CHAPTER 4

EFFECT OF GLUCOSE CONCENTRATION ON LIGHT TRANSMISSION

4.1 Introduction:

The present chapter represents the optical clearing effect of blood glucose levels on the light transmission trends.

The refractive index between the scattering agents and their respective adjacent media decreases with increase in blood glucose concentration levels.

This phenomenon causes smaller scattering coefficients and accordingly shorter optical path lengths leading to increased optical clearing effects [Amir *et al.* (2007); Kohl *et al.* (1995)].

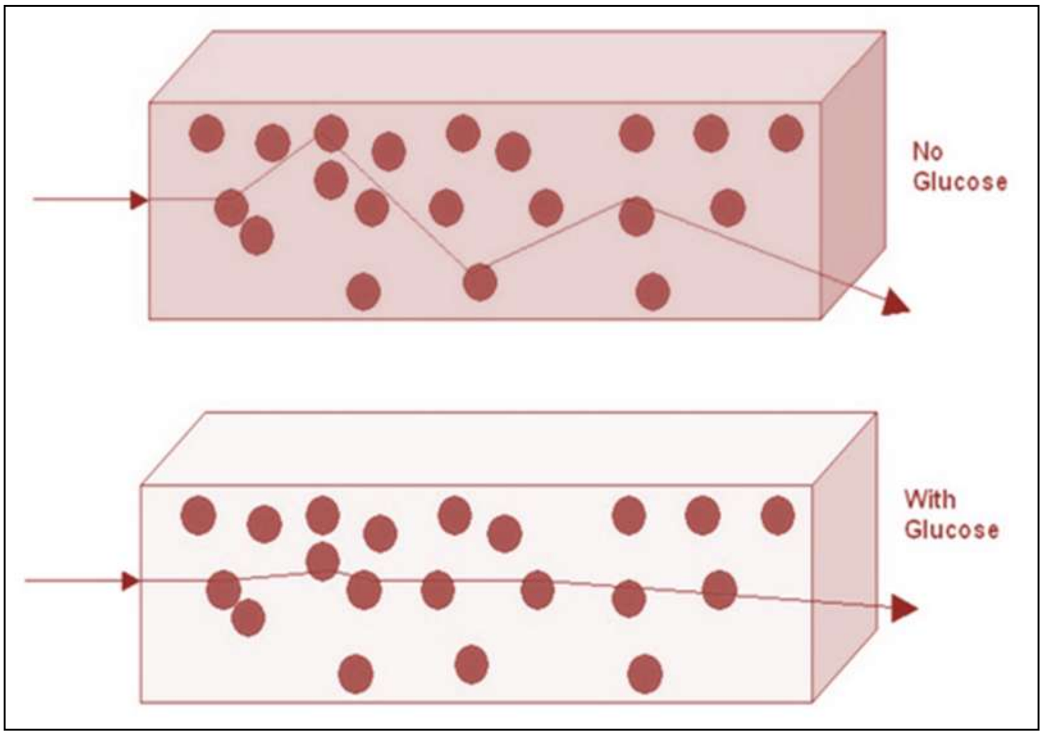

Figure 4.1: Diagrammatic representation of the effect of glucose concentration on light transmission phenomenon [Amir *et al.* (2007)].

The figure 4.1 depicts the glucose concentration effect on light transmission. In this present work, to prove this concept we have performed the clinical study by our noninvasive technique based prototype (MUS-IR) unit over healthy and diabetic subjects.

Further, the characteristics of blood glucose molecules to influence transmission of light optical signals has been investigated here and quantified by means of mathematical parameters (Absolute and Square value) computed on the transmitted optical signals.

