Biomedical Sciences
2021; 7(2): 47-52
http://www.sciencepublishinggroup.com/j/bs
doi: 10.11648/j.bs.20210702.12
ISSN: 2575-3924 (Print); ISSN: 2575-3932 (Online)

Non-Invasive Measurement of Glucose Concentration Using Red and Near-Infrared Light-Emitting Diodes

Semi Oh[1], Min-Seok Kim[1], Beom-Rae Noh[2], Hyung-Hwan Baik[1, *], Kyoung-Kook Kim[2, *]

[1]Department of Medicine, Kyung Hee University, Seoul, Republic of Korea

[2]Department of Nano & Semiconductor Engineering, Korea Polytechnic University, Siheung, Republic of Korea

Email address:
ohsemi1230@gmail.com (Semi Oh), mskim9262@naver.com (Min-Seok K.), rnqlrnal@naver.com (Beom-Rae N.), hhbaik@khu.ac.kr (Hyung-Hwan B.), kim.kk@kpu.ac.kr (Kyoung-Kook K.)

[*]Corresponding author

To cite this article:
Semi Oh, Min-Seok Kim, Beom-Rae Noh, Hyung-Hwan Baik, Kyoung-Kook Kim. Non-Invasive Measurement of Glucose Concentration Using Red and Near-Infrared Light-Emitting Diodes. *Biomedical Sciences.* Vol. 7, No. 2, 2021, pp. 47-52. doi: 10.11648/j.bs.20210702.12

Received: April 15, 2021; **Accepted**: April 30, 2021; **Published**: May 14, 2021

Abstract: Many diabetic mellitus patients envision a non-invasive method of blood glucose measurement since they require periodic monitoring of their blood glucose levels to ensure that it is stable and within the normal range. In this study, we detected glucose concentration using commercial light emitting diodes (LEDs) with a wavelength of 700–1600 nm. Light of long wavelengths (e.g. NIR) infiltrate human skin and reach the blood vessel lining, thereby aiding in the non-invasive measurement of blood glucose concentration. To demonstrate this, the concentration of glucose solutions was measured using red and NIR-LEDs in a non-invasive manner. The sensitivity of glucose detection was greater when light of wavelength below 1000 nm was used, owing to the absorption of wavelengths above 1000 nm by water. Furthermore, we controlled the input current of the red and NIR-LEDs to confirm the light intensity deviation with increasing glucose concentrations and suggested the optimum wavelength of light using this in-vitro system. Among various LEDs, the 700 nm LED showed higher light intensity deviation with change in injection current compared to LEDs with the other wavelengths. In particular, compared to other LEDs, a stark difference was observed in the light intensity of the 700 nm LED while measuring glucose concentrations in the range of 50–100 mg/dl.

Keywords: Non-Invasive, Glucose, NIR-LED, Diabetic Mellitus, Water Absorption

1. Introduction

Currently, diabetes mellitus is one of the significant public health issues affecting more than 400 million people worldwide. Moreover, this number is expected to rise by approximately 55% within the next 25 years [1]. Diabetes mellitus is a type of metabolic disease in which the blood glucose (blood sugar) level increases dramatically from the standard base value, leading to a condition known as hyperglycaemia [2, 3]. It occurs primarily due to lifestyle changes such as the consumption of unhealthy food, smoking, drinking, and stress [4, 5]. These lifestyle changes increase the blood sugar level due to inadequate insulin production in blood cells or improper cellular response to the insulin produced. Diabetes can lead to significant health complications such as cardiovascular diseases, kidney damage, stroke, amputation of arms or legs, and blindness [6]. Therefore, it is essential to monitor the blood glucose level periodically and ensure that it is stable and within the normal range.

Diabetic patients usually use a glucose meter to measure the blood glucose level. This is an invasive detection method involving the pricking of fingers using a lancet to obtain a few drops of blood [7-10], which is placed on a stripe and inserted into the glucose meter. Inside the glucose meter, a series of chemical reactions occur, resulting in the formation of potassium ferrocyanide, which interacts with the metals on the electrode and causes the flow of electric current between the electrodes. The more the concentration of glucose in the blood, the more the amount of potassium ferrocyanide produced and more the current flow between the electrodes. The strength of this current determines the blood glucose level [7-10]. However, these devices are expensive and involve an invasive procedure.

