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Fourier Transform Infra-Red spectrophotometry observation to find appropriate wavelength for non-invasive blood glucose level measurement optical device

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Abstract. The appropriate wavelength is essential for non-invasive blood glucose level measurement optical device. We conducted this experimental observation to find the usable wavelength candidate for non-invasive blood glucose level measurement optical device in 1000 nm to 2500 nm range. We run this observation in Prodia Bogor and Food Processing and Crops Technology Lab, Faculty of Agricultural Engineering, IPB University, July 2019. We obtained fasting, 15 mnt postprandial, and 30 mnt postprandial blood sample from 10 randomly selected consenting non blinded healthy adult subjects between 18 to 60 years old. We measured spectrophotometric absorbance for each blood sample. We did the measurement using BUCHI NIR FLEX 500. We compared the result to blood glucose level by standard gold measurement. We also compared the Pearson correlation, and the standard deviation of all samples to then-existing wavelength source LED provided by Thorlabs. We found that the highest absorbance and standard deviation wavelength is at 1939 nm. Wavelength LEDs candidates that represent measuring blood glucose levels is 1200, 1300, 1450, 1750, and 1950 nm. We did not find a severe adverse effect from each participant. Researchers should confirm the trial results with in vivo human observation.

1. Introduction

Most people already aware of the general risk of conventional phlebotomy-based method, such as physical and psychological trauma, disease spread, or simple malpractice, as well as relatively high cost for daily use [1–3]. This fact fosters researchers to find generally safer methods to measure blood glucose level. Researchers have seen spectrophotometry-based methods as potent methods for blood glucose level measurement due to their potential to eliminate consumable costs [4–6]. We were previously done a review on wavelength for non-invasive blood glucose level measurement optical device using bio-assayed blood control sample. The result is promising, yet we are aware that we should verify these results with real human blood samples [7,8]. We have done this review to support our development research for non-invasive blood-glucose-level measurement device [8,9]. We have done this because the appropriate wavelength is directly related to blood-glucose-level measurement accuracy, sensitivity, and specificity [10,11]. We have done this experimental observation to find the usable wavelength candidate for non-invasive blood glucose level measurement optical device in 1000 nm to 2500 nm range.

2. Methods

2.1. General Methods
This article describes a quantitative experimental observation of wavelength absorbance for subject blood between 1000 to 25000 nm. We focus our observation on the change of absorbance due to the change in blood glucose level. Human Research Ethical Committee of IPB University has approved this research protocol, which we have register under ethical clearance 076/IT3.KEPMSM-IPB/SK/2018. Lembaga Pengelola Dana Pendidikan has supported this study using Riset Inovatif Produktif Invitasi, with grant number PRJ-78/LPDP/2019, 2 December 2019. This research protocol is a modification from our previous researches [7,12,13], adapted to live human blood glucose level sample in the infrared range.

2.2. Blood Sample Procurement
We have done the blood sample procurement in Prodia Office in Bogor, in July 2019. There are ten volunteers for this study which already read the research information the day prior. They also have signed informed consent before participating in this study. We did not implement randomisation nor blinding in this study. Subjects are male or female between 18 to 60 years old and did not under glucose disorder medication. We also exclude those who are pregnant or breastfeeding in the duration of this observation. The Subjects underwent eight hours of fasting before blood taking procedure. We have done the blood taking procedure three times, at fasting state and 15 and 30 mins postprandial. The Subjects are taking 75 mg of pure glucose in 200 ml water solution after first blood taking session. Each blood taking procedure yields 3 ml of the blood sample, and the whole procedure yields 30 samples. Each sample is observed three times, in total yields 90 samples, which would enough for typical spectral observation study.

2.3. Blood Observation
We run this observation in Prodia Bogor and Food Processing and Crops Technology Lab, Faculty of Agricultural Engineering, IPB University, West Java, July 2019. We have observed each blood samples three times using Buchi NIRFlex N-500 (BÜCHI Labortechnik AG, Switzerland). We then calculated the Pearson correlation and standard deviation of all samples. We superimposed the data with the available LED from Thorlabs (Thorlabs inc., USA). We have used GNU R (The R Foundation, USA), RKward (KDE e.V., Germany), and RStudio (RStudio PBC, USA) for data analysis.