4.2 Study subjects:

In total eight adult subjects (seven males and one female) participated in this study. Four subjects are healthy normal (age = 33.8±4.2 years, height = 174.8±2.8 cm, weight = 66.6±3.1 kg, and, Random Blood Glucose Level = 85±10.0 mg/dl). Other four subjects had diabetes (two Type I-male diabetic, two Type II-male diabetic, age = 42.3±11.9 years, height = 169.6±2.9 cm, weight = 60.1±2.5 kg, Random Blood Glucose Level = 275±25 mg/dl). The clinical study reported here are in accordance with the standard ethical procedures and performed with the informed consent of all the respective study subjects. The local ethical committee approved the clinical study.

4.3 Experimental protocol:

(i) Tuning of modulated ultrasound signal parameters such as carrier and modulating signal in the indigenously developed Prototype (MUS-IR) unit (Modulated Ultrasound-Infra Red) unit. Adjustment of infrared LED and its infrared detector for modulated ultrasound based optical signal acquisition purposes.

(ii) Acquisition of the optical sample signals from all the above-mentioned eight study subjects.

(iii) Determination of the mathematical parameters such as Absolute and Square values from the acquired optical sample signals.

The figure 4.2 depicts the Mathematical parameters based calculations (Absolute value Square value calculations) for all the acquired signals to determine the influence of blood glucose levels upon the light transmission.

