



Determination of hydrogen peroxide concentration in antiseptic solutions using portable near-infrared system

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Abstract

Hydrogen peroxide (H_2O_2) concentrations in antiseptic solutions (normally 3% H_2O_2) has been determined non-destructively using a portable near-infrared (NIR) analyzer. The spectral variation due to $-\text{OH}$ band around 1400 nm in the second derivative spectra has been found as H_2O_2 concentration changes. Both multiple linear regression (MLR) and partial least squares (PLS) were employed to generate calibration models over the 1100–1720 nm range. The PLS calibration model showed the better calibration performance with a standard error of prediction (SEP) of 0.16%. In order to validate the developed PLS calibration model, H_2O_2 concentrations in commercial antiseptic solutions were predicted and compared with values from a conventional redox titration method. The results showed that NIR predictions had good correlation with conventional analysis values. The rapid and non-destructive determination of H_2O_2 in the antiseptic solution was successfully performed using portable NIR analyzer without any hazardous chemical solvents.

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1. Introduction

Hydrogen peroxide (H_2O_2) solution is colorless, transparent, and odorless. Usually it easily decomposes into water and the oxygen when it is exposed to open air for many hours or shake seriously. H_2O_2 is being more unstable by increasing temperature and the dissociation increases 2.2 times

per 10 °C increase in the 10–100 °C range. H_2O_2 has been widely used in the textile and paper industries as a bleaching agent. Recently, its demand is increasing in the fields of semiconductor manufacture as an oxidant. Different H_2O_2 concentrations are prepared depending on its usage such as disinfecting oxidizer or decolorizing. In pharmaceutical area, H_2O_2 solutions are being used as an antiseptic solution with 3% H_2O_2 .

Continuous inhalation of H_2O_2 can cause nausea, arterial embolism (sudden blocking of an artery), and irreversible lung damage. Recently, central nervous system damage and death have

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been reported after inhalation of H_2O_2 . Conventionally, H_2O_2 is measured by titration using 0.02 mol/l potassium permanganate (KMnO_4) solution. With titration method, analysts are always exposed to H_2O_2 vapor as well as toxic redox solvents during experiment, so it can cause diverse health problems listed above. Additionally, it requires a long analysis time due to the preparation of chemical standard solutions. Therefore, there is a strong demand of new analytical method that can quickly measure H_2O_2 concentrations without any threat for health.

Near-infrared (NIR) spectroscopy is an excellent analytical method that can replace the conventional titration analysis since it can provide fast, non-destructive and reproducible analysis without requiring chemical reagents. Additionally, it is possible to expand it to on-line measurement that can diminish the exposure of chemicals to human [1–3]. Several NIR researches in pharmaceutical area, such as H_2O_2 vapor permeability of different pharmaceutical packaging materials [4], quantification of active components [5–8], and intact tablet analysis [9,10], blend evaluation [11,12], the differentiation of crystalline of piroxicam [13], and the quantification of crystallinity [14] have been widely studied.

In this publication, determination of H_2O_2 concentrations in antiseptic solutions (normally 3 wt.%) has been studied using a portable NIR analyzer. H_2O_2 standards were prepared (0–25.6 wt.%) and corresponding NIR spectra were collected. Both multiple linear regression (MLR) and partial least squares (PLS) were utilized to build calibration models over the 1100–1720 nm range. With this calibration model, H_2O_2 concentrations in commercial antiseptic solutions were predicted to investigate the actual applicability of NIR spectroscopic method.

2. Experimental section

2.1. Materials

H_2O_2 (30 wt.%, reagent grade) used in this experiment was purchased from Waco Chemical

& Supply Co., Ltd. (Osaka, Japan). KMnO_4 , sodium hydroxide (NaOH) and sulfuric acid (H_2SO_4) were achieved from Yakuri Pure Chemicals Co., Ltd. (Osaka, Japan). Thirty-one aqueous standard solution (0–25.6 wt.%) were prepared as the calibration data set for quantitative calibration models. To minimize any analytical errors in sample handling, spectra were collected immediately after samples were prepared. For the test of commercial samples, four different brands of antiseptic solutions (about 3 wt.%) from four different manufacturers were purchased in normal market. To determine the concentration of H_2O_2 for these commercial samples, the conventional redox titration using KMnO_4 was performed.

