International Journal of
Health Systems and Medical Sciences

ISSN: 2833-7433
Volume 2 | No 5 | May -2023

Determination of Glucose Level in Blood and Aqueous Solution using Fourier Transform Near Infrared Spectroscopy

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Abstract: Fourier transform near infrared spectroscopy is frequently utilized because it can measure a variety of solid and liquid samples, including components that are water soluble. The measurements of glucose concentrations in aqueous solutions are helpful to explore how near-infrared spectroscopy can be used for non-invasive assessments of glucose levels in the blood and how low concentrations of glucose in water may be determined using it. This study uses Fourier transform near-infrared spectroscopy to present an alternate method for estimating the glucose concentration in aqueous solutions below 1000 mg/dL. This method benefits from being non-destructive and less labor-intensive sample preparation. We carefully produced aqueous solutions of glucose at concentrations of 0–100 mg/dL at intervals of 5 mg/dL, 110–500 mg/dL at intervals of 10 mg/dL, and 525–1000 mg/dL at intervals of 25 mg/dL. As a result, 81 standard solution samples overall are produced for the calibration and validation sample sets. Inferring that the near-infrared prediction model is enough to estimate glucose content in the aqueous solutions below 1000 mg/dL, PLSR analysis to near-infrared spectra demonstrates that glucose content in aqueous solutions can be predicted effectively with a maximum variance of 6 mg/dL. While building a non-destructive glucose level measurement system employing a near-infrared light source, the NIR's capacity to detect glucose concentration below 1000 mg/dL is very crucial.

1. Introduction

In recent years, Near-infrared spectroscopy (NIRS) has become increasingly popular due to its ease in workflow analysis and ability to measure large quantities of samples. NIRS can measure one or more constituents, which can be identified by their fingerprints using a single spectrum [1]. The vibrations of O-H, C-H and N-H bonds, which are present in most substances with covalent hydrogen bonds, are present in the near-infrared region. The harmonic overtones absorptions are generally broader in the NIR region than in the infrared (IR) region, and their intensities decrease as the overtone order increases. IR is highly sensitive to the O-H vibration mode, making constituents measurements in aqueous solutions with IR impossible. Fortunately, NIR can measure the concentrations of constituents in aqueous solutions [2,3], due to the significant decrease in the intensity of the O-H overtone vibration mode compared to the fundamentals in the IR region. However, the broadening of the overtone absorption bands and the combination of vibrations in the NIR region make the analysis of absorption bands complex and require more complex processes. Nonetheless, the amenability of NIR to chemometrics makes it suitable for complex processes.

Samples containing functional groups such as OH, CH, and NH are susceptible to NIR because overtones of their fundamental vibrations (R-H) in the IR region correspond to the NIR absorptions. Although the C = C and C-C bonds do not appear in the NIR region, their C-H vibrations frequencies can reflect the C=C and C-C bond. Because all organic materials contain hydrogen bonds, NIR spectroscopy has been used widely in the pharmaceutical field such as discrimination and analysis of the medicinal components [1–3]. Simeone et al. [4] used NIR spectroscopy to measure sucrose, glucose, and fructose of sweet sorghum juice. Yano et al. [004] employed NIR spectroscopy for the simultaneous prediction of glucose and a citric acid aqueous solution of a blood anticoagulant. The validity in measuring blood glucose was then discussed by Zhang et al. [6] using two-dimensional correlation spectroscopy (2DCS) to improve the data analysis. Recently Saleh et al. [005] examined the glucometer design to measure glucose in blood non-invasively using NIR at a single wavelength.

This technique is quite promising, but various other organic materials on the tissue affect the accuracy of the determination. In other words, it needs spectrum-based measurements. Efforts to advance noninvasive measurement of blood glucose continue to carry out, starting from a fundamental investigation of the NIR glucose spectrum [7,8]. Various measurement techniques were also developed, including NIR Raman spectroscopy [9,10], direct diagnostics using a chip NIR detector implanted beneath the skin [11,12], and the possibility of long-term continuous observation using wireless detector [13,14]. The NIRS approach with an analysis of various spectral range and other measurement techniques have also been studied [15] and analyzed using chemometric. In this study, we examined the use of NIRS to determine glucose content in aqueous solution with a physiological range of concentrations from 0 to 1000 mg / dL. This examination is intended to see at the possibility of NIRS as an alternative approach to constructing non-invasive blood glucose apparatus.