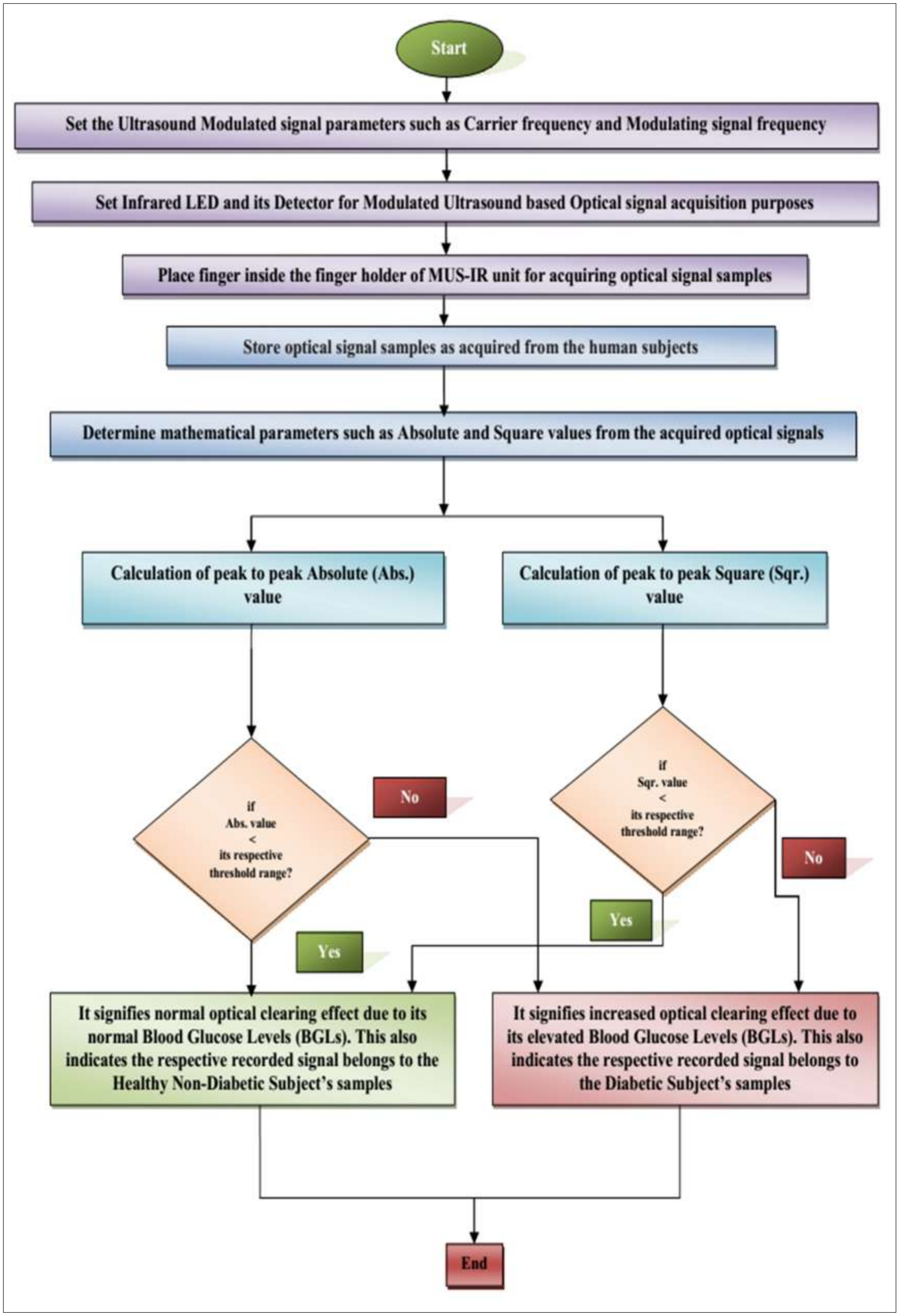

Figure 4.2: Flowchart for quantification of glucose level induced light transmission

4.4 Peak to peak amplitude measurements for Absolute and Square value calculations:

Peak to peak amplitude calculation is the difference between highest peak amplitude and lowest peak amplitude values, when the cursors are placed between those two certain locations within the waveform.

If "$S_{pp} = S_{peak\ to\ peak}$" represents the real or complex signal, then peak-to-peak amplitude calculation has been performed as follows [Ward *et al.* (1971)]:

$$S_{pp} = s_{max} - s_{min}$$ Equation (4.1)

Here, s_{max} signifies the acquired signal highest amplitude value and s_{min} signifies the acquired signal lowest amplitude value, when the cursors are placed between those two certain locations within the waveform.

4.4.1 Absolute value calculations:

For all the acquired signal samples, the Absolute (Abs) value mathematically expressed as follows:

For any signal, 'x' is a real input then absolute value or modulus of 'x' represented as $|x|$ and mathematically expressed as [Bartle *et al.* (2011); Schechter *et al.* (1997)]:

$$|x| = \begin{cases} -x, if\ x < 0 \\ x, if\ x \geq 0 \end{cases}$$ Equation (4.2)

Whereas, in case of complex signal input,

$$z = x + iy$$ Equation (4.3)

When, x and y signifies real signal input, the absolute value, or modulus of z represented as $|z|$ and mathematically expressed as [Bartle *et al.* (2011); Schechter *et al.* (1997)]:

$$|z| = \sqrt{x^2 + y^2}$$ Equation (4.4)

When complex part equals to zero, it resembles as the absolute value of real number x repectively.

The peak-to-peak Absolute (abs) value measurements were performed on the acquired signal samples of the study subjects by the Math function of SW-340 software.

