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A real time non-invasive cholesterol monitoring system.

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Abstract. Hypercholesterolemia causes cardiovascular disease which is a disorder of the heart and blood vessels, one of the most significant causes of death in the world, and this needs to be anticipated by monitoring blood cholesterol levels regularly. The current method of monitoring blood cholesterol levels is using invasive technique by collecting blood samples. A simple device is needed to measure blood cholesterol levels that can be done without collecting blood samples. This study aims to develop a non-invasive technique for monitoring blood cholesterol levels using sensors utilizing infrared light absorption in body tissues, in order to simplify measuring blood cholesterol levels regularly for patients with hypercholesterolemia. The application of a non-invasive technique focused on developing a total blood cholesterol monitoring device using an infrared sensor with IR LED - 940nm wavelength as a transmitter. A photodiode was used as a detector with the wavelength range of 400-1100 nm and a microcontroller as the minimum system for controlling the value of the output voltage in the form of digital data and then converted onto total blood cholesterol. The measurement results using non-invasive technique was compared to the results using invasive technique.

1 Introduction

The development of science in field of health is very rapid, many studies have explained the correlation between the increase of blood cholesterol levels and the occurrence of cardiovascular diseases, such as arteriosclerosis and hypertension.[1, 2].

In 2012, there were 17.5 million deaths and it was predicted to increase up to 23.4 million in 2030 [3, 4], 80% will be caused by heart attacks and strokes, and more than 75% will occur in low and middle income countries. Deaths due to cardiovascular disease are around 34% at the age of 70 years [3]. Excessive protein brought by cholesterol and triglycerides or low-

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density lipoprotein (LDL) that flows in the blood plasma can cause myocardial infarction (heart attack), stroke or peripheral vascular disease.[5, 6]. To prevent this, it is necessary to conduct routine cholesterol check-up.

Device for measuring total cholesterol available in general clinical laboratories is the one with invasive techniques. Invasive technique procedures require blood samples collection which poses a risk of bruising and inflammation. Research using measurement methods with non-invasive techniques have been widely research such as; to estimate total cholesterol with bioelectric impedance [6, 7]. Measurement of total blood cholesterol uses a near-infrared sensor [4, 8], using a smart phone camera as a scanner to scan a blood sample in a container to determine total blood cholesterol [9]. This non-invasive method has attracted attention because it is easy to use and inexpensive. At present, there are many individuals who do not pay attention to their cholesterol levels because invasive blood cholesterol monitoring is quite expensive.

Research on non-invasive techniques using near infrared sensors (NIR) to measure blood components including blood glucose, NIR sensors with Emitter LED 1550E, FGA10 photodiode with 800 - 1800nm wavelength [10], wavelength 940 nm with NIR radiation in 700 -1100nm [11, 12]. Measurement of blood cholesterol uses optical sensors IR LED Photodiode wavelength 800 nm - 1800 nm [8]. The development of simple measuring devices with non-invasive techniques to monitor total blood cholesterol is required.

Cholesterol has a chemical formula $C_{27}H_{46}O$, a small biological molecule called lipid such as wax, mixed in blood plasma. In water, cholesterol is almost insoluble (0.095 mg/L at $30^{\circ}C$) so that it moves in the bloodstream with a very small concentration [6]. Cholesterol requires lipoproteins to be able to flow in the bloodstream, where hydrophilic proteins attached to cholesterol and formed a lipoprotein. The accumulation of this lipoprotein can cause clogged arteries. Lipoprotein which causes atherosclerosis is called atherogenic. Lipoproteins are classified into Low density lipoprotein (LDL) and High density lipoprotein (HDL) [13]. In 2013, The Ministry of Health of Republic Indonesia referred to the National Cholesterol Education Program - Adult Treatment Panel (NCEP-ATP III) to determine the standard of reference value for total blood cholesterol [14], as shown in table 1 below.

Table 1. Total cholesterol reference value.