2.2. Instrumentation

All the spectra were collected using a diode array based portable infrared spectrometer (Model: HN 1100, Spectrontech Co., Ltd., Korea) equipped with a tungsten halogen source and InGaAs microdetector. The spectra were collected using a rectangular quartz cuvette (pathlength: 1 mm) with a temperature control unit. Each spectrum was acquired after an accumulation of 30 scans in the 1100–1750 nm range with 2 nm data interval. All the spectra were collected using CHEMO HN1100 (Spectrontech Co., Ltd.) software.

2.3. Data processing

A total of 31 NIR spectra were divided into 21 spectra for calibration and ten spectra for the prediction data set, which served as a validation set. The division of samples was intended to assign randomly two thirds of the total spectra into the calibration set. All data processing, including second derivative and MLR and PLS regression were accomplished by using CHEMO HN1100 and WINISI (Foss NIRsystem, Silver Spring).

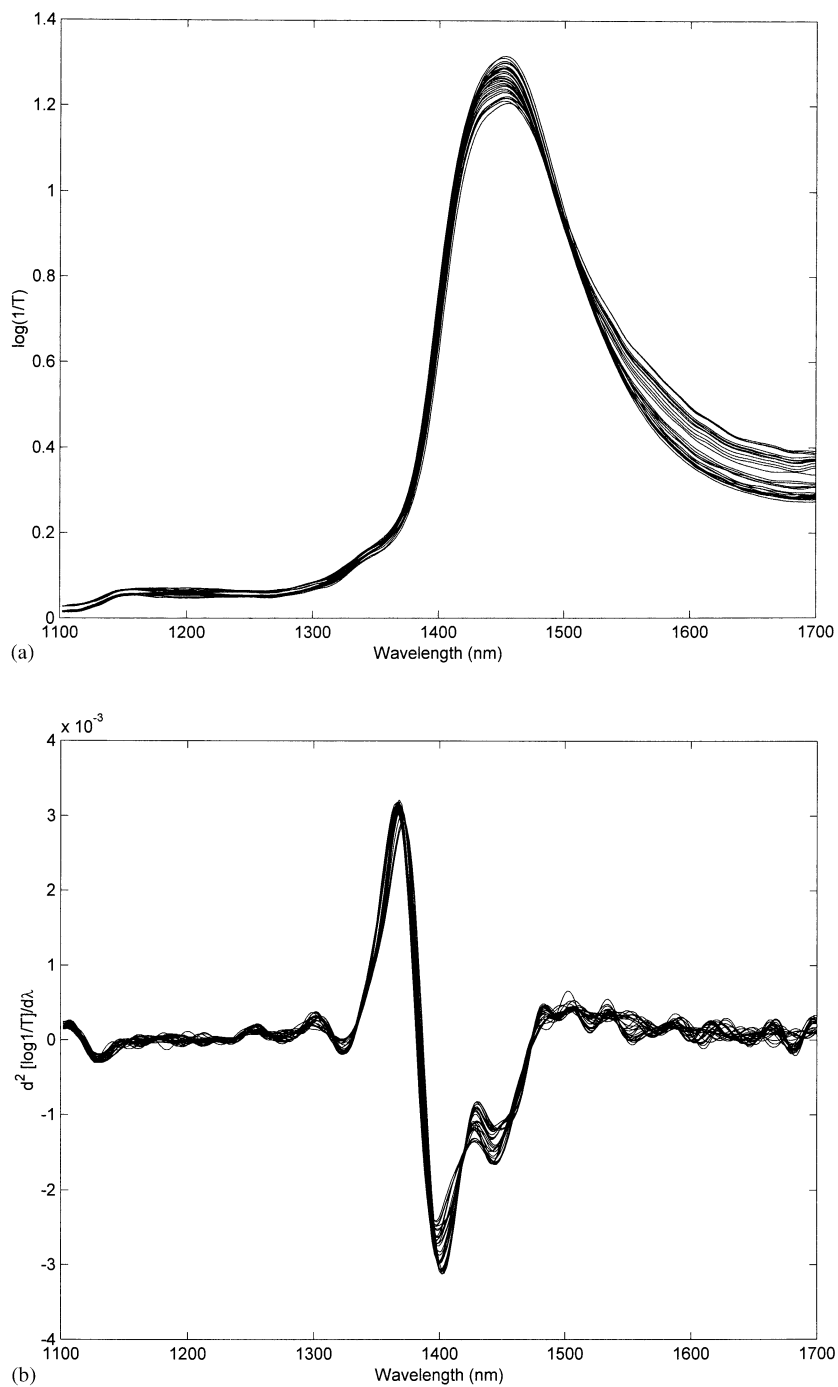


Fig. 1. (a) NIR absorbance spectra of all standard samples (0–25.6 wt.% range). (b) Second derivative spectra of (a).

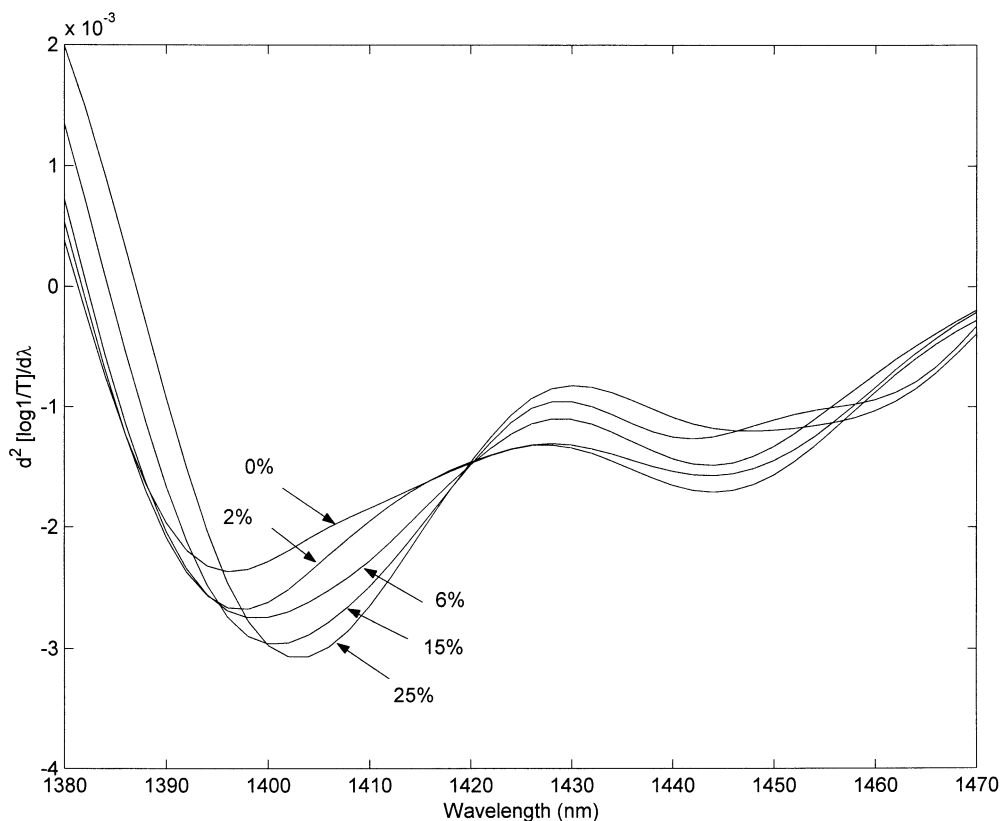


Fig. 2. Second derivative spectra of 0, 2, 6, 16, and 25% of H_2O_2 , respectively, from 1380 to 1470 nm.