Recently, specific non-invasive techniques have been

introduced to measure blood glucose levels. These serve as an excellent alternative to the glucose meter, which involves removing a few drops of blood. These techniques possess specific optical, transdermal, and thermal properties, which aid in non-invasive blood glucose concentration [11-15]. Some of the key advantages of these non-invasive measurement methods include relief from pain, comfort, and the lack of infection due to the absence of finger pricking. Specific non-invasive methods of glucose measurement, such as infrared (IR) spectroscopy, have been popular for several years. However, the establishment of a method producing further reliable results has not been achieved yet. Furthermore, these systems still have a more significant volume and the full bandwidth of the IR spectrum. Moreover, it can be easily absorbed by water and other organic human tissue components such as hemoglobin, fat, protein, and lactic acid.

In this study, we determined the concentrations of various glucose solutions using commercial red and near-IR (NIR)-light-emitting diodes (LEDs) in the wavelength of 700–1600 nm. The LEDs have a narrow bandwidth, portable, and overcome the limitations of other light sources [16, 17]. For glucose detection, we used red, and NIR-LEDs of wavelengths below 1000 nm since light above 1000 nm wavelength is absorbed by water. Furthermore, we controlled the input current of the red and NIR-LEDs to confirm the light intensity deviation with increasing glucose concentrations and suggested the optimum wavelength of light using this in-vitro system.

2. Experimental Procedures

Glucose solutions of various concentrations, including 30, 50, 110, 150, 250, and 400 mg/dl were prepared by dissolving pure D–(+)–glucose ($C_6Hq_{12}O_6$; Sigma Aldrich) in deionized (DI) water. The amount of light absorbed by the solution was measured using a non-invasive system comprising of red and NIR-LEDs, glucose solution in a cuvette, a power source, and a spectrophotometer. The wavelengths of the red and NIR-LEDs (purchased from Thorlabs) used in the experiments include 700, 730 (red), 780, 851, 870, 910, 940, 1200, 1300, 1450, 1550, and 1600 nm (NIR). Keithley 2400 served as the power source that provided the current for the red and NIR-LEDs. The amount of light transmitted through the glucose solutions was measured by a spectrophotometer (Ocean optics flame wave 2000 and BWSpec).

3. Results and Discussion

According to American Diabetes Association, the preprandial blood glucose level of normal, healthy individuals must be between 80 and 130 mg/dl, that is, 4-6 mmol/l, and the postprandial blood glucose level must be less than 180 mg/dl, that is, 10 mmol/l [18]. We prepared six glucose (dextrose monohydrate) solutions of concentrations 30, 50, 110, 150, 250, and 400 mg/dl, using equation (1).

$$X \text{ mg/dl} = X \text{ mg of glucose} + 100 \text{ ml of DI water} \quad (1)$$

The concentrations of the glucose solutions were also confirmed using a commercial digital measurement system that is used for detecting blood glucose levels. We transferred 2.2 ml of each glucose solution into a cuvette and measured the change in light intensity caused by each of these solutions.

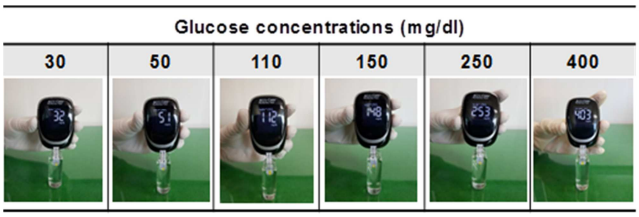

Figure 1. *Actual glucose concentrations and glucose meter measurement of glucose concentrations.*

Figure 1 shows the various glucose concentrations used in the experiment and the actual concentration of the solutions obtained using a glucose meter. We found that the glucose concentrations used in the experiment were similar to that of the glucose meter reading. The output light intensity of the red and NIR LEDs after passage through the different glucose solutions was recorded to determine the correlation between the measured value and the expected glucose concentration.