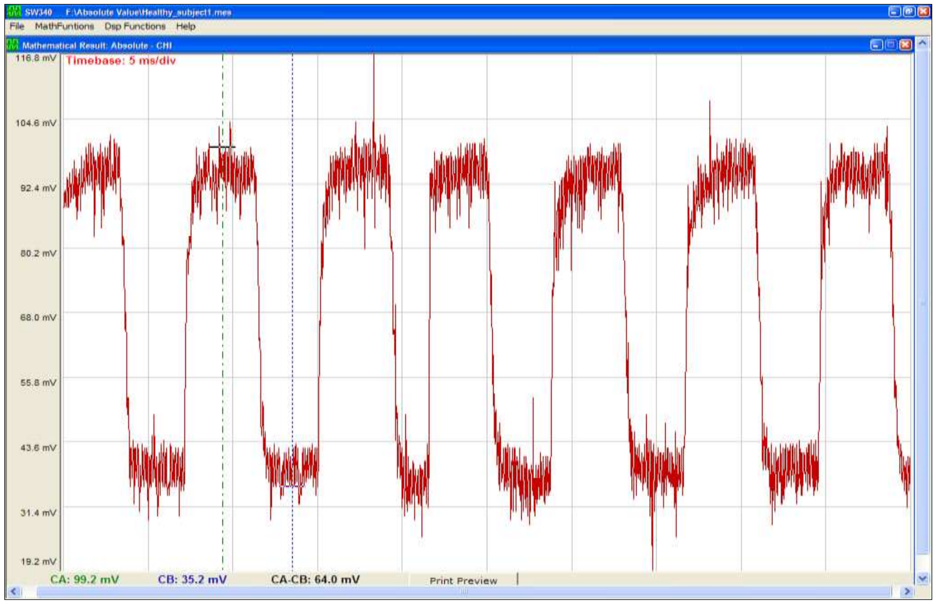

Figure 4.3: Absolute value calculation from the signal waveform as acquired from the healthy subject

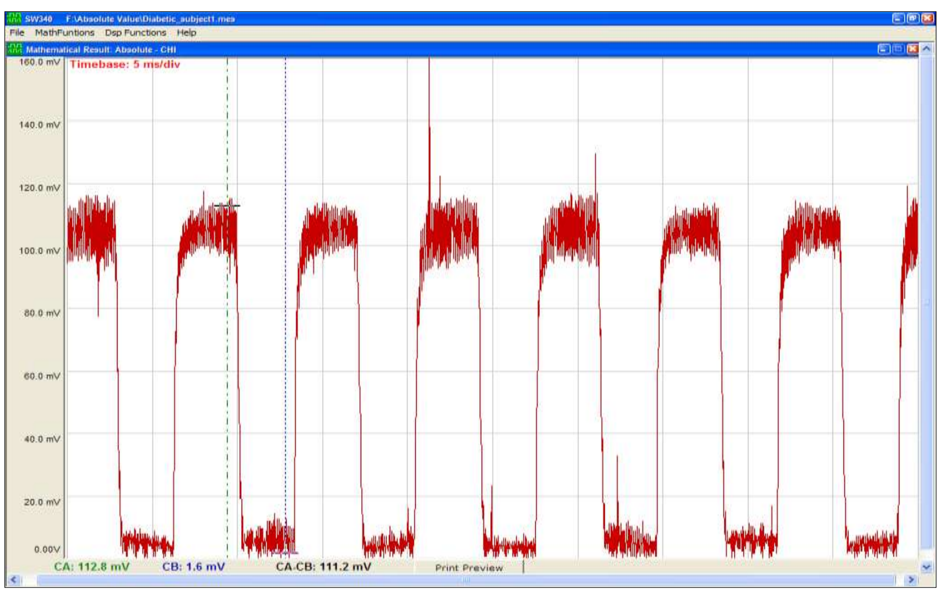

Figure 4.4: Absolute value calculation from the signal waveform as acquired from the diabetic subject

The figure 4.3 depicts one sample signal file for the absolute value calculation in the healthy subjects. Similarly, the figure 4.4 depicts one sample signal waveform for the absolute value calculation in the diabetic subjects. The threshold range allotted for Absolute value measurement for healthy and diabetic subject's signal samples are as follow:

If the Absolute peak-to-peak value of the recorded signal is lesser than its respective threshold range between 85 mV to 90 mV then it belongs to the healthy subjects respectively. It also signifies normal optical clearing effect due to normal Blood Glucose Levels in Healthy Subjects as depicted in figure 4.1 respectively. Now, if the Absolute value of the recorded signal is greater than its respective threshold range between 85 mV to 90 mV then it belongs to the Diabetic Subjects. It also signifies increased optical clearing effect due to elevated Blood Glucose Levels in Diabetic Subjects as depicted in figure 4.1 respectively [Tuchin (2009].