3. Results and discussion

3.1. The spectral feature of hydrogen peroxide

The most significant vibration of both water and H_2O_2 is $-\text{OH}$ stretching. Because molecular structure is very similar each other, it is expected that resulting NIR spectral features of both compounds are close. Fig. 1(a) shows NIR absorbance spectra of all samples (0–25.6 wt.% range). The band shown in the figure is the first overtone band of $-\text{OH}$ stretching in infrared region. The spectral features in the 1100–1720 nm range are broad and the $-\text{OH}$ vibration spectral information from water and H_2O_2 was not separated. However, based on the previous publication [15,16], first overtone $-\text{OH}$ vibration wavelength of H_2O_2 is slightly higher than that of water. As shown in the Fig. 1, when H_2O_2 concentration increased, the absorption at 1440 nm from water is clearly

decreasing as well as peak position is moving to higher wavelength.

To investigate the spectral variations more clearly, all raw absorbance spectra were converted to second derivative spectra. All the second derivative spectra are shown in Fig. 1(b). The most significant variations are observed at 1400 and 1442 nm. Fig. 2 shows the second derivative spectra of 0, 2, 6, 16, and 25% of H_2O_2 solutions, respectively. It is clearly shown that absorption is increasing and peak in moving to higher wavelength with the increase of H_2O_2 concentration. In overall, the spectral variations can provide sufficient quantitative analytical information when multivariate calibration is employed.

3.2. MLR and PLS calibration models

MLR is simple, easy to understand, and possible to clearly rationalize the relationship between the