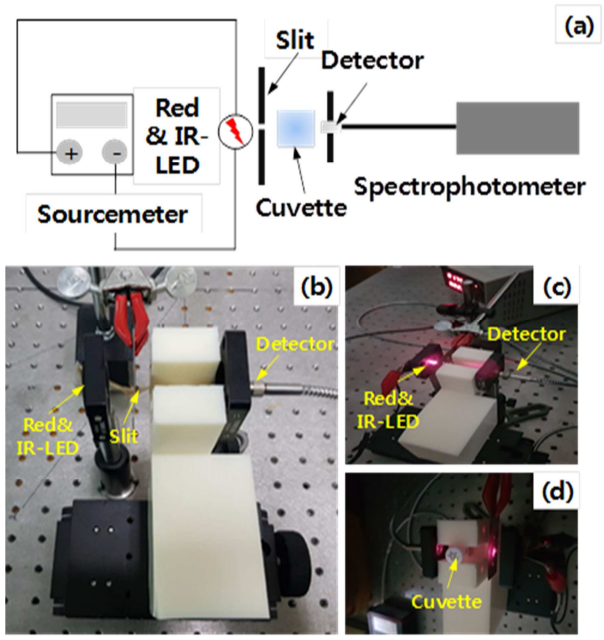

Figure 2. *(a) Schematic representation of the non-invasive measurement system. (b)-(d) Images of the non-invasive measurement system.*

A schematic representation of the non-invasive system is shown in Figure 2 (a). The cuvette was surrounded by the block and put in the fixed site in the block to prevent the other scattered light. Scattered light can be in any direction/angle (from backscattering to forward scattering), and is affected by material structure and energy of incident light. In addition, to block any interference between the LED light and the cuvette wall, we placed a dark slit with a micro-hole in front of the cuvette.

A normal optical measurement system has several issues.

First is the absorption of light by water [19, 20], and the other is the absorption of light by other biological materials such as hemoglobin and nutrients [21, 22]. The total blood volume in our body consists of approximately 60% plasma that includes water (90%), proteins (7%), inorganic salts (0.5%), lipids (0.4-0.7%), and only 0.07-0.01% of glucose [23]. Furthermore, some major optical parameters such as wavelength and power of the incident light affect the interaction between the light and the glucose solution in the cuvette [24].

As light enters the glucose solution, it interacts with glucose particles and is absorbed, transmitted, or scattered. When a material absorbs light, the light or photon's energy is used up as a result of the interaction between the light and the material. The scattering of light by the particles in a solution is referred to as Rayleigh scattering. Rayleigh scattering can be caused by sufficiently small particles of any shape [24].

Additionally, the absorption of light by these particles strongly depends on the wavelength of light transmitted. When the light of a particular wavelength strikes particles in solution, the bond between the component atoms vibrate and absorb specific wavelengths. Besides, the amount of light absorbed by a substance is directly proportional to the effective path length [25]. In glucose solutions, the absorbance depends on the amount of glucose in water. The remaining light is transmitted. Therefore, the concentration of glucose solution can be determined by analyzing the wavelength or intensity of transmitted light.