2. Methods

2.1. Sample Preparation

The D-glucose sample used in this study was ordered from Sigma-Aldrich with 99.5 purity without any treatment before use. A total of 81 samples D-glucose in distilled water were prepared with a concentration of 0-100 mg/dL with intervals of 5 mg/dL, 110-500 mg/dL with intervals of 10 mg/dL and 525-1000 mg /dL with intervals of 25 mg/dL. The D-glucose in each sample solution was completely dissolved by using a magnetic stirrer. The 81 samples were then divided into two groups: (i) samples with even concentration (consists 41 samples) were used for calibration and (ii) samples with odd concentrations (consists of 40 samples) were used for validation. Before uploaded into a 1 mm pathlength cuvette, each sample was stirred again or about 1 minute to ensure that D-Glucose dissolved evenly.

2.2. Data acquisition

The NIR transmission spectrum of each sample solution was scanned using a Fourier transform nearinfrared spectrometer (Buchi NIRFLEX 500 solid) in a spectral region of 4000-9000 cm^{-1} and intervals of 4 cm^{-1} (thus, each spectrum consists of 1250 data points). During the measurements, the sample temperature was maintained at 25 ^{o}C. Each sample spectrum was obtained from an average of 32 measurements.

2.3. Data analysis

Both calibration and validation spectra were smoothed using the Savitzky-Golay method employs third order polynomial at a frame size of 21. Spectral normalizations were applied to eliminate multiplicative scattering and baseline variation. The calibration spectra were employed to construct a prediction model using the partial least square regression (PLSR) method. PLSR tries to model relations between sets of observed variables and latent variables. A detailed description of PLRS has been published elsewhere [3,21]. In the PLSR algorithm, the data matrix was mean-centered in order to remove strong transmittance background from water. Validation spectra were used to cross-validate, by utilizing the PLSR parameters, to predict the concentrations validation samples.

3. Results and Discussions

Glucose dissolves well in water but experienced much less NIR absorption compared to water. Since the main portions of the samples comprise water, their NIR transmission spectra resembled the NIR spectrum of water which is characterized by two strong absorptions; the combination band, and overtone in the area of about 4700-5400 cm-1 and 6500-7500 cm-1. Figure 1 shows the transmittance spectra of the glucose in aqueous solution with a concentration of 0, 60 and 490 mg/dL. The diffuse reflectance spectrum of glucose powder is also shown for comparison. Noted that the transmission spectra of water in the spectral region of 4700-5400 cm-1 were saturated due to the extreme water absorption; therefore, the transmission spectra in that of the particular region were omitted in the subsequent analysis. All spectra appear to be similar even though they represent samples with various concentrations. It is because of the subtle change due to the difference in glucose concentration hindered by a strong water absorption background. However, the NIR spectrum of powder glucose shows a noticeable difference between water and glucose absorptions.

