CHAPTER 4

GLUCOSE INDUCED OPTICAL TRANSMISSION EFFECT ON INTRALIPID™ BASED PHANTOM

4.1 Introduction:

This present work describes the results of experimentation, carried out on Intralipid™ phantom to study the optical clearing properties of glucose. Intralipid™ phantom with different concentration of dextrose levels have been used and the analysis based on selected mathematical parameters have been obtained using our indigenously designed amplitude modulated ultrasound and infrared system. The results shows that dextrose minimizes the refractive index dissimilarity between scatterers and their surrounding media, leading to a smaller scattering coefficient, consequently, a shorter optical path. Hence, it is concluded that light clearing effect in relation with glucose (dextrose) concentration can be principally utilized for the design of amplitude modulated ultrasound and infrared light based non-invasive blood glucose meter.

4.2 The effect of glucose on the optical properties of tissue phantom:

Presence of glucose in an aqueous suspension of inert scattering particles can vary number of physical parameters such as absorption, scattering and transmission (a brief detail of these factors dependency on glucose is summarized in Table 4.1), further, the alteration in these properties effects the propagation of light in the scattering medium [Kohl *et al.* (1995); Kohl *et al.* (1994)].

Glucose reduces the absorption coefficient (μ_a^w) of the water in the aqueous solution because it displaces water (that is reduces the molar concentration of water molecules). At the same time it adds the intrinsic glucose absorption coefficient (μ_a^g) (Table 4.1 (a), (b)).

The refractive index 'n' of the aqueous solution increases with the glucose concentration (Table 4.1 (c)), resulting in a reduced velocity of light and a changes of the scattering properties of particles (scattering coefficient (μs) phase function (p) and (g) value) suspended in the solution (Table 4.1 (d)-(f)). In tissue-simulating phantoms when glucose is added Light Transport property like Transmittance (T) and Phase shift (ϕ) increases (Table 4.1 (g)-(h)) [Kohl *et al.* (1995); Kohl *et al.* (1994)].

Table 4.1: A summary of the effect of glucose upon the basic optical properties of a tissue phantom and the light transport within this tissue phantom [Kohl *et al.* (1995); Kohl *et al.* (1994)].

No.	Effect of Glucose on Basic Optical Properties of Tissue Phantom		
I.	Change in Absorption Properties	Notations	Effect
	(a) Water Absorption Coefficient	μ_a^w	Decreases
	(b) Intrinsic Glucose Absorption Coefficient	μ_a^g	Increases
II.	Change in Scattering Properties		
	(c) Refractive Index of Suspending Medium	Δg^n	Increases
	(d) Scattering Coefficient	μ_s	Decreases
	(e) Phase Function (P)	g value	Increases
	(f) Modified Scattering Coefficient	$\mu_s^{'} = \mu_s(1-g)$	Decreases
III.	Effect of added Glucose on Light Transport in Tissue-Simulating Phantoms		
	(g) Transmittance	T	Increases
	(h) Phase Shift	Φ	Increases

4.3 *In-vitro* experimental procedure:

In order to test the optical clearing effect in Intralipid™ phantom (tissue based) with respect to different glucose (dextrose) concentration, Intralipid™ phantom has been prepared here as mentioned in Chapter 3 of this present thesis. The dedicated prototype and the mathematical parameters (absolute value and square value) based algorithmic concept as shown in figure 4.1 was designed and developed. Our method utilizes amplitude modulated ultrasound and Infrared technique for detecting this optical clearing effect of dextrose in Intralipid™ tissue phantoms based on mathematical parameters. The Intralipid™ phantom was prepared with the help of soybean oil, lecithin, glycerin, distilled water. The 100 ml of this tissue phantom is used to carry out experimentation with different concentrations like blank 0 mg, 500 mg, 1000 mg and 1500 mg of dextrose anhydrous purified powder to verify optical clearing property of glucose (dextrose). The prepared 2 ml of dextrose mixed with Intralipid™ phantom sample is placed for measurement in indigenously developed

prototype. The signal acquired is processed in our developed algorithm for data analysis. The mathematical functions, absolute and square function were used here. The value obtained was interpreted to validate the acquired data with respect to the sample concentration.