3. Result and Discussions
We have included all ten subject's data in this data analysis. We have conducted each blood sample procurement and blood observation procedure within four hours - the whole event taking two days. We stop the procedure after we have taken and observed all sample. We did not find a severe adverse effect from each participant. We have found that there are five absorption peaks from the near-infrared test results, namely at a wavelength of 1159, 1450, 1797, 1939 and 2170 nm (**Figure 1**). The most significant absorption is at a wavelength of 1939 nm with a standard deviation value of 0.17296 (**Figure 2**). The positive correlation value is in the 1000 - 1876 nm range, which means that the absorbance and concentration of blood glucose at this wavelength have a directly proportional value, with the highest correlation value of 0.0453. The negative correlation value is shown in the range 1878 - 2500 nm with a high absorbance value against low blood glucose concentrations. This wavelength range has the highest correlation value, namely, -0.1703 (**Figure 3**). The wavelength at the most considerable standard deviation value makes it the best measurement for measuring blood glucose levels. The 1950 nm LED had the highest absorbance correlation values (**Figure 4**).

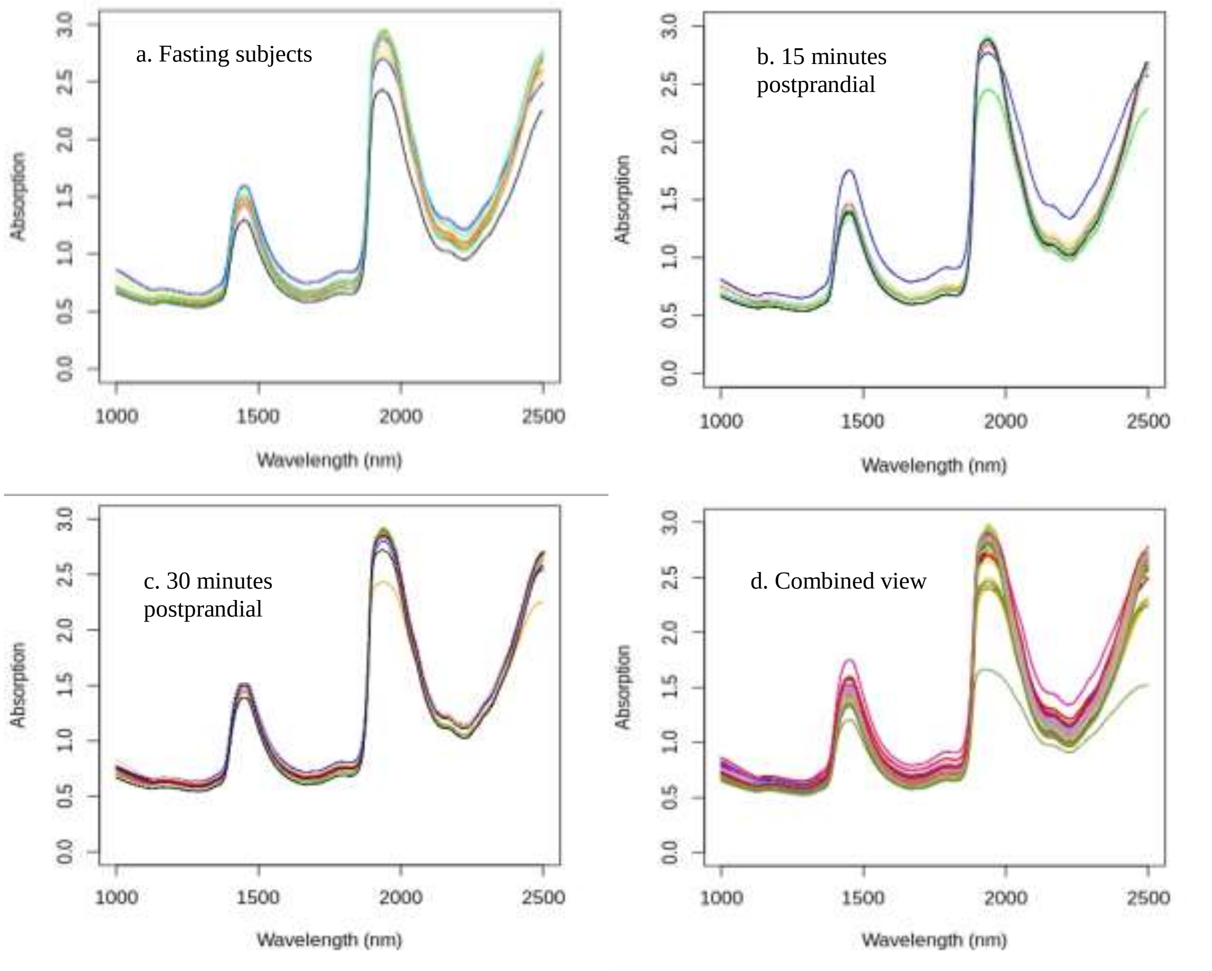

Figure 1. The absorbance of blood samples in three different subject extraction.

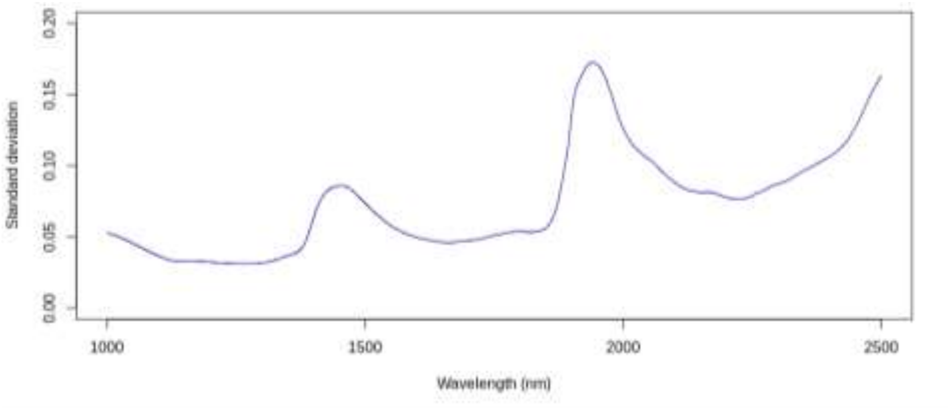

Figure 2. Combined view of absorbance, standard deviation, and absolute Pearson correlation of blood samples, projected to [0, 1] ratio.