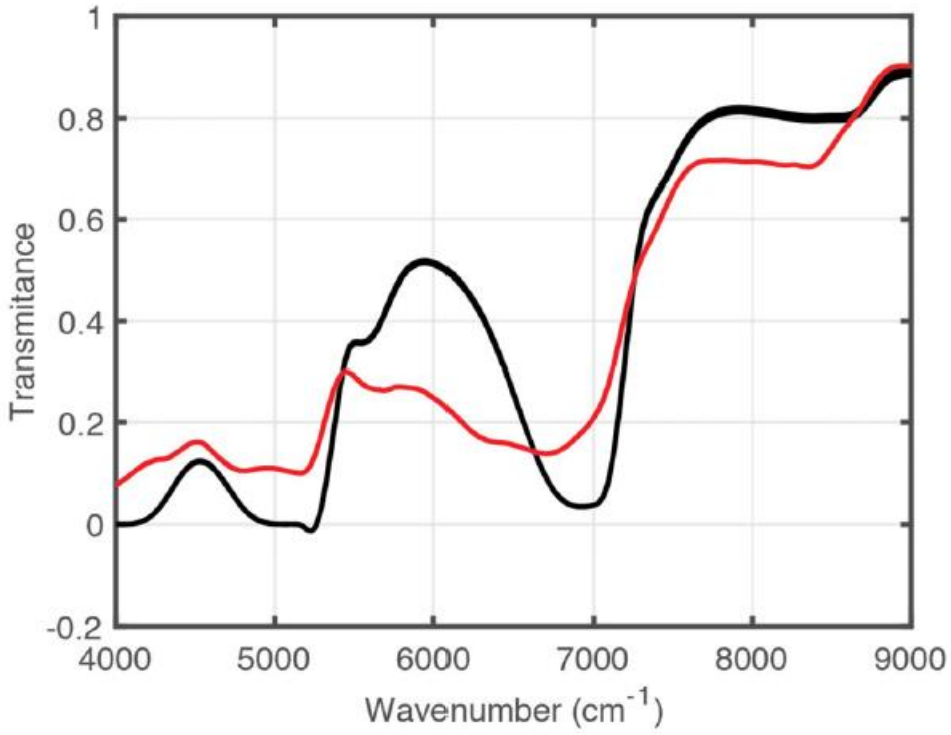

Figure 1. Near-infrared transmittance spectra of glucose in aqueous solution (black) with concentrations 0, 60, and 490 mg/dL. The diffuse reflectance spectrum of powder glucose (red) is shown for comparison. Note that the intensity of reflectance spectrum for powder glucose is not scaled.

NIR spectra often suffer from baseline variation and multiplicative scattering. Therefore, it is necessary to normalize the spectra by subtracting each spectrum with their corresponding transmittance at 4080 cm^{-1} followed by dividing the resulted spectrum with its corresponding transmittance intensity at 9350 cm^{-1}. These normalization steps produced spectra with transmittance between 0 and 1. The normalized spectra at a concentration of 0, 60, and 490 mg/dL shown in Figure 2. One sees in the figure that all spectrum are similar and practically overlapped each other. However, when the spectra subtracted with the spectrum from pure water, the difference spectra left behind revealed a typical glucose spectrum with difference transmittance magnitude. They are featuring broad absorption in a region of 7000-8700 cm-1, 5500-6800 cm^{-1}. In Figure 2, the red and green line representing spectra from the samples of 60 mg/dL and 490 mg/dL, respectively, indicating NIRS distinguishes samples with different glucose concentrations.

The singular values decomposition analysis of the spectral data matrix was applied to obtain a region that substantially contributed to the regression model. Calculations of PLSR were then performed using that of a substantial spectral region. Figure 3 shows the loading plot of the first three

components in the spectral region of 4000 - 9000 cm^{-1}. The plot suggests that significant contribution to PLSR may arise from the full spectral region.

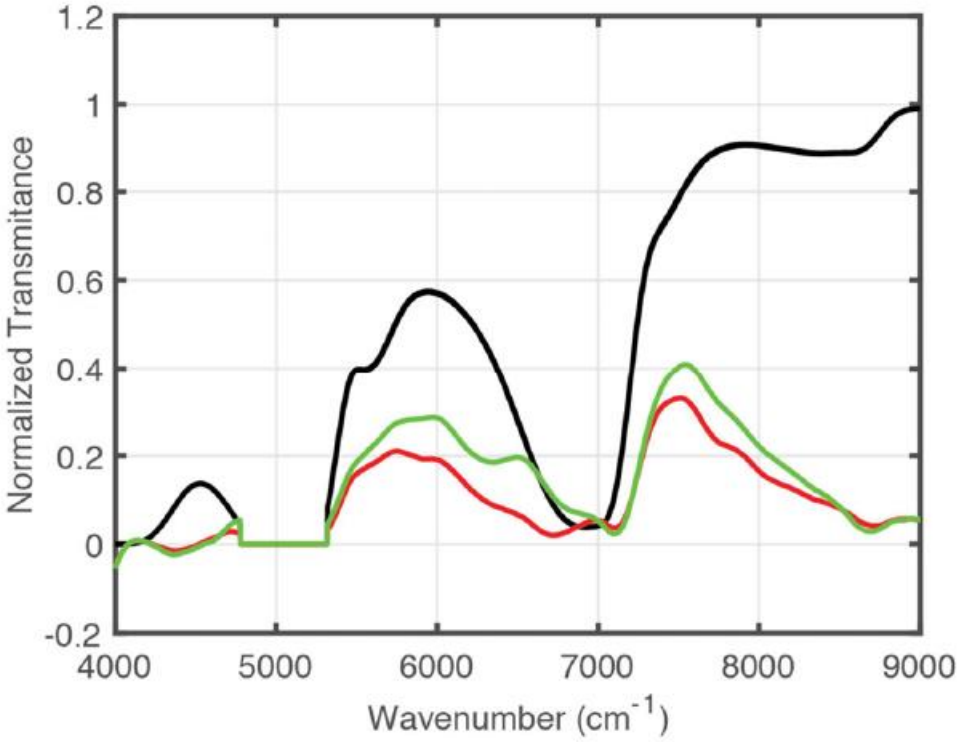

Figure 2. Normalized near-Infrared spectra of glucose in aqueous solution (black) for concentration 0, 60, and 490 mg/dL. Difference normalized spectra, i.e., normalized spectra of glucose in aqueous solution minus normalized spectrum of water, are shown in red and green for glucose concentrations of 60 and 490 mg/dL, respectively. The difference spectra were magnified 100x for clarity.