4.4.2 Square value calculations:

For all the acquired signal samples, the Square value calculations have been defined as follows [Bartle *et al.* (2011)]:

$$S^2=[real(x^2)+imag(y^2)] \qquad \text{Equation (4.5)}$$

The Math function of SW-340 software performed the peak-to-peak Square (sqr) value calculations on the acquired signal samples of the study subjects.

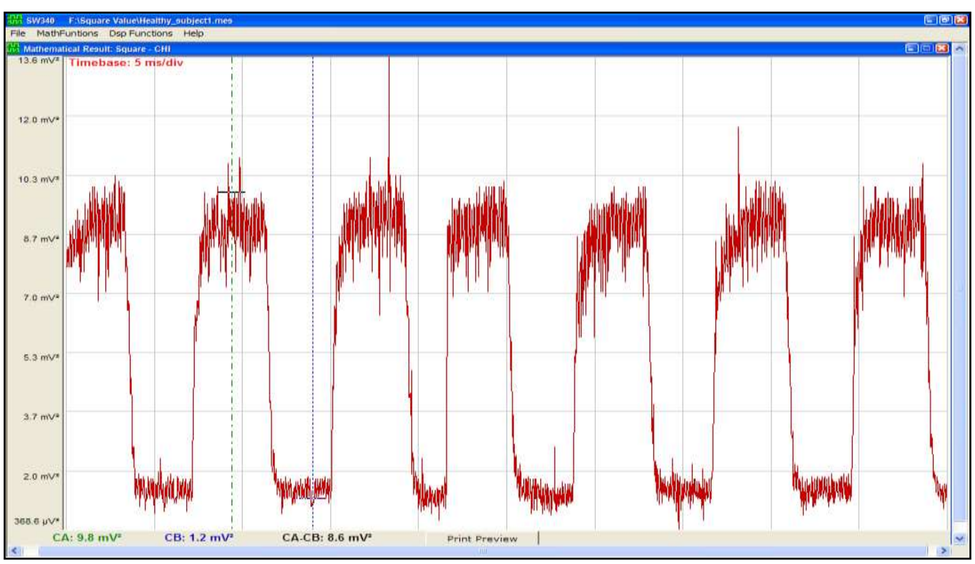

Figure 4.5: Square value calculation from the signal waveform as acquired from the healthy subject.

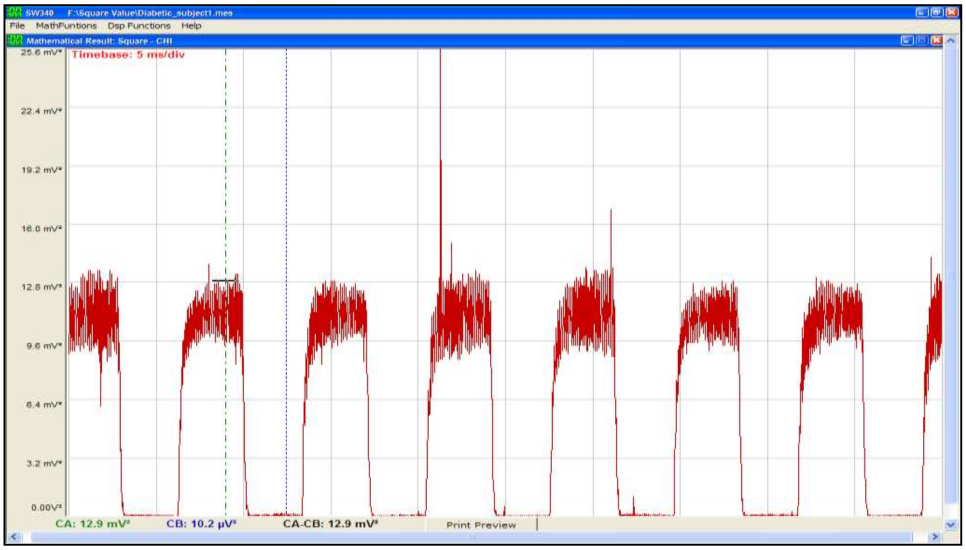

Figure 4.6: Square value calculation from the signal waveform as acquired from the diabetic subject

The figure 4.5 depicts one sample signal file for the square value calculation in the healthy subjects. Similarly, the figure 4.6 depicts one sample signal waveform for the square value calculation in the diabetic subjects.