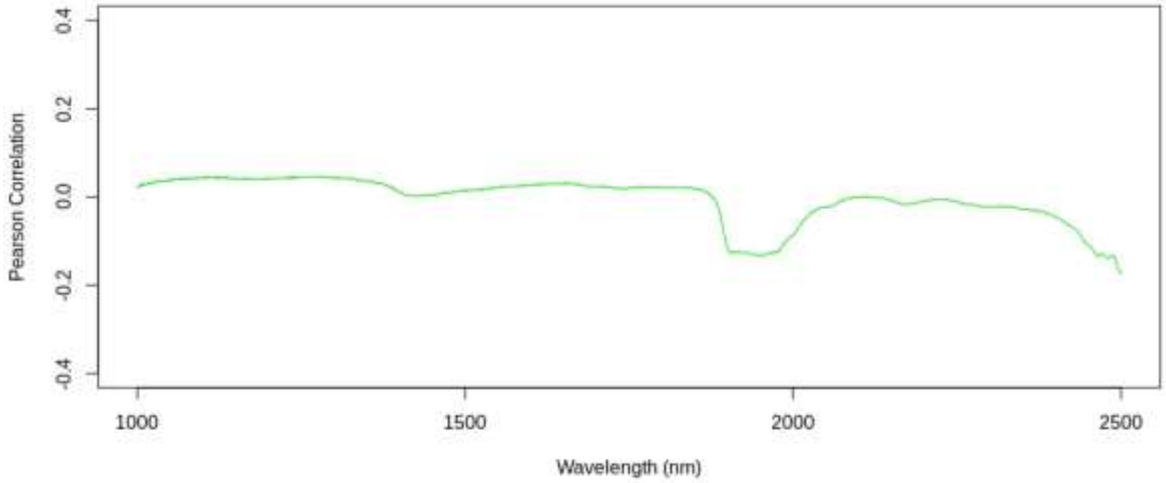

Figure 3. Pearson correlation of absorbance of blood samples to blood glucose level.

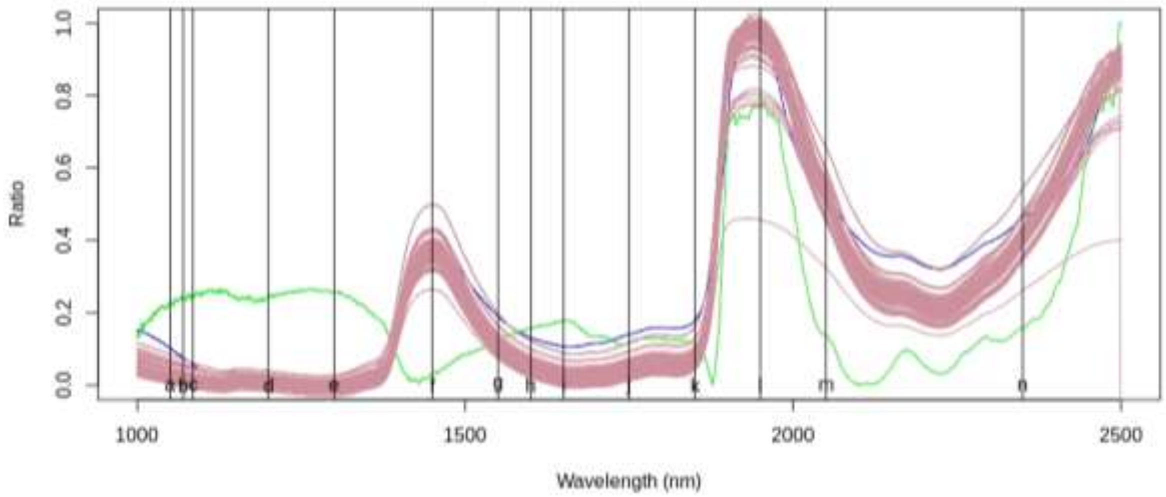

Figure 4. Combined view of absorbance, standard deviation, and absolute Pearson correlation of blood samples, projected to [0, 1] ratio.

The study confirms our previous observations [7,8]. This result confirms the result of Goodarzi (1500 to 1800 nm, 2050 to 2300 nm) [14], Ryckeboer (1530 to 1820 nm) [15], and Krushinitskaya (2000 to 2500 nm) [16] explicitly for reflectance-based blood glucose level measurement, due to high absorbance. On the other hand, this research also confirms the study by Abdallah (360 to 1200 nm) [17], McEwen (454 to 1200 nm) [18], Momose (700 to 1050 nm) [19], Smith (800 to 1600 nm) [20], Song (850, 950, and 1600 nm) [21], Lawand (900 to 1550 nm) [22], So (1100 to 1400 nm) [23], and Yu (1300 nm) [24] for transmittance based measurement, due to low absorbance. We take the fact that the study was only taking account of healthy Subjects as a limitation. Further verification should include those with blood glucose level disorders as well. We also plan to confirm this result using in vivo human observation.

Conclusions

The 1950 nm LED had the optimal absorbance correlation values at -0.17, which make it appropriate for non-invasive blood glucose level measurement. Researchers should confirm the trial results with in vivo human observation.

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