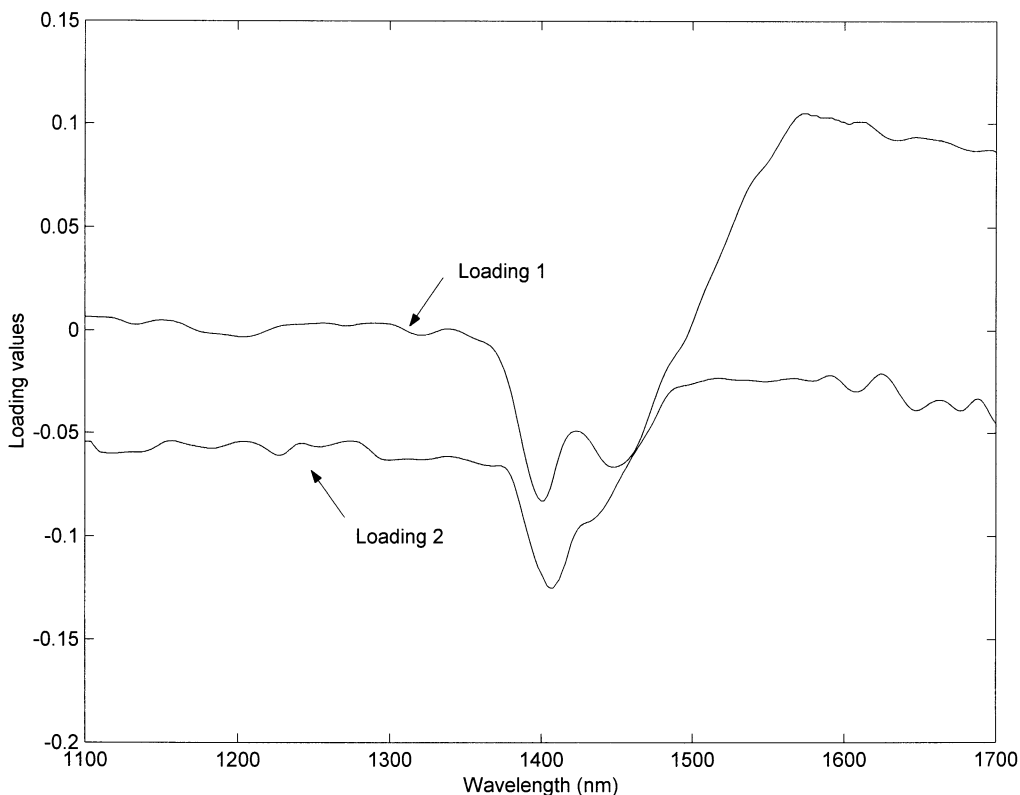


Fig. 3. First and second loading plot for calibration of H_2O_2 using PLS.

NIR spectral features and the concentration of analyte. However, in the presence of multicollinearity, estimates of least square methods including MLR are unstable and tend to lead to poor prediction. PLS regression, factor based calibration method, can eliminate the collinearity problem. Additionally, it is effective in extracting analytical information and useful when many variables (full or fairly wide range of spectrum) are available even though minor components of sample system change. An optimal number of PLS factors should be identified to avoid possible overfitting of a model.

In this paper, both MLR and PLS regression was used to develop calibration models in the 1100–1720 nm range. All the spectra were auto-scaled with standard normal variate (SNV) treatment before performing MLR and PLS. Even though we got better spectral features after second derivatives, the derivative spectral data did not

give much better results for calibration and prediction than original data. Using autoscaling, possible calibration errors from baseline variations, resulted from the change of the sample density, temperature and particle size. For MLR, the effective variables (wavelengths) were selected, as added to the model stepwise from one until both standard error of calibration (SEC) and standard error of prediction (SEP) have the lowest values.

In PLS regression, we first investigated loadings information as shown in Fig. 3. It is noticeable that the first loading shows the negative peaks at 1400 and 1445 nm by using PLS with original spectral data, which also are found in the second derivative spectra. The first peak explains the variance of water concentration and the second one describes that of H_2O_2 as mentioned in the second derivative spectra. The second loading has also the peak at the 1400 nm. The optimum number of factors can be identified as the number

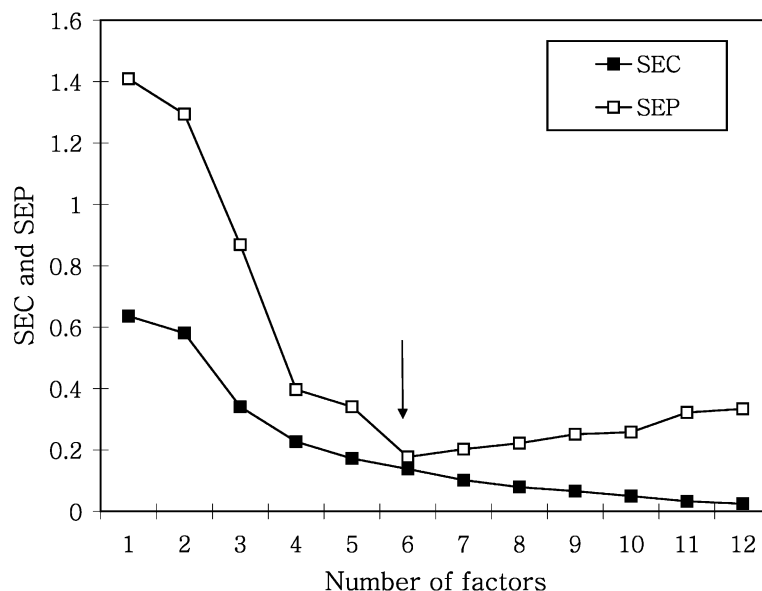


Fig. 4. SEC (filled circles) and SEP (open circles) plotted as functions of the number of PLS factors used for the determination of H_2O_2 within the 1100–1720 nm range.