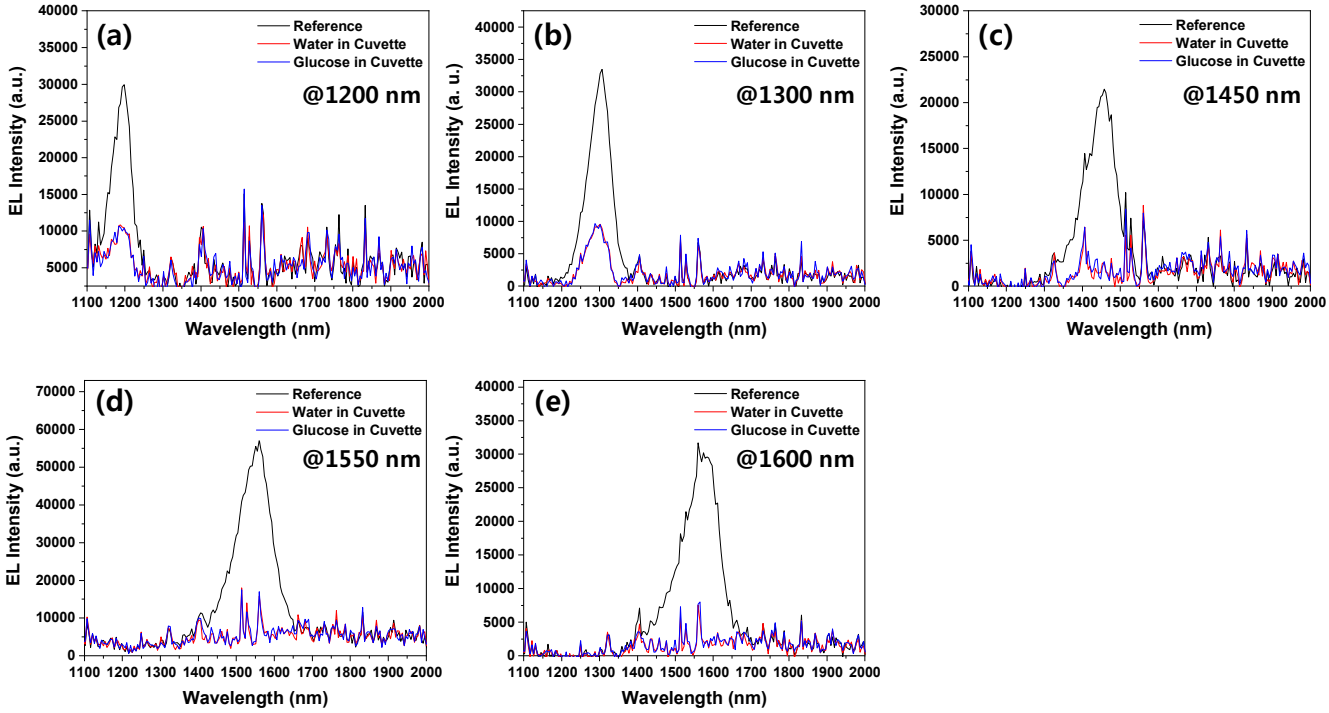

Figure 3. *EL intensity in the absence of glucose solution, with water, and glucose solutions of different concentrations when an LED light of (a) 1200 nm, (b) 1300 nm, (c) 1450 nm, (d) 1550 nm, and (e) 1600 nm wavelengths were injected.*

Figures 2 (b)-(d) show the non-invasive measurement system consisting of red and NIR-LEDs, with and without a cuvette. Figure 3 shows that when wavelengths greater than 1000 nm was used to measure the concentration of the glucose solutions, the light was almost entirely absorbed by the water in the solution. These graphs show the light intensities detected by the spectrophotometer without a non-invasive system, with water in the cuvette, and glucose solutions in the cuvette. The wavelengths between 1200 and 1600 nm were almost entirely absorbed by water. Therefore, we used red and NIR-LEDs of wavelength below 1000 nm.

The maximum intensity was set close to 65,000 values in the spectrophotometer, and the injection current to reference current ratio was divided into four categories, as shown in Table 1.

Table 1. *Four categories of injection current to reference current ratio (%) at various LED wavelengths.*

LED Wavelength (nm)	Current I (mA) @ Injection Current/Reference Current*(%)			
	I (mA)@25%	I (mA)@50%	I (mA)@75%	I (mA)@100%
700	3	6	9	12
730	2	3	4	5
780	0.5	0.8	1.1	1.4
851	2	5	8	10
870	3	5	7	9
910	1	2	3	4
940	6	12	18	24

*Reference current: the applied current with LED intensity near the 65,000 value

The peak intensity of light transmitted through water (blank) and glucose solutions of 30, 50, 100, 150, 250, and 400 mg/dl were measured at various wavelengths of red and NIR-LEDs by changing the injection current, as shown in Figure 4.