4.3.1 Algorithm concept:

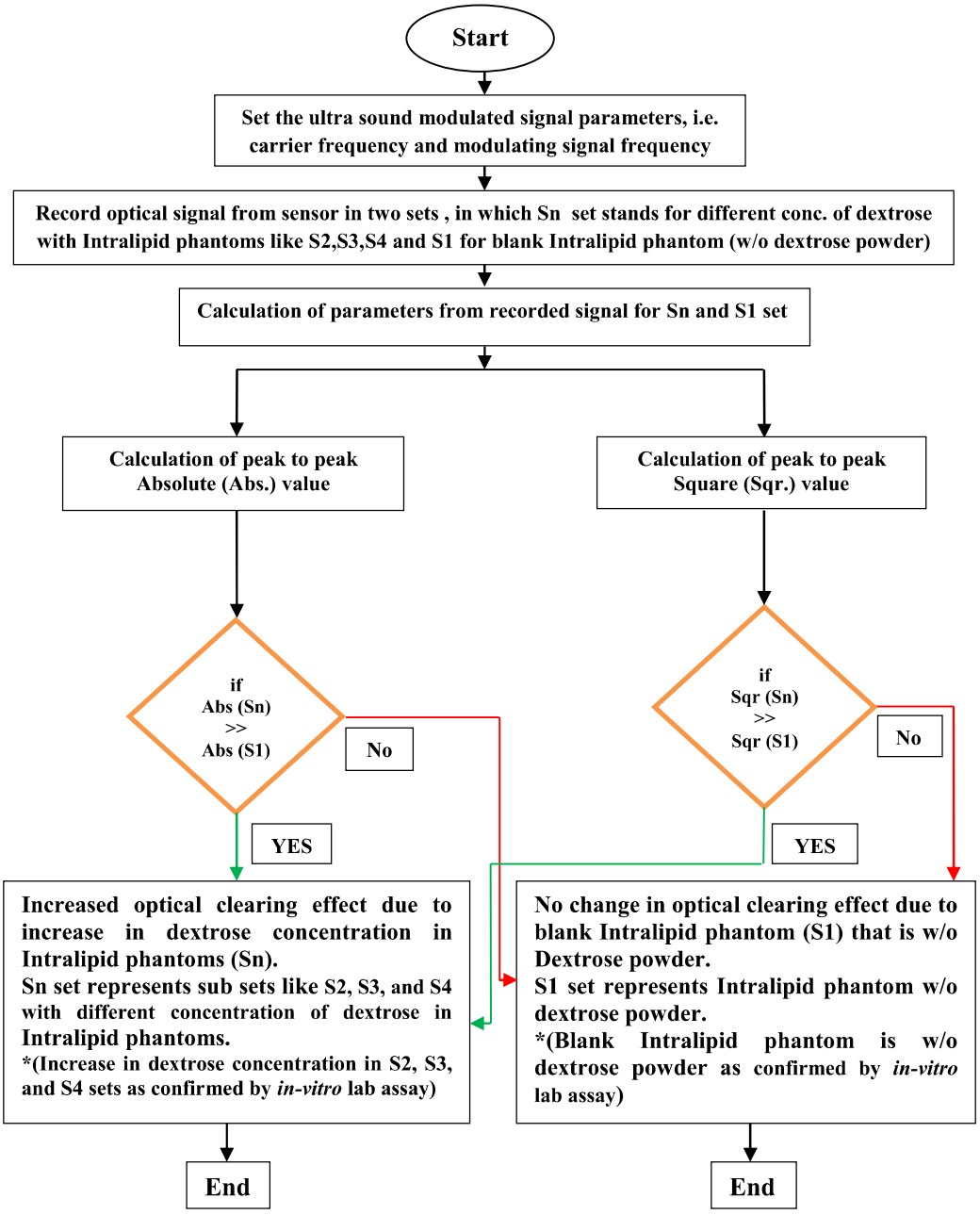

Figure 4.1: Flowchart depicting the algorithmic concept.