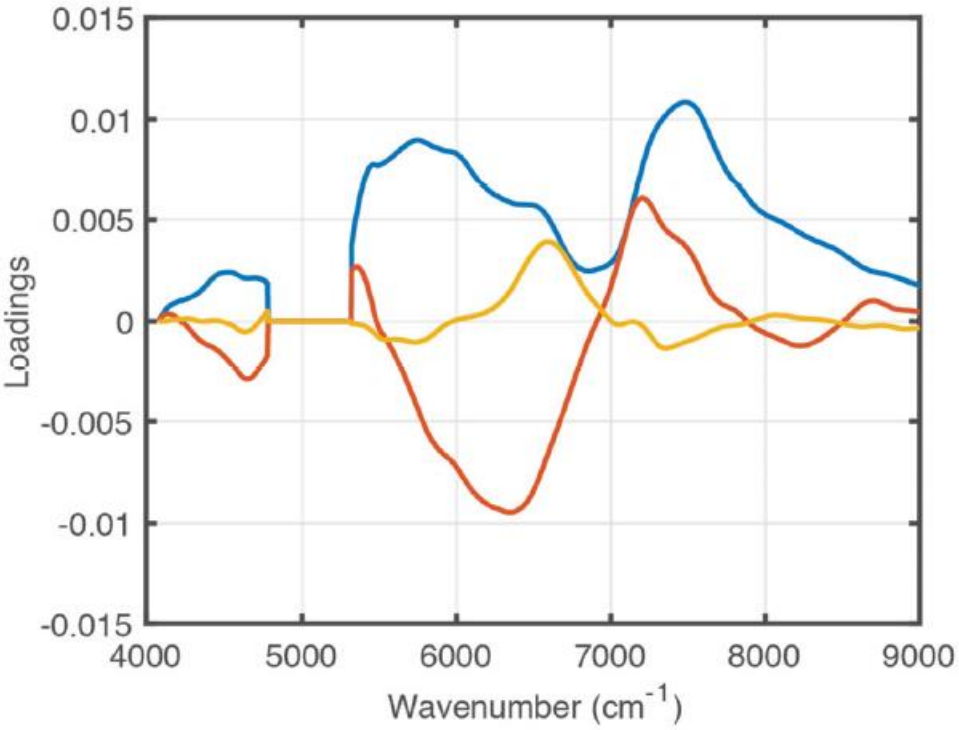

Figure 3. The 1st (red), 2nd (blue) and 3rd (yellow) showing loading plots of the calibration data matrix extracted by singular value decomposition.

The number of the latent variable, N, to be used in PLSR calculations were also carefully selected by finding the prediction residual error sum of square (PRESS) to be a minimum. In this case, N = 8 provides the minimum PRESS of the validation data set, as shown in Figure 4.