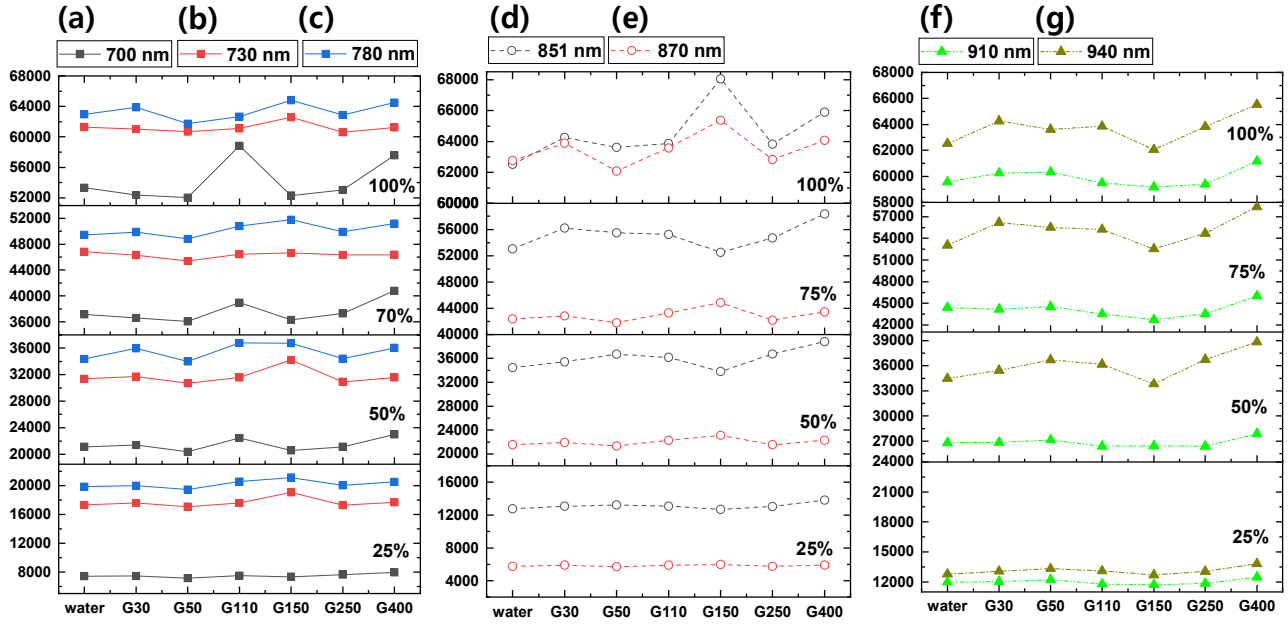

Figure 4. *EL peak intensities obtained by passing LED light of different wavelengths through as glucose solutions of various concentrations and water. The LED wavelengths used in the experiments: (a) 700 nm, (b) 730 nm, (c) 780 nm, (d) 851 nm, (e) 870 nm, (f) 910 nm, and (g) 940 nm.*