In figure 4.1 represents the utilization of mathematical function parameters such as absolute and square calculation based analysis for determination of the glucose (dextrose) different concentration (0 mg), (500 mg), (1000 mg) and (1500 mg) mixed with each 100 ml of Intralipid™ phantom medium in w/v proportions respectively. The absolute and square value parameters are provided in the mathematical function library of the digital oscilloscope (DSO) SW 340 software. For the analysis we developed the algorithmic concept for recognizing the glucose-induced changes according to the different concentration of glucose (dextrose) mixed with Intralipid™ samples. The flowchart describes the steps followed for the analysis purpose. Initially, the amplitude modulated ultrasound wave (using of carrier frequency and modulating signal frequency) are used to excite the Intralipid™ phantom with dextrose mixed samples. This specific vibration pattern in the sample has been used for identifying the glucose molecules, which is detected by infrared light technique.

The obtained optical signals from our prototype are categories in two sets. The first set indicated as “Sn” set which stands for different concentration of dextrose with Intralipid™ phantom samples such as S2 (500 mg), S3 (1000 mg) and S4 (1500 mg) of dextrose powder mixed with 100 ml of Intralipid™ phantom medium. The second set signifies as “S1”, which stands for blank (0 mg) of dextrose powder with Intralipid™ phantom sample. Further, the acquired signal from the Sn and S1 set samples undergoes the analysis processes. The calculation is based on the mathematical function of SW 340 DSO software. The peak-to-peak value of Sn and S1 set samples is calculated by Absolute (Abs.) and Square (Sqr.) functions respectively. In absolute parameter function, the calculation of set Sn indicates increase value in S2, S3, and S4 samples, which implies that when the dextrose concentration increases, it causes the optical clearing effect. Further, in S1 sample no change in absolute parameter function which indicates the absence of dextrose and there is no change in optical clearing effect. Therefore, S1 sample has been as the blank sample. Similarly, this pattern is observed for square value parameter in S2, S3, and S4 samples that also shows the increased optical clearing effects. Both the calculation parameter were performed here to identify the glucose concentration induced optical clearing effects.

4.3.2 Peak to peak amplitude calculation:

Peak-to-peak amplitude is the change between peak (highest amplitude value) and trough (lowest amplitude value, which can be negative). With appropriate circuitry, peak-to-peak amplitude oscillation can be measured by meters or by noticing the waveform on an oscilloscope. Peak-to-peak is a straight forward measurement on an oscilloscope, the peaks of the waveform has been identified and measured against the graticule. This remains a common way of specifying amplitude [Ward (1971)]. If 'S' is the real or complex signal input then the peak to peak amplitude value for the signal 'S' is calculated as

$$\mathbf{S = S_{max} - S_{min}} \qquad \text{Equation (4.1)}$$

Where $\mathbf{S_{max}}$ stands for highest amplitude value and $\mathbf{S_{min}}$ stands for lowest amplitude value.

4.3.2.1 Absolute value (Abs) calculations:

For all *in-vitro* acquired samples signals, the Absolute (Abs) value scientifically represented as follows:

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

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

Whereas, in case of complex acquired signal input,

$$z = x + iy \qquad \text{Equation (4.3)}$$

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

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

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

4.3.2.2 Square value (Sqr) calculations:

For all acquired *in-vitro* sample signals, the Square value measurement has been represented as follows [Bartle *et al.* (2011)]:

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

4.4 *In-vitro* measured spectra results:

In this present work Intralipid™ phantom (tissue based) with similar optical characteristic to finger has been prepared as proposed by Van Staveren *et al.* (1991). Light transport data based on mathematical function (Absolute value and Square value) of different concentration of dextrose (blank 0 mg, 500 mg, 1000 mg and 1500 mg) in Intralipid™ phantom (tissue based) (w/v) are shown in figure (4.2 to 4.9) respectively.

