Development of a near-infrared spectroscopic system for monitoring urine glucose level for the use of long-term home healthcare

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ABSTRACT

We have been developing a new technique for measuring urine glucose concentration using near infrared spectroscopy (NIRS) in conjunction with the Partial Least Square (PLS) method. In the previous study, we reported some results of preliminary experiments for assessing feasibility of this method using a FT-IR spectrometer. In this study, considering practicability of the system, a flow-through cell with the optical path length of 10 mm was newly introduced. Accuracy of the system was verified by the preliminary experiments using urine samples. From the results obtained, it was clearly demonstrated that the present method had a capability of predicting individual urine glucose level with reasonable accuracy (the minimum value of standard error of prediction: SEP = 22.3 mg/dl) and appeared to be a useful means for long-term home health care. However, mean value of SEP obtained by the urine samples from ten subjects was not satisfactorily low (53.7 mg/dl). For improving the accuracy, (1) mechanical stability of the optical system should be improved, (2) the method for normalizing the spectrum should be reconsidered, and (3) the number of subject should be increased.

Keywords: urine glucose level, near-infrared spectroscopy, chemometrics, PLS method, home healthcare

1. INTRODUCTION

Although there are several drawbacks of urine glucose test compared to blood testing [1], daily monitoring of urine glucose level has still been widely used as a rough indicator of high blood glucose levels [2]. For this purpose, there are several kinds of commercially available items such as test strips [3], a pen-shaped enzyme sensor [4] and a sensor system installed in a toilet [5]. Among these, the third one would be an ideal type for long-term home healthcare, however, there are several drawbacks [5] such as a limited sensor life (4 months or 700 measurements), cumbersome maintenances and a high cost. To overcome these practical drawbacks, we have been developing a new technique for measuring urine glucose concentration using near infrared spectroscopy (NIRS) in conjunction with the Partial Least Square (PLS) method. In the previous study, we reported some results of preliminary experiments for assessing feasibility of this method using a FT-IR spectrometer. In this study, considering practicability of the system, a flow-through cell with the optical path length of 10 mm was newly introduced and accuracy of the system were assessed using glucose solution and urine samples.

2. MATERIALS & METHODS

2.1 System description

Figure 1 shows an outline of the newly designed NIRS system for monitoring urine glucose level using a commercially available flow-through cell. All of the optical components were obtained from “Ocean Optics, Inc., USA” including the light source, the NIR spectrometer, the optical fibers and the flow cell. Optical path length of the flow cell was 10mm and the UV-grade fused silica with the thickness of 1 mm was used for the window material. The dead volume of the cell was 50 μl. The connectors of “SMA 905” were used for the fiber connection. Wavelength range of the spectrometer (NIR512) was 900-1700nm with the resolution about 3nm. For the other detailed specifications, see Figure 1. For measuring urine glucose level, near infrared spectroscopy in conjunction with the chemometric method of

partial least squares (PLS) was adopted and performance of the system was assessed by the experiments described below.

2.2 Calibration and validation using glucose solution

Calibration and validation studies were carried out using glucose solution. Altogether 55 samples with various glucose concentrations (36-1000 mg/dl) were prepared by dilution. Transmitted light intensity (Is) of each samples were collected over the spectral range of 900-1750 nm using the newly developed system. Before these measurements, the spectra of water (Iw) was also measured, and the differential spectrum (ΔAbs) were obtained using the equation of ΔAbs = log (Iw/Is). Each spectra was normalized by the ΔAbs value at 1105 nm for the PLS analysis. PLS calibration models were generated by the PLS Toolbox 3.5 of MATLAB (Eigenvector Inc., USA). The leave-one-out cross validation method was applied to obtain the Standard Error of Calibration (SEC) for assessing the validity of the model. The glucose concentration was predicted using this model, and the accuracy of the model was assessed by the values of the Standard Error of Prediction (SEP) and the correlation coefficient (r). 44 samples were used for obtaining PLS calibration model and 11 samples were used for the accuracy assessment.