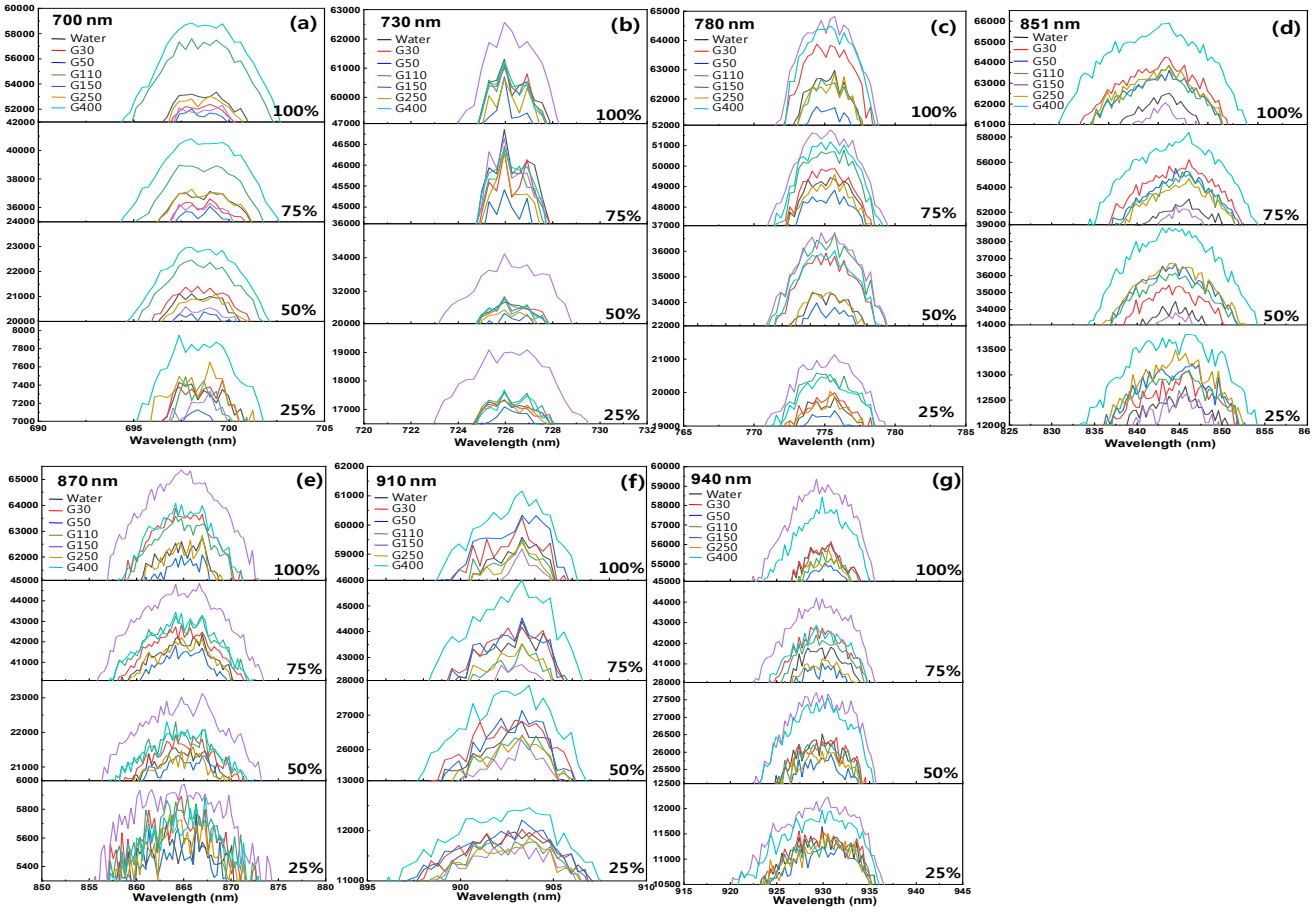

Figure 5. *EL intensities of LED light of different wavelengths when passed though glucose solutions of various concentrations and water. The LED wavelengths used in the experiments were: (a) 700 nm, (b) 730 nm, (c) 780 nm, (d) 851 nm, (e) 870 nm, (f) 910 nm, and (g) 940 nm.*

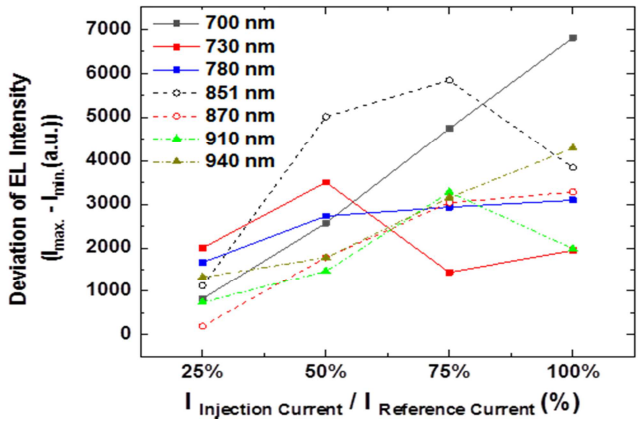

Figure 6. *Plot of the deviation of EL intensity ($I_{max.}$-$I_{min.}$) of the glucose solutions versus $I_{Injection\ current}/I_{Reference\ current}$ ratio.*

As the injection current increased, all wavelengths of the two LEDs showed higher light peak intensity and similar peak positions. In particular, when the injection current to reference current ratio was above 50%, light wavelengths of 700, 780, 870, and 940 nm showed a relatively large deviation in light intensity compared to other wavelengths of 730, 851, and 910 nm. Graphs of the whole light intensity versus injection current are shown in Figure 5.

The range of glucose solutions between 50-110 mg/dl and 110-150 mg/dl are significant for the patient of diabetic Mellitus, as mentioned above. The 700 nm wavelength of light showed the abrupt change in those ranges when the injection current was increased. Moreover, the light detection results show a similar tendency in the 700 nm wavelength of LEDs than other wavelengths in all injection currents.