Category	LDL (mg/dl)	Total (mg/dl)
Optimal	<100	
Desirable		<200
Near optimal/above optimal	100-129	
<i>Borderline High</i>	130 - 159	200 - 239
<i>High</i>	160 - 189	>240
<i>Very High</i>	> 190	

LDL value can be determined if the total cholesterol, HDL and triglyceride values are identified, all of which are measured directly in blood [6, 8, 13] following equation (1).

$$L = C - H - kT \tag{1}$$

$H =$ HDL cholesterol, $L =$ LDL cholesterol, $C =$ total cholesterol, $T =$ triglycerides and $k = 0.20$ if it measured in units of mg/dl and $k = 0.45$ if it measured in units of mmol/l.

When radiation interacts with biological tissue, the light is weakened by absorption and scattering, so light attenuation can be described [11]. The description of light propagation in a similar medium as described by the Lambert Beer law is the absorptions of

light at specific wavelengths in homogeneous solution which can be determined accurately using the following equation (2):

$$I_x = I_o e^{-\varepsilon(\lambda)\beta L} \tag{2}$$

Equation (2) I_x is the reflected light intensity, I_o the incidence of light intensity, ε is media absorption and media absorption coefficient, β is the concentration of absorption and L is the length of the light path. The correlation between light absorbed by the material and transmitted is described by the following equation (3) :

$$T_s = I/I_o = 10^{-\varepsilon\beta L} \tag{3}$$

$$A = \varepsilon * \beta * L = \text{Log} (T)$$

Where T_s is transmittance, A is absorbance. Definition of the reflected light using input voltage V_{in} and output voltage V_{out} are substitution of the light intensity and light incident described (4) as described in the following linear equation (4).

$$\frac{V_{in} - V_{out}}{V_{in}} = 10^{-\varepsilon\beta L} \tag{4}$$

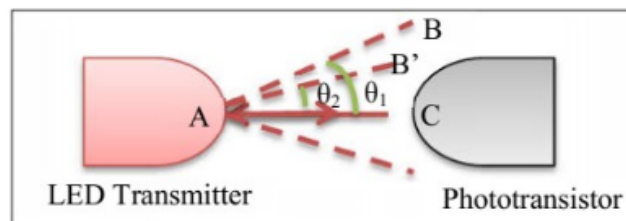


Fig. 1. IR LED light reflection angle.

Determining blood cholesterol concentration is related to the light reflectance angle. Direct correlation between light intensity J and output voltage V_{out} is described (5). Figure 1 describes the refractive index (η_2) to measure cholesterol levels by connecting points A, B and C. The increase of cholesterol levels in the blood can reduce the reflection angle (θ_2), so that the line AB moves closer to line AC and creates the new line AB'. Mathematically, the refractive index (η_2) can be calculated using Snell's law. The reflection angle (θ_2) decreases when the blood cholesterol level increases which reduces the reflected index (η_2) and increases output voltage (V_{out}) because many photons touch the photodiode. As a result

of the decrease in the reflection angle (θ_2), the radius of BC in LED light also decreases when light rays curving to AC which causes the increase of cholesterol levels according to Snell's law [12].

$$V_{out} = \frac{nKT}{q} \ln\left(\frac{I_{SC}}{I_o}\right) = \frac{nKT}{q} \left[\ln\frac{I_{SC}}{I_o} + \ln J \right] \quad (5)$$

$$V_{out} = V + \frac{nKT}{q} \ln J$$

Where: I_o is Backflow saturation, I_{SC} is Short circuit current, V is Initial voltage $nKT/q =$ is a constant value at T temperature, while K value = $1,380 \cdot 10^{-23}$ and $q = 1,602 \cdot 10^{-19}$.

The transfer of light energy to the material carried by each photon, as described in the following equation (6):

$$E = hc/\lambda \quad (6)$$

Where h is Plank's Constant ($6,620 \cdot 10^{-34}$ m²kg/s), C is Light Speed ($2,9 \cdot 10^8$ m/s), and λ is the light wavelength (940 nm).