2.3 Calibration and validation using urine sample

Calibration and validation studies were conducted using urine samples obtained from ten young healthy adults. Total volume of about 400 ml of first morning urine specimens were collected from each subject. In order to obtain urine samples with various glucose concentration levels (36-1000 mg/dl), appropriate amount of glucose was added. Altogether 55 samples were prepared for each subject. Near infrared spectra of each sample were collected in the same way, and 44 samples were used for obtaining PLS calibration model and 11 samples were used for the accuracy assessment.

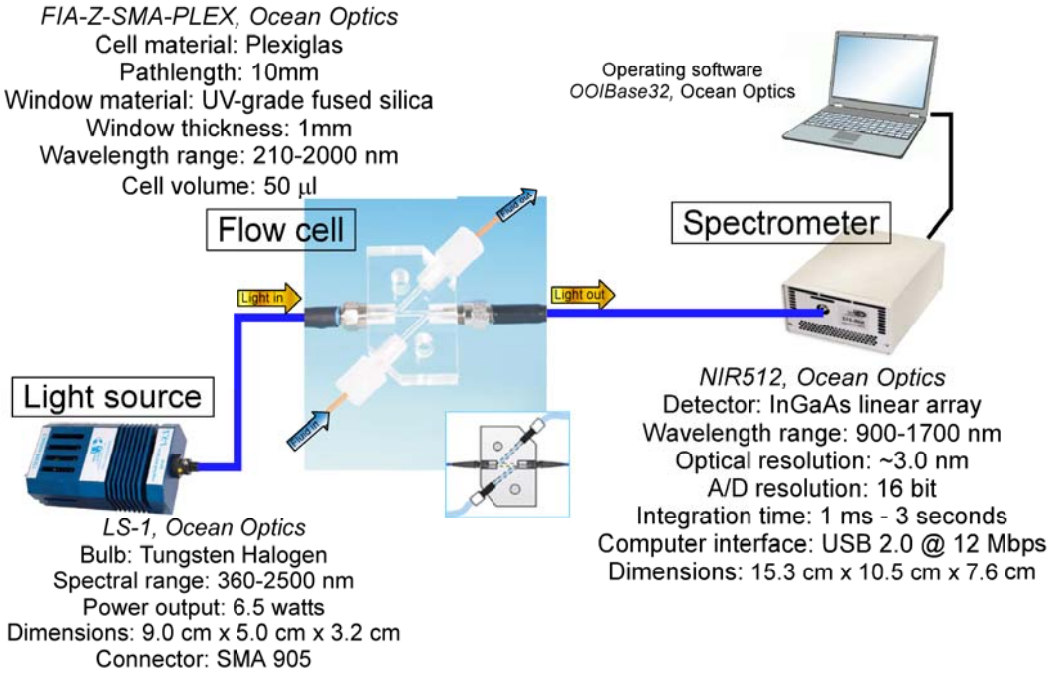

Figure 1 Outline of the newly designed NIRS system using flow-through cell for measuring urine glucose level.

3. RESULTS & DISCUSSION

3.1 Calibration and validation using glucose solution

Figure 2 shows the results of the glucose model calibration (upper) and validation (lower) obtained by the glucose solution measurements. From these results, validity of the calibration model could be confirmed and, using this model, we could estimate concentration of the glucose solutions. In our previous study [6], we used an FT-IR spectrophotometer (Spectrum One NTS; Perkin Elmer Co. Ltd., USA) with the spectral range of 1100-1830 nm and a transmission cell with the path length of 0.5 mm. In this study, on the other hand, a conventional near-infrared spectrometer and a flow-through cell were used considering practicability of the system. Even such a "down grade" of the spectrophotometer, we could obtain reasonable accuracy for estimating glucose level, presumably due to the increase in the path length of the cell used (twenty times larger than the previous study).