Dextrose minimizes the refractive index dissimilarity between scatterers and their surrounding media, leading to a smaller scattering coefficient and, consequently, a shorter optical path. As a result, with the increasing concentration of dextrose, fewer photons are absorbed and the light intensity increases [Kohl *et al.* (1995); Kohl *et al.* (1994)].

Table 4.2 to 4.5 shows the mathematical function values of various dextrose mixed with Intralipid™ phantoms (tissue based). In mathematical functions (absolute value and square value) the magnitude of amplitude (light transport) increases with increase in dextrose concentration at different frequency positions. Thus optical clearing effect increases with increase in dextrose concentration in Intralipid™ phantoms (w/v). The corresponding mathematical function (absolute value and square value) of different Intralipid™ phantom samples as obtained by the developed prototype and algorithmic concept are shown in figure 4.10 and 4.11 respectively. Figure 4.12 expresses the different concentration of dextrose in different samples of Intralipid™ phantom (w/v) [Intralipid™ Phantom (ILP) Sample (sp1) to Intralipid™ Phantom (ILP) Sample (sp4)]. The above stated experimentation is processed and analyzed by developed prototype and algorithm.

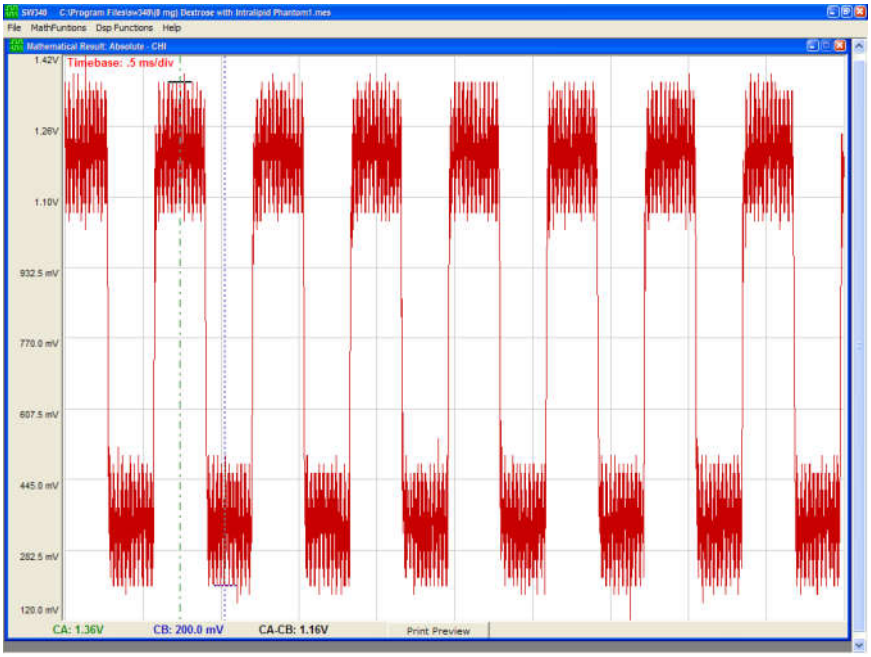

Figure 4.2: Shows mathematical function of absolute value of blank (0 mg) dextrose with Intralipid™ phantom (tissue based).