of factors that gives a minimum SEP for a separate set of validation samples, which were not used in the calibration set. An SEP is an excellent index to represent the ability of a calibration model to predict analyte concentrations independently. Fig. 4 shows SEC (filled circles) and SEP (open circles) plotted as the functions of the number of PLS factors used for the determination of H_2O_2 within the 1100–1720 nm range. As expected, both the SEC and SEP decrease sharply with the initial factors and gradually decrease as more H_2O_2 -dependent spectral variation is incorporated into the calibration model. As the number of factors increases further (i.e. the 7th factor in Fig. 4), the SEC continues to drop slightly while the SEP begins to increase. This is general for factor-based multivariate calibrations. An increase in the SEP indicates that the calibration is overmodeled by incorporating spectral variation that is not related to H_2O_2 . In this case, the optimum number of factors is six.

The results of MLR and PLS calibration are summarized in Table 1. We tried to observe the change of SEC and SEP to decide the optimal factor number. For MLR, the model using three wavelengths (1376, 1436 and 1588 nm) gave the

Table 1

The results of MLR and PLS calibration for determination of H_2O_2 concentration

	SEC (%)	SEP (%)
<i>MLR, selected wavelengths (nm)</i>		
1376, 1436, 1588	0.26	0.28
<i>PLS, number of PLS factor</i>		
6	0.15	0.16

best result. The three wavelengths were selected by step-up MLR. For PLS, six factors were chosen as an optimum using the wavelength region from 1100 to 1720 nm. A fewer factors were also investigated using the narrower wavelength region from 1300 to 1500 nm. However, its prediction result for product analysis was worse than when using entire wavelength ranges. It could be supposed that the model with more factors with wider ranges have some information of other measuring conditions such as temperature, giving more robustness to calibration in this study. Therefore, we cut out only the above 1720 nm region which is

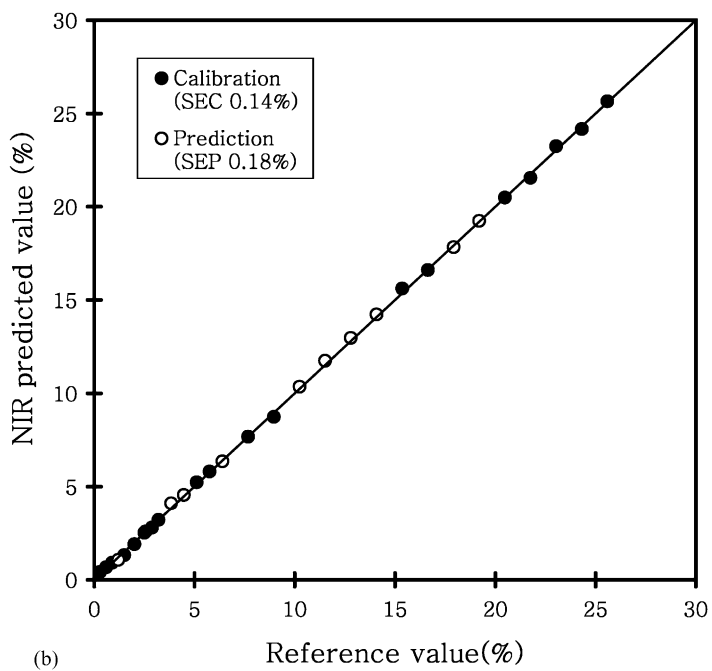
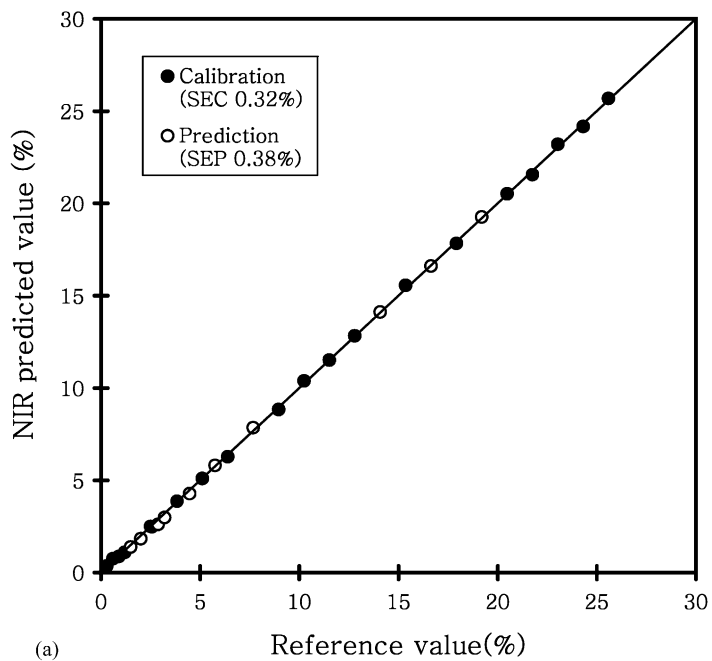