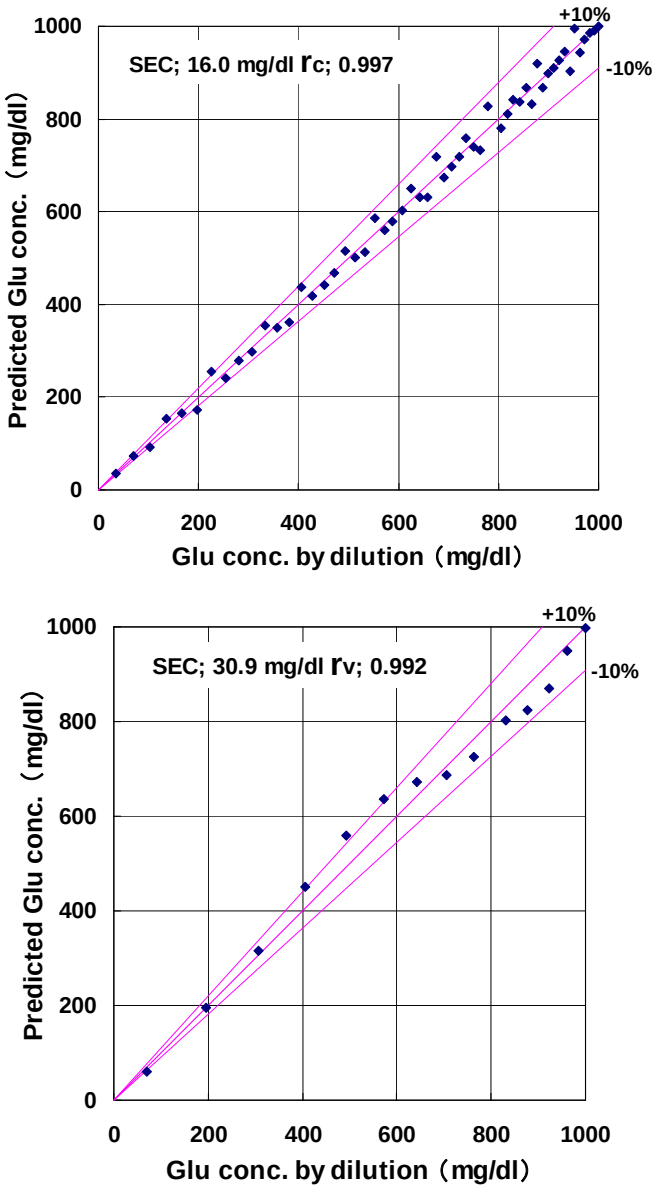

Figure 2 NIRS predicted vs. reference values for glucose model calibration (upper) and validation (lower) using glucose solution

3.2 Calibration and validation using urine sample

In Figure 3, examples of the results of the glucose model calibration (left) and validation (right) obtained from the urine samples of a single subject are shown. As shown in the upper part of Figure 3, quite good linear relationship (r_c =0.999) and the low value of SEC (7.3 mg/dl) were obtained, indicating validity of the PLS calibration model obtained. Regarding the accuracy of the glucose level prediction, the SEP between predicted and measured glucose concentration was 35.9 mg/dl (see the upper figure of Figure 3). This value is much lower than the value reported by Pezzaniti et al [7] (4.3 mmol/l = 77.4 mg/dl). This difference may cause from the difference in the used spectral range. They used the range of 2100-2400 nm because they tried to measure not only glucose but also other four analytes, *i.e.*, urea, ketone, creatinine and protein.