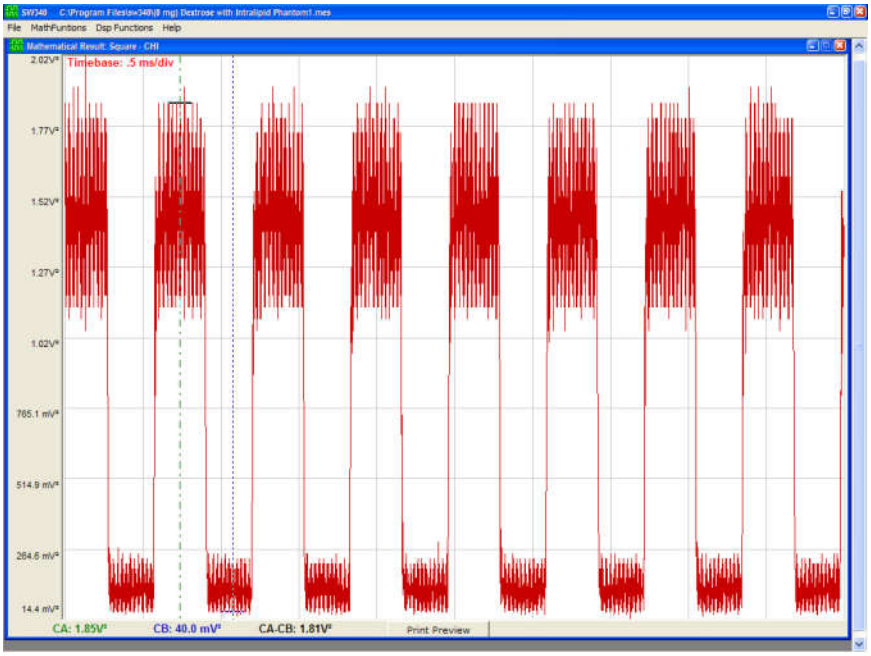

Figure 4.3: Shows mathematical function of square value of blank (0 mg) dextrose with Intralipid™ phantom (tissue based).

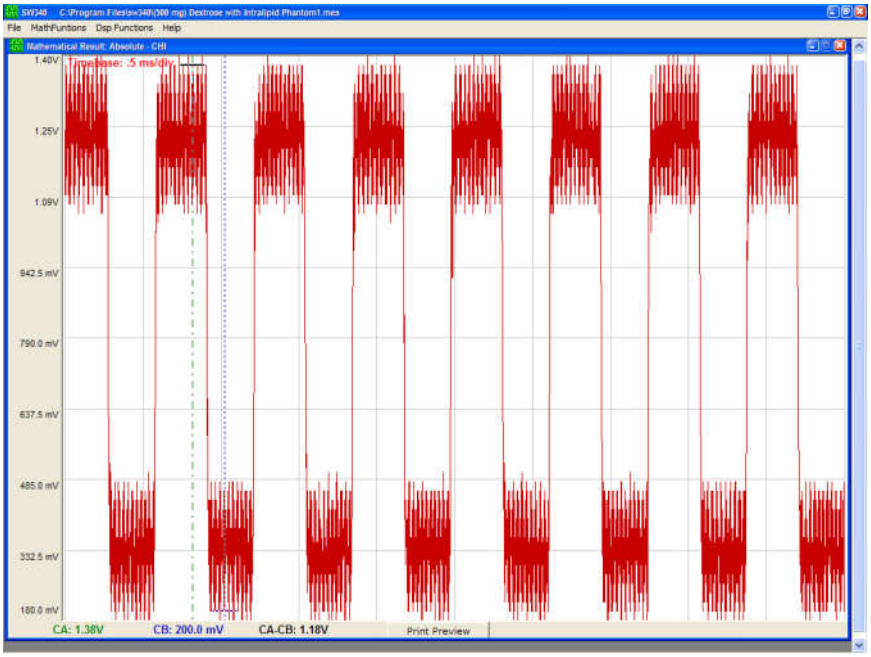

Figure 4.4: Shows mathematical function of absolute value of (500 mg) dextrose with Intralipid™ phantom (tissue based).