Figure 6 shows a graphical representation of the deviation in electroluminescence (EL) intensity ($I_{max.}$-$I_{min.}$) of the glucose solutions versus $I_{Injection\ current}/I_{Reference\ current}$ ratio. The red and NIR-LED wavelengths of 700, 780, 870, and 940 nm show a linear increase in light intensity. In particular, the 700 and 940 nm wavelengths show a radical increase in the light intensity deviation curve compared to other wavelengths. Generally, the 780 and 940 nm wavelengths have been used to detect glucose concentration, since these wavelengths match the absorption wavelengths of the chemical bonds in glucose [26]. The 700 nm wavelength has not been well known due to the need to fabricate a high-efficiency light source. However, this wavelength is not absorbed by water or other organic contaminants such as hemoglobin, fat, and protein [16, 27]. Moreover, the linear increase in light intensity aids in the precise detection of glucose concentration by blending with other wavelengths. Therefore, we have suggested the 700 nm red LED as a probable candidate for detecting blood glucose levels.

4. Conclusions

We measured the intensity of light transmitted through glucose solutions of various concentrations using red and NIR-LEDs and a light detector to measure the amount of injection current. We found that wavelengths beyond 1000 nm were almost entirely absorbed by water. Red and NIR-LEDs of different wavelengths less than 1000 nm were used as the light source, and the amount of light transmitted light through glucose solutions of different concentrations was measured using a spectrophotometer. Through these measurements, we can found that the 700 nm wavelength of the red LED is a probable candidate for blood glucose level detection detect compared to other LED wavelengths of LEDs, as shown by the deviation in EL intensities and maximum and minimum intensity in the presence of injection current. The 700 nm wavelength is not absorbed by water and other organic contaminants such as hemoglobin, fat, and protein. Therefore, to aid in the precise detection of glucose concentration, the light source of the non-invasive measurement system can be combined with an LED of 700 nm wavelength or other wavelengths below 1000 nm. Although, the requirements have yet to be met, and there is still a long way to go for these novel approaches to replace the current finger-prick glucose meters, we believe that this work provides a more advanced detection system to monitor the blood glucose level of diabetics in a non-invasive manner.

Acknowledgements

This study was supported by Technology Innovation Program (or Industrial Strategic Technology Development Program), (No. 10079634) funded by the Ministry of Trade, Industry and Energy (MOTEI) and Korea Institute for advancement of Technology (KIAT) grant funded by the Korea Government (MOTIE) (P0008458, The Competency Development Program for Industry Specialist) and the MSIT (Ministry of Science and ICT), under the ITRC (Information Technology Research Center) support program (IITP-2021-2018-0-01426) supervised by the IITP (Institute for Information & Communications Technology Planning & valuation), Republic of Korea.

References

[1] http://www.diabetesatlas.org/ (2015).

[2] Ong, W. M., Chua, S. S., Ng, C. J. (2014). Barriers and facilitators to self-monitoring of blood glucose in people with type 2 diabetes using insulin: a qualitative study. Patient Prefer. Adherence, 8, 237-246.

[3] http://www.diabetes.co.uk/diabetes_care/blood-sugar-level-ranges.html (2019).

[4] Kennedy, L. (2001). Self-Monitoring of Blood Glucose in Type 2 Diabetes Time for evidence of efficacy. Diabetes Care, 24 (6): 977–978.

[5] American Diabetes Association, (2015). Standards of Medical Care in Diabetes—2015 Abridged for Primary Care Providers. Clinical Diabetes, 33 (2): 97-111.

[6] http://www.diabetesnet.com/diabetes-technology/metesr-monitors/continuous-monitors/compare-current-monitors (2018).

[7] McMillin, J. M. (1990). Clinical methods: The history, physical, and laboratory examinations Blood Glucose, 3rd ed., Boston, MA, USA: Butterworth, ch. 141, 662-665.

[8] Wang, H. -Ch., Lee, A. R. (2015). Recent developments in blood glucose sensors. J. Food Drug Anal., 23 (2): 191–200.

[9] Klonoff, D. C. (2007). The Benefits of Implanted Glucose Sensors. J. Diabetes Sci. Technol., 6, 797-800.

[10] Mamkin, I., Ten, S., Bhandari, S., Ramchandani, N. (2008). Real-time continuous glucose monitoring in the clinical setting: the good, the bad, and the practical. J. Diabetes Sci. Technol., 2 (5): 882-889.