The threshold range allotted for square peak-to-peak value measurement in healthy and diabetic subject's recorded signal samples are as follow:

If the Square peak-to-peak value of the recorded sample signal is lesser than its respective threshold range between 11 mV^2 to 12 mV^2 then it belongs to healthy subjects respectively. It also signifies normal optical clearing effect due to normal Blood Glucose Levels in Healthy Subjects as depicted in figure 4.4 respectively. Now, if the Square peak-to-peak value of the recorded signal is greater than its respective threshold range between 11 mV^2 to 12 mV^2 then it belongs to diabetic subjects respectively. It also signifies increased optical clearing effect due to elevated Blood Glucose Levels in diabetic subjects as depicted in figure 4.1 respectively [Tuchin (2009].

4.4.3 Result and Discussion:

In this present work, our noninvasive technique based prototype (MUS-IR) unit measures the influence of blood glucose level upon light transmission effects over eight study subjects. The figures 4.7 and 4.8 depicts the mathematical function (Absolute value and Square value) based results as obtained from healthy and diabetic subjects following the schematic in figure 4.1 respectively.

Further, the figure 4.9 shows the comparison of Random Blood Glucose Level of both the healthy and diabetic subjects as measured during the above experiments (by the invasive glucometer Accu-Chek Active of Roche Diagnostics GmbH, Mannheim, Germany) respectively. The figure 4.7 and figure 4.8 depicts that the diabetic subject's signal samples based absolute and square peak-to-peak values possess higher values as compared to the healthy subject's signal samples respectively. Further, in all these respective situations, the diabetic subject's blood glucose levels are much higher than the healthy subjects are as depicted from figure 4.9. High blood glucose levels in diabetic subjects causes minimum scattering effects, subsequently smaller optical path lengths, reduces absorption characteristics, which in turn causes increased light transmission effects [Amir *et al.* (2007)]. Similarly, in figure 4.1 as mentioned above represents this particular phenomenon also called as glucose concentration induced light clearing effects.

Hence, the present work strongly reveals that with increase in blood glucose concentrations, refractive index mismatches between the scatters like blood cells and surrounding media like body fluids minimizes, which facilities the increased optical clearing effect with increase in light transmission phenomenon and vice versa respectively [Tuchin (2009); Amir *et al.* (2007); Kohl *et al.* (1995)].