Equation (6) shows that the amount of energy carried by photons depends on the wavelength where the NIR is at 400-1400 nm, the shorter the wavelength, the higher the wave number and the photon energy.[15].

Real-Time System is a system that must generate the right response and display monitoring within the specified time limit. Real-time system implementation on blood cholesterol total monitoring devices with non-invasive techniques is needed. Blood cholesterol levels are determined by detection of a NIR sensor with a predetermined time limit. When the limit time has been reached the device must display the precise measurement results on the monitor, and users can quickly find out the total blood cholesterol value at that time.

2 Methodology

Measurement of blood cholesterol levels with non-invasive techniques was done by conducting blood irradiation on body tissues such as at the earlobe and fingers using the wavelength. Near infrared spectroscopic sensors using infrared LEDs and photodiode was developed to determine blood components such as SPO₂, Glucose, Hemoglobin and Heartbeat. Previous research showed good results. Light absorption at wavelengths is utilized by measuring transmission or reflectance. The use of Infrared is a spectroscopy technique employing the infrared wavelength region of an electromagnetic spectrum. Non-invasive techniques analyse absorption ratios at various sets of these wavelengths.

The flow diagram of this study, starting from initialization by converting analog to digital by processing the signals from infrared LED sensors, placing sensors at the fingertips, emitting light into body tissues which then absorbed by the bloodstream and the one not absorbed is reflected and accepted by the photodiode. The voltage from the photodiode is supplied to the ADC microcontroller and calculated using logarithmic equation to determine the total cholesterol value and the readings are displayed on the LCD monitor and sent to the user's smartphone.

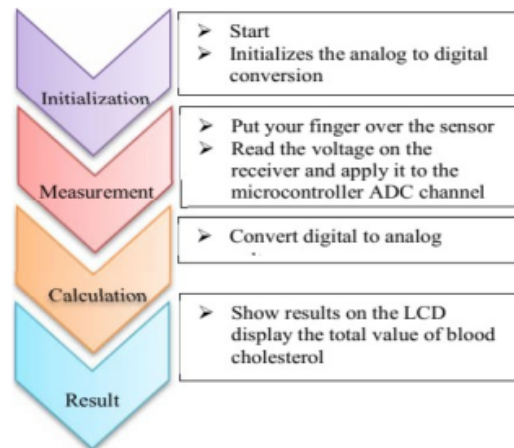


Fig. 2. Diagram of methodology process.

This research used Near Infrared (NIR) sensors with IR LED 333-A Ever light as an emitter with a wavelength of 940nm, 100mA continuous current, and 1A peak current. The detector used was PT 333-3C Ever light photodiode with a spectral bandwidth of 400nm - 1100nm, and spectral sensitivity at a wavelength of 940nm and maximum voltage of 5 volts. The photodiode absorbed the reflected light emitted by the LED emitter, then converting it into output voltage to the microcontroller. The blood cholesterol monitor device was designed to convert the output voltage into the total cholesterol value in mg/dl.



Fig. 3. Diagram block of the blood cholesterol level monitor

Figure 3, a series of sensors consists of IR LED 940 nm as emitter that emits infrared light. Photodiode is used as a detector that absorbs or receives light. When the sensor is installed at the finger, the light from the LED will be absorbed by the tissue in the finger, and the one not absorbed is reflected and received by the photodiode detector. The light received by the photodiode becomes a light attenuation value and is converted into an electric current, then becomes a voltage due to the presence of a load resistor on the anode. The voltage released by photodiode depends on the amount of light received, the more light is received, the greater the voltage released by the photodiode that is between 0 V and 5 V. The voltage value of the photodiode is still too low, so the variation in voltage values is less noticeable. To deal with this, an IC LM358N amplifier circuit is installed to strengthen the voltage from the sensor. The voltage value of the photodiode from the sensor circuit is read by a 10-bit ADC microcontroller and this ADC value is reconverted into a voltage value. Then, it is entered into a linear equation to change it into total blood cholesterol value.

