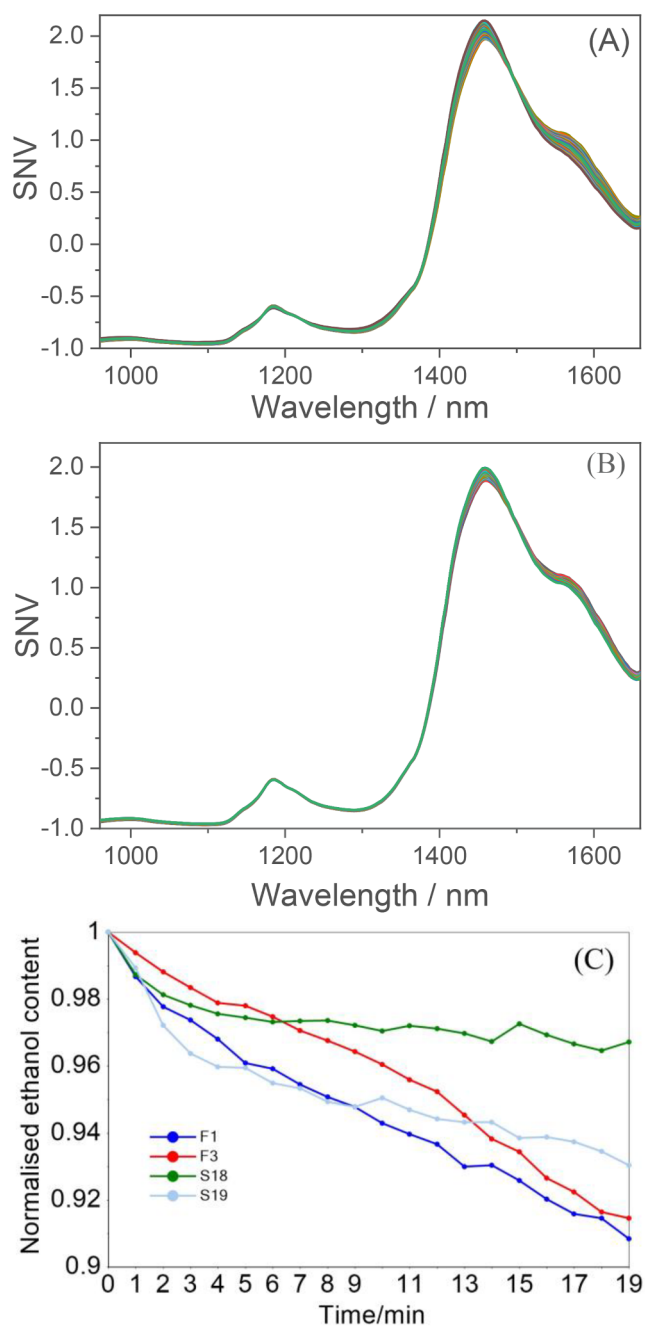
Fig. 5. (A) and (B), pre-treated spectral data set obtained during the volatilization experiment for a F1 (sample prepared in the laboratory, containing 70% ethanol) and S18 (commercial sample, containing 68% ethanol); (C) Normalized change in the concentration of ethanol due to evaporation of the four tested samples showing different composition.

Several factors, such as the presence of additives, composition and the viscosity of the gel, can influence the volatilization rate of ethanol [2].

Therefore, the F1 and F3 formulations and two commercial products (S18 and S19) employing different gel-forming (*Astragalus gummifer,* and hydroxypropyl methylcellulose), containing ethanol close to 70% (m/m), as recommended by ANVISA, were evaluated for their volatilization rate using NIRS. Fig. 5A and 5B show the pre-treated spectrum sets obtained for the volatilization experiment carried out using the F1 sample and the commercial S18, which employs *Astragalus gummifer* as gel-forming, respectively.

The content of ethanol associated with each spectrum obtained during the volatilization experiments was determined using the joint

F1 + F3 PLSR model. The use of this model should cause a bias in the ethanol concentration results because the model was constructed using the closed-cell. Nevertheless, the results permit to evaluate the volatilization rate in a relative way.

As can be seen in Fig. 5C, the F3 formulation presents a lower volatilization rate of ethanol than F1. This characteristic may be attributed to the gel matrix. Sample S18, based on *Astragalus gummifer* gel-forming, shows the lowest rate of volatilization.

Although based on a preliminary study, the results obtained demonstrate that NIRS can be used to assess other parameters associated with the efficacy of the ethanol-based sanitizer. Not only the content of active substance can be determined by NIRS. The effect of other quality parameters associated with concomitant factors such as formulation as a gel or not, and gel characteristics can also be assessed.

Considering these preliminary results, perhaps, under more controlled conditions, the volatilization rate assessed by NIRS may be used as a quality test for ethanol-based sanitizers in the future.

4. Conclusion

The use of near-infrared spectroscopy (NIRS) for quality control of the most frequent used ethanol-based hand sanitizers assisting the fight against the CoVID-19 disease was evaluated comprehensively.

The performance of the multivariate models based on NIR spectral data permits the determination of the ethanol content of the three more common formulations of sanitizers with an estimated absolute error of 0.83% (m/m) or 1.0% (v/v), according with the RMSEP obtained, if the model is developed with samples prepared in the laboratory to match the product composition. Probably, the error increases to close to 1.3% (m/m) when the models are applied to real commercial samples, as demonstrated by the interference study. The repeatability of the method is better than 0.3% (m/m).

The cost of the spectrophotometer (~US$ 1000) and the sample cell employed in this work is affordable to small manufacturers which are helping to fight the CoVID-19 outbreak. The instrument has been previously evaluated by its long-term performance with excellent results considering the cost/benefit ratio [16]. The chemometrics software package "R" [19] available free of charge can be used to perform the necessary multivariate analysis of spectral data in case a commercial software is not available.

The analytical procedure is straightforward, and manufacturers can produce their models (with the desired composition, including additives not studied in this work) to improve the performance, and effectively control the quality of the raw substances employed for fabrication and of the final product. The measurement takes about 1 min, and requires around 120 μL of a sample.

On the other hand, agents of the sanitary vigilance can count on a low-cost means for inspection, including in-field, of commercial ethanol-based sanitizer products, aiming at the identification of frauds and non-conformities. The projection of new samples into the two-dimension PCA model constructed with the database of samples prepared in the laboratory allows rapid identification of possible frauds and non-conformities. The distance of the score in the first and second PC of the tested samples from those with the expected composition for each formulation is used to this end.

Finally, the proof of concept of NIRS as an efficient and practical tool to be used in volatilization studies aiming to estimate the efficacy of different formulations of ethanol-based sanitizers was presented.

5. Author statement

CP and MCH proposed the use of NIR low-cost portable instrument for monitoring the quality ethanol samples, contributed to experimental part, and wrote the manuscript. KAMLC and AFP contributed to experimental part of the manuscript. CP performed the chemometrics analysis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.microc.2020.105421.

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