Fig. 5. Scattering plots showing correlation between reference values and NIR measurements for H₂O₂ using MLR (a) and PLS (b).

Table 2
The prediction results of H₂O₂ concentrations for commercial samples of four different manufacturers

Company	Reference (%)	NIR (%)	Residuals
A	2.77 (0.06) ^a	2.58	0.19
B	2.83 (0.18)	2.99	−0.16
C	3.09 (0.14)	3.09	0.00
D	3.27 (0.20)	3.25	0.02

^a The number in parenthesis corresponds to S.D. of each titration analysis.

noise area due to the performance of the cooled InGaAs detector.

As shown in the table, PLS provides the better calibration performance over MLR. Fig. 5 presents the MLR and PLS scattering plots showing correlation between reference values and NIR measurements for H₂O₂ solutions. Filled and open circles represent calibration and prediction data, respectively. For both MLR and PLS regression, the calibration and prediction data correlate well with the conventional reference data and many points fall on or close to the unity line. However, PLS provides the better correlation over MLR.

3.3. Application to commercial hydrogen peroxide solutions

To investigate the actual applicability of the developed PLS model to practical usage, the H₂O₂ concentrations of commercial antiseptic solutions ($\approx 3\%$) were predicted. If there is a compositional difference between standards for modeling and commercial samples, a model will predict H₂O₂ concentration with high error for classical calibration such as univariate calibration. However, when the composition of sample system is not exactly same, the PLS model will keep the same accuracy. Conventionally, commercial solutions contain small amount of organic stabilizer to minimize decomposition of H₂O₂. The typical organic stabilizers such as amino trimethylene phosphonic acid (ATMP) or hydroxy ethylidene diphosphonic acid (HEDT) are used for the protection of H₂O₂. Even with the existence of organic stabilizers, the collected spectra are similar to the spectrum of

pure H₂O₂ solution. The concentration of organic stabilizer is low and the absorption band of stabilizer would not affect on overall spectra and no significant deviation would be expected in PLS prediction. It was shown that PLS prediction based on the factor analysis is robust for the changes of minor components because the PLS model was designed to use mainly the spectral information from H₂O₂. Table 2 shows the prediction results of H₂O₂ concentrations using commercial samples from four different manufacturers. The reference concentrations were determined by a redox titration method. In the table, standard deviations (S.D.) (uncertainty) of each titration measurement are also presented. Comparison of each S.D. of titration and the corresponding prediction residual reveals that NIR predictions match well with the results from titration.

4. Conclusion

The PLS calibration model developed using lab-prepared standards accurately predicted the H₂O₂ concentrations of commercial samples. Even the presence of low amount of organic stabilizer, there was no significant chemical difference with standard method for the commercial samples. Therefore, the PLS model can predict commercial samples with accuracy without any transfer functions or re-development of a model. The rapid and non-destructive determination of H₂O₂ in the antiseptic solution was successfully performed using the portable NIR analyzer without using any hazardous chemical solvents.

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