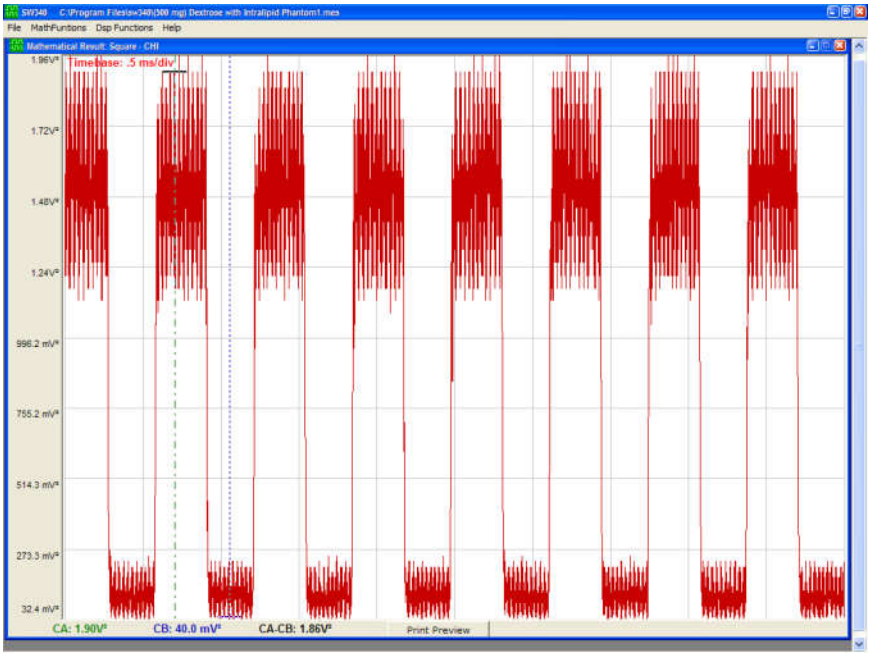

Figure 4.5: Shows mathematical function of square value (500 mg) dextrose with Intralipid™ phantom (tissue based).

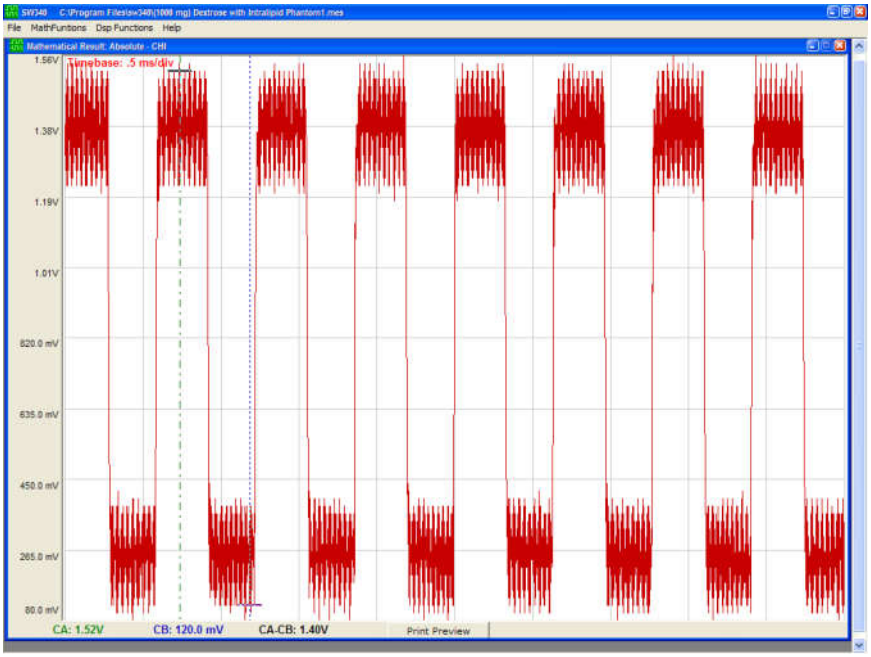

Figure 4.6: Shows mathematical function of absolute value of (1000 mg) dextrose with Intralipid™ phantom (tissue based).