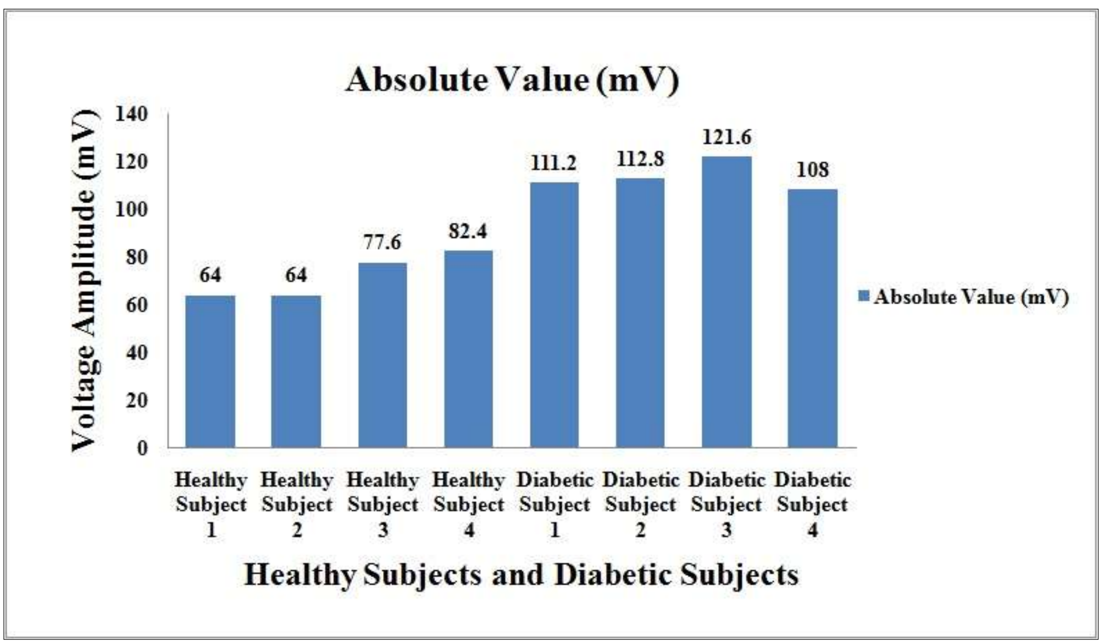

Figure 4.7: Absolute value peak to peak as obtained from Healthy and Diabetic Subjects

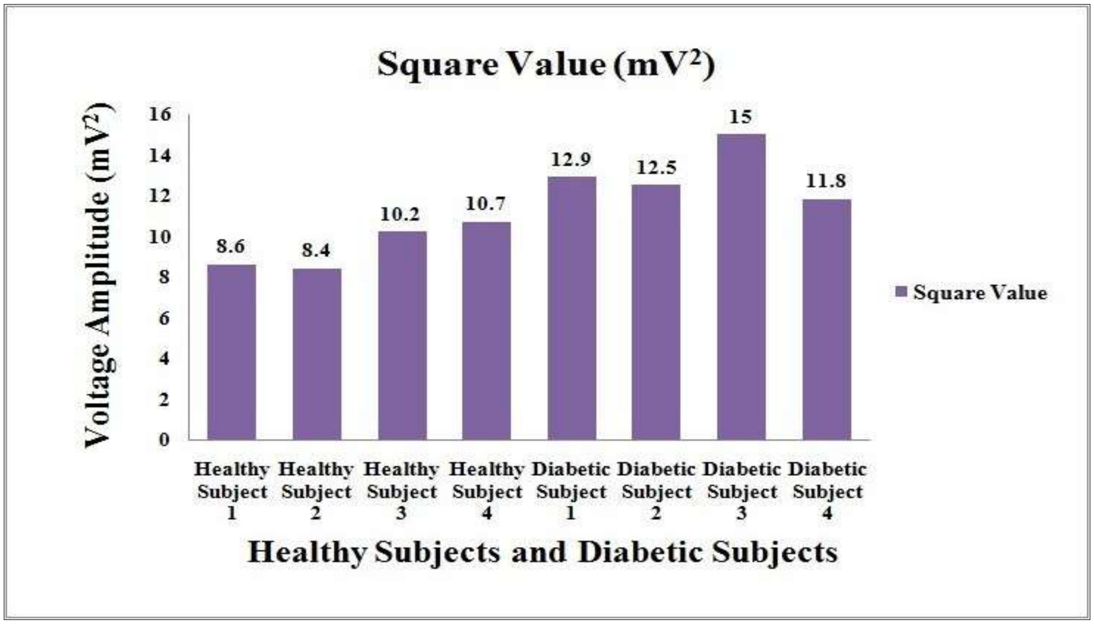

Figure 4.8: Square values peak to peak as obtained from the Healthy and Diabetic Subjects