[11] So, C.-F., Choi, K.-S., Wong, T. K. S., Chung, J. W. Y. (2012). Recent advances in noninvasive glucose monitoring. Med. Devices Evidence Res., 5, 45-52.

[12] Tura, A., Sbrignadello, S., Clanciavicchia, D., Pacini, G., Ravazzani, P. (2010). A Low Frequency Electromagnetic Sensor for Indirect Measurement of Glucose Concentration: In Vitro Experiments in Different Conductive Solutions. Sensors, 10 (6): 5346-5358.

[13] Yatim, N. N. M., Yatim, M., Zain, Z. M., Jaafar, M. Z., Yusof, Z. Md. (2014). Noninvasive glucose level determination using diffuse reflectance near infrared spectroscopy and chemometrics analysis based on in vitro sample and human skin. In Proc. IEEE Conf. Syst., Process Control, Kuala Lumpur, Malaysia, 30-35.

[14] Shao J., Lin, M., Li, Y., Li, X., Liu, J., Liang, J., Yao, H. (2012). In Vivo Blood Glucose Quantification Using Raman Spectroscopy, PLoS One, 7 (10): e48127.

[15] Helse H. M., Winzen, R., Fundamental chemometric methods. In Near Infrared Spectroscopy: Principles, Instruments, Applications, (2002). H. W. Siesler, Y. Ozaki, S. Kawata, and H. M. Heise, Eds. Weinheim, Germany: Willey, ch. 7, 125-162. Yung, R., & Khoo-Lattimore, C. (2019). New realities: a systematic literature review on virtual reality and augmented reality in tourism research. Current Issues in Tourism, 22, 2056 - 2081.

[16] T. Kossowski, K. Kossowska, R. Stasiński, (2017). Non-invasive measurement of chemical compounds levels in human body. Measurement Automation Monitoring, 63 (06): 200-202.

[17] S. Robiah, R. P. Jenie, M. Dahrul, N. M. Nurdin, J. Iskandar, A. Kurniawan, E. Rustami, H. Syafutra, H. Alatas, Irzaman, E. Damayanthi, Rimbawan, D. Sukandar, Evriyanti, and S. Budiarti, (2017). Infra Red Light Emitting Diode in 1200 nm Range have Moderate Performance in Detecting Glucose in Human Blood Glucose Model, IOP Conf. Series: Earth and Environmental Science, 58 (012021): 1-4.

[18] American Diabetes Association. Standards of Medical Care in Diabetes (2015). Diabetes Care, 38 (Suppl. 1), S1-S94.

[19] R. Hotmartua, P. W. Pangestu, H. Zakaria, Y. S. Irawan, (2015). Noninvasive blood glucose detection using near infrared sensor. The 5th International Conference on Electrical Engineering and Informatics, IEEE, 978, 687-692.

[20] Sekar, S. K. V., Bargigia, I., Mora, A. D., Taroni, P., Ruggeri, A., Tosi, A., Pifferi, A., Farina, A., (2017). Diffuse optical characterization of collagen absorption from 500 to 1700 nm, J. Biomed. Opt., 22 (1): 015006.

[21] S. K. Vashist, (2012). Non-invasive glucose monitoring technology in diabetes management: a review, Anal. Chim. Acta, 750, 16-27.

[22] S. Perrey, (2008). Non-invasive NIR spectroscopy of human brain function during exercise, Methods, 45, 289-299.

[23] Zirk, K., Poetzschke, H. (2004). On the suitability of refractometry for the analysis of glucose in blood-derived fluids. Med. Eng. Phys., 26, 473-481.

[24] O. S. Abdalsalam, A. A. Awouda, (2014). Noninvasive glucose monitoring using scattering spectroscopy. Am. J. Biomed. Eng., 4 (3): 53-59.

[25] Haxha, S., Jhoja J. (2016). Optical Based Noninvasive Glucose Monitoring Sensor Prototype. IEEE Photonics J., 8 (6): 6805911.

[26] McEwen, M. P., Reynolds, K. J. (2014). Noninvasive Monitoring With Strongly Absorbed Light. OPT. APPL., XLIV, 2, 177-190.

[27] Khalil, O. S. (1999). Spectroscopic and clinical aspects of noninvasive glucose measurements. Clin. Chem., 45 (2): 165-177.