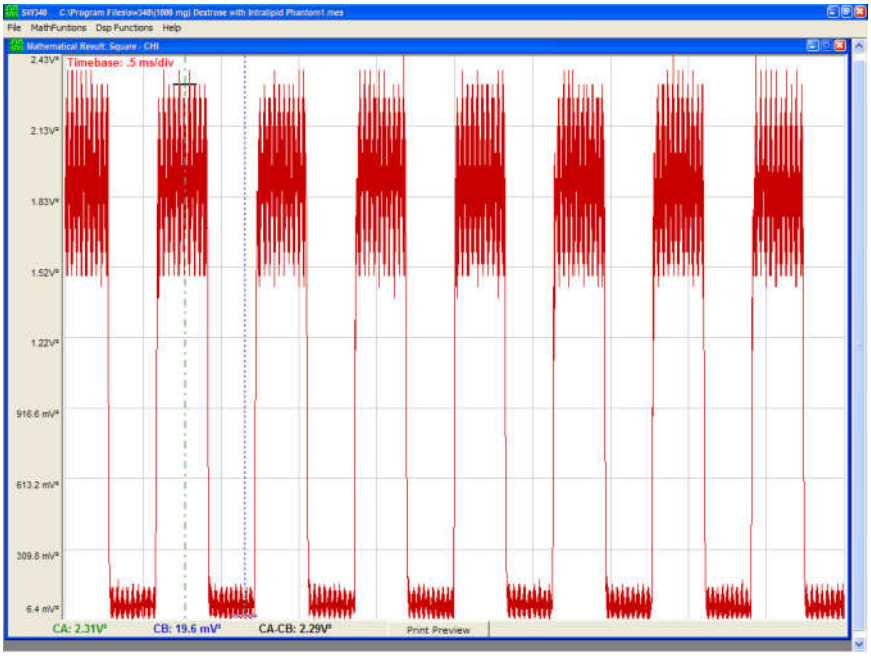

Figure 4.7: Shows mathematical function of square value (1000 mg) dextrose with Intralipid™ phantom (tissue based).

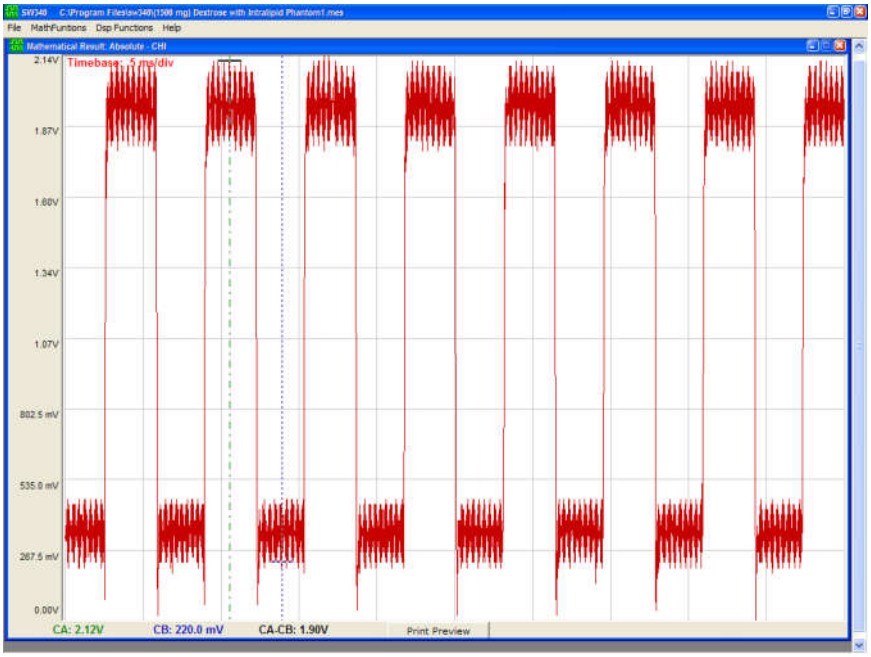

Figure 4.8: Shows mathematical function of absolute value of (1500 mg) dextrose with Intralipid™ phantom (tissue based).