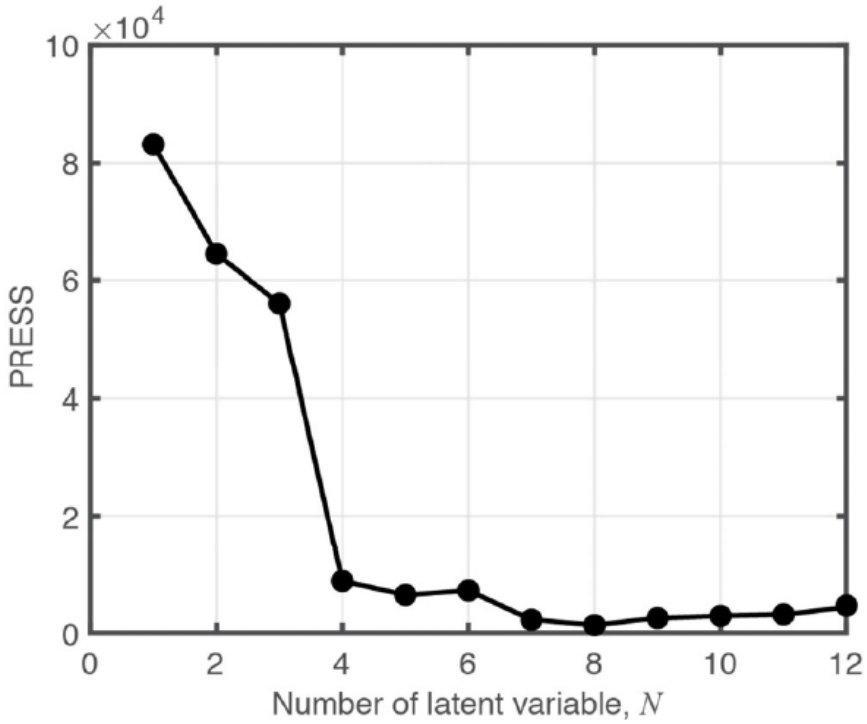

Figure 4. Prediction residual error sum of square (PRESS) of validation data set. Minimum PRESS was achieved at N=8.

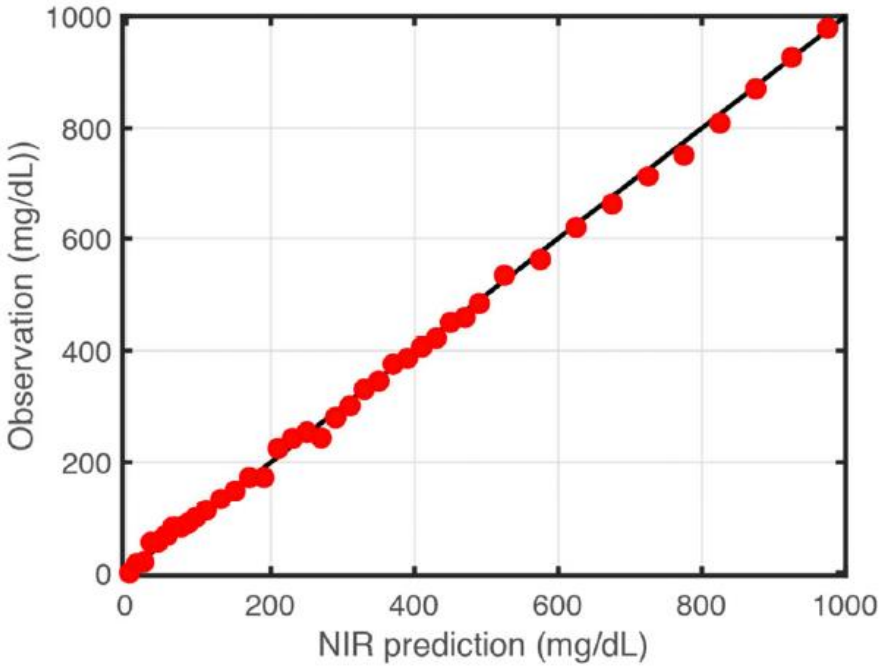

Figure 5. Comparison of Observation (actual) concentration to that of NIR prediction (close red circle). The black straight line shows the expected prediction.

In the examine the accuracy of the PLSR model, the regression parameters derived from the calibration data set were used as an estimator to predict glucose concentrations of the validation samples set (cross-validation) based on their corresponding NIR spectra. Figure 5 shows the validation plot, comparing observations (ordinate) and NIR predictions (abscissa) of glucose concentrations. This plot shows that NIR predictions are very similar to observation ones. The coefficient of determination of the above plot is given by at R^2 = 0.99 with a maximum error of less

than 6 mg/dL. These results are equivalent to previous studies [3] showing that NIR spectroscopy with PLSR can be used to predict glucose concentrations in glucose-water solutions within physiological concentrations of 0-1000 mg/dL. In blood, the measurement of glucose levels certainly more complicated as it contains blood suspended cells, white blood cells, platelets, salt, and dissolved protein. These constituents are sensitive to the NIR so that they require more accurate spectral handling and analysis.

4. Conclusion

Measuring glucose content in aqueous solutions can be done by utilizing NIRS followed by PLSR analysis. The reasonably accurate prediction of glucose concentration in the range of 0-1000 mg /dL was confirmed. The useful spectral region for calibration and detection for glucose content is considerably broad, i.e., 4000-9000 cm-1. In that particular region, NIRS may provide an effective and non-invasive approach to measuring blood glucose levels.

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