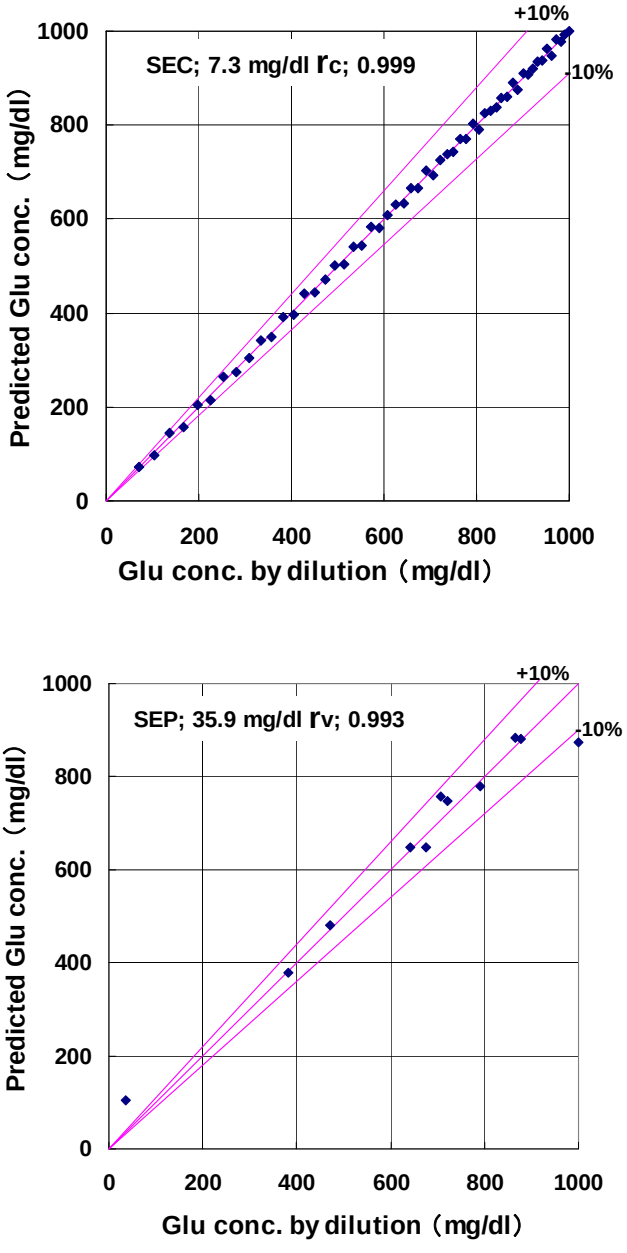

Figure 3 NIRS predicted vs. reference values for glucose model calibration (upper) and validation (lower) using urine sample

In Table 1, the results of calibration and validation studies using urine sample were summarized. As shown here, quite good

linear relationship (mean r_c; 0.994, mean r_v; 0.982) and the low value of SEC (mean; 16.8 mg/dl) were obtained, indicating validity of the PLS model obtained in each subject. However, in several subjects, high value of SEP (about 100 mg/dl) was observed and the mean value of SEP was not satisfactorily low (53.7 mg/dl).

Table 1 Summary of calibration and model validation using PLS regression for urine sample

Subject	Calibration		Validation	
	SEC (mg/dl)	r_c	SEP (mg/dl)	r_v
AA	15.7	0.995	31.8	0.996
BB	15.9	0.997	52.3	0.991
CC	56.0	0.969	99.5	0.954
DD	15.2	0.997	22.3	0.999
EE	2.3	0.999	91.9	0.946
FF	12.5	0.997	56.4	0.981
GG	7.3	0.999	35.9	0.993
HH	4.7	0.999	44.0	0.993
II	30.3	0.990	55.8	0.987
JJ	7.7	0.999	47.0	0.984
Mean	16.8	0.994	53.7	0.982
S.D.	15.9	0.009	24.7	0.018

4. CONCLUSION

A NIRS system using flow cell with the optical path length of 10 mm was developed for measuring urine glucose concentration. Accuracy of the system was verified by the preliminary experiments using glucose solution and urine samples. From the results obtained, it was clearly demonstrated that the present system had a capability of predicting urine glucose level and appeared to be a useful means for long-term home health care. However, mean value of SEP obtained by the urine samples from ten subjects was not satisfactorily low (53.7 mg/dl). For improving the accuracy, (1) mechanical stability of the optical system should be improved, (2) the method for normalizing the spectrum should be reconsidered, and (3) the number of subject should be increased. Moreover the problems to be solved for the home healthcare use will be (i) reduction of the number of the wavelength for spectral collection, (ii) shift of the present complicated optical system to the convenient LED-photo diode multi-array sensor system, and (iii) development of a urine sampling system which could be installed in a toilet.

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