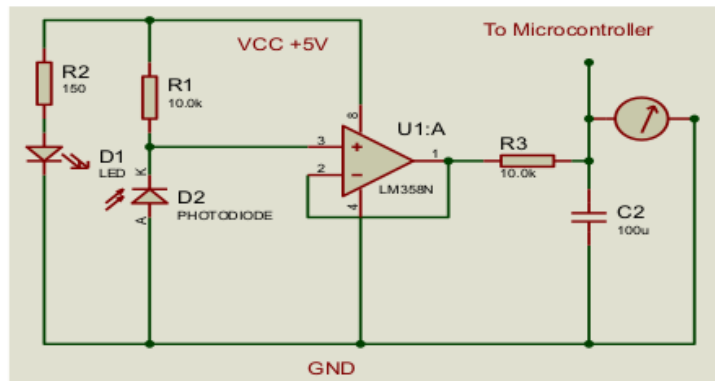


Fig. 4. Transmission Circuit

The measurement results are displayed on the LCD and smartphone. A compatible LCD with a microcontroller and a 4 x 16 LCD screen is used and installed directly on pin 4 on the main board of the microcontroller. The results are sent to smartphone using **SIM900A Mini V4.0 Wireless Data Transmission Module GSM GPRS Board Kit** installed on the ports available on the main board of the microcontroller.

In order to test the device, a sample was taken from 40 people with ages varied from 20 - 70 years of male and female participants. Blood cholesterol total data was collected using invasive measuring devices, and then continued with measurement of voltage using the designed NIR sensor a few minutes later. For data collection of sensor voltage output values, each participant was measured five times. The data collection was conducted by measuring the sensor output voltage twice before taking a blood sample for an invasive technique measurement and then thrice afterwards. Sensor output voltage stability, as long as the sensor was on the finger for about 20-40 seconds, the output voltage value was averaged. Data collection techniques and measurement results are shown in Figure 5 and table 2 respectively.



Fig. 5. Data collection with invasive and sensors devices.

Tabel 2. Measurement of the sensor output voltage and total blood cholesterol

SUBJECT	INVASIVE AUTOCHECK (mg/dl)	NIR SENSOR OUTPUT VOLTAGE (Volt)				
		SI	SI	NI	NI	NI
1	128	1.98	1.97	1.98	1.97	1.98

2	132	2.08	2.08	2.08	2.08	2.08
3	166	2.16	2.16	2.17	2.16	2.16
4	226	2.25	2.28	2.27	2.26	2.25
5	256	2.35	2.34	2.33	2.30	2.35
6	267	2.39	2.25	2.39	2.38	2.38
7	290	2.42	2.43	2.43	2.43	2.43
8	304	2.52	2.51	2.53	2.52	2.53
9	313	2.65	2.65	2.65	2.65	2.65
10	350	2.70	2.71	2.71	2.70	2.70

3 Result and Discussion

The results of measurements carried out on male and female participants showed a correlation between sensor voltage output and total cholesterol values, and invasive measurement techniques. The difference in sensor output voltage was found due to the absorption of light in the body's tissues and different light reflections. Blood cholesterol of each person caused this difference. The simple correlation of the total cholesterol values and sensor output voltage with algorithm equation $Y = 878.85 \ln(x) - 502.81$, with regression correlation coefficients $R^2 = 0.9656$. The NIR sensor output voltage has not been linear with blood cholesterol values measured with invasive techniques. Factors influencing the measurement result include the inconsistent of sensor installation, the possibility of other light received by the photodiode producing impure light reflection and the thickness of the skin affecting the absorption of light in the finger tissue.