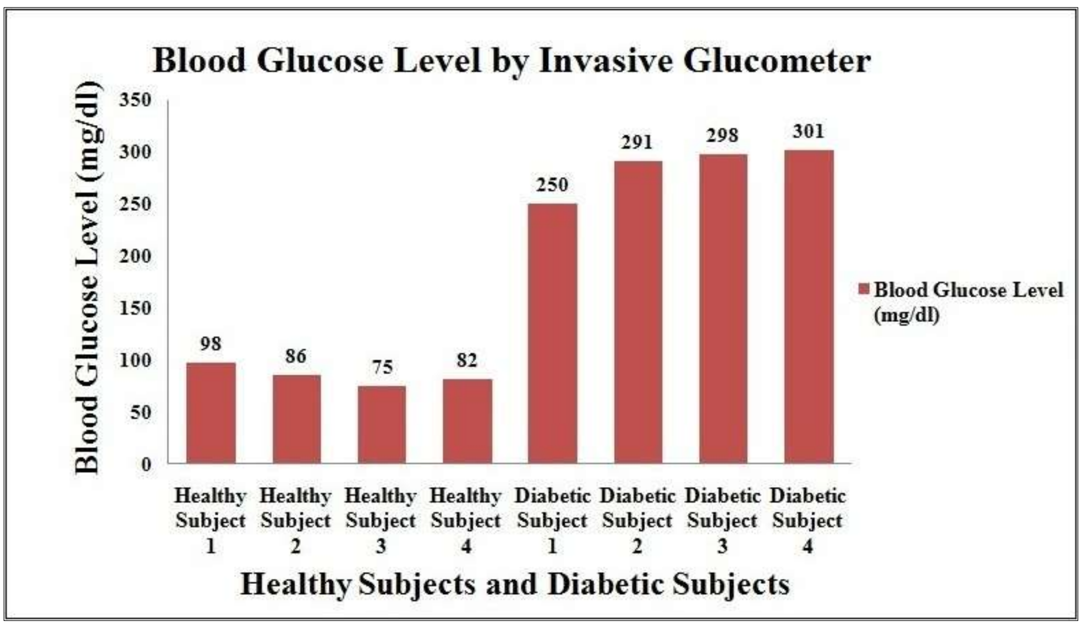

Figure 4.9: Invasive Random Blood Glucose Levels as obtained from Healthy and Diabetic Subjects

In diabetic subjects, the malfunctioning of glucose homeostasis mechanism occurs. At the same time, extra glucose concentration can influence solute concentration variations in both the extracellular and intracellular fluids affecting the overall metabolism systems [Kohl *et al.* (1995)]. In diabetic subjects, the glucose level associated rise in body fluid osmolality and change in their respective compositions such as ketone body, blood urea, body electrolytes, etc. occurs [Kohl *et al.* (1995); Wilson *et al.* (1991)]. For accurate estimations of blood glucose changes, the consideration of all these contributing aspect is important. Further, the increase in glucose levels and body fluid osmolality effects the body fluid balance and renal functions. This entire phenomenon induces the change in light transmission phenomenon. Other parameters like blood oxygenation, blood hematocrit level, body temperature influences this phenomenon [Kohl *et al.* (1995); Tuchin (2009)]. All this aspects directs towards the real time complexity that occurs during noninvasive blood glucose level estimations.

4.5 Conclusion:

This chapter describes that the change in blood glucose concentrations influences the change in the optical property of the blood tissue matrix. Our noninvasive technique based prototype (MUS-IR) unit has been capable in detecting the glucose concentration induced light clearing effects.

Hence, this phenomenon proves that due to the glucose concentration induced optical clearing effect, the peak amplitude in FFT domain increases with increase in blood glucose levels and vice-versa. Further, this principle aspect forms the benchmark of our noninvasive technique for measuring noninvasive blood glucose levels in the human subjects. Various clinical studies performed based up on this principle are reported in the Chapter 5 of this present thesis work.