In order to determining the total blood cholesterol values showed on the LCD according to the sensor output voltage, a linear equation was needed. Simple data processing with linear regression has the equation $Y = 355.87x - 591.46$, with a regression correlation coefficient $R^2 = 0.9747$. The function of this equation was to design a program on a microcontroller. Performance improvements are needed to maintain the stability of the input voltage with the addition of a voltage stabilizer to obtain a high degree of accuracy.

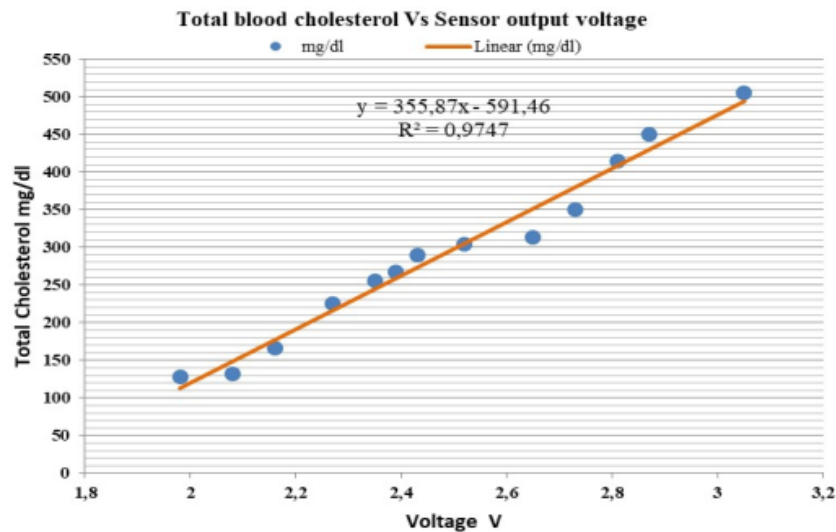


Fig. 6. Linear regression of sensor output voltage and total cholesterol.

Subsequent experiments were conducted to validate by comparing the measurements results of total blood cholesterol obtained using an invasive and a designed non-invasive measuring device. Data obtained using invasive measuring devices is very accurate because it uses blood samples. The results of a non-invasive measuring device depend on the NIR sensor detection. Testing the device by conducting validation was done by measuring total blood cholesterol with non-invasive techniques twice before and after collecting blood samples for invasive techniques.

Table 3. The Measurement Results Using Invasive and Voltage with Non-Invasive Sensors.

SUBJECT	NON- INVASIVE (mg/dl)		INVASIVE (mg/dl)	NON- INVASIVE (mg/dl)		VARIANCE
	1	2	3	4	5	
A	150	155	158	154	157	3,1
B	219	224	226	227	225	3,1
C	250	258	252	255	250	3,5
D	270	275	267	280	278	5,4
E	295	289	290	294	290	2,7
F	301	310	306	300	305	4,0

From Table 3, it can be seen that the data differences between the two devices still exist with variants 2,7 to 5,4. This tolerance value shows a great accuracy, and still needs continuous improvement. The perfect variant is zero, the farther away from zero, the condition of the data is uneven, meaning the greater the value of the variance, the higher the

fluctuation of data with other data. In subject E, the smallest data variant shows the results relative same between invasive and non-invasive measurements; the accuracy of non-invasive measurements is quite good. Subject D and other subjects showed that the results of non-invasive measurements were still varied; there is high-value data and low-value data from invasive measurements. Factors that influence the measurement results are not evenly distributed on non-invasive techniques such as; finger sensor mounting inconsistent; the sensor is not strong enough to clamp a finger, the possibility of other light entering and being captured by the photodiode and finger thickness can also affect the results of sensor detection.

4 Conclusion

The data presented in this paper are results of cholesterol measurements using non-invasive techniques that have been developed using sensors consisting of IR LED emitters and Photodiode detectors. These measurement results were compared with the results taken from invasive technique procedures measurement. The results of this device development are alternative innovations that can be used to measure cholesterol, which are easy to use, not painful, and low cost because it does not use cholesterol strips. The accuracy of the tool has developed quite well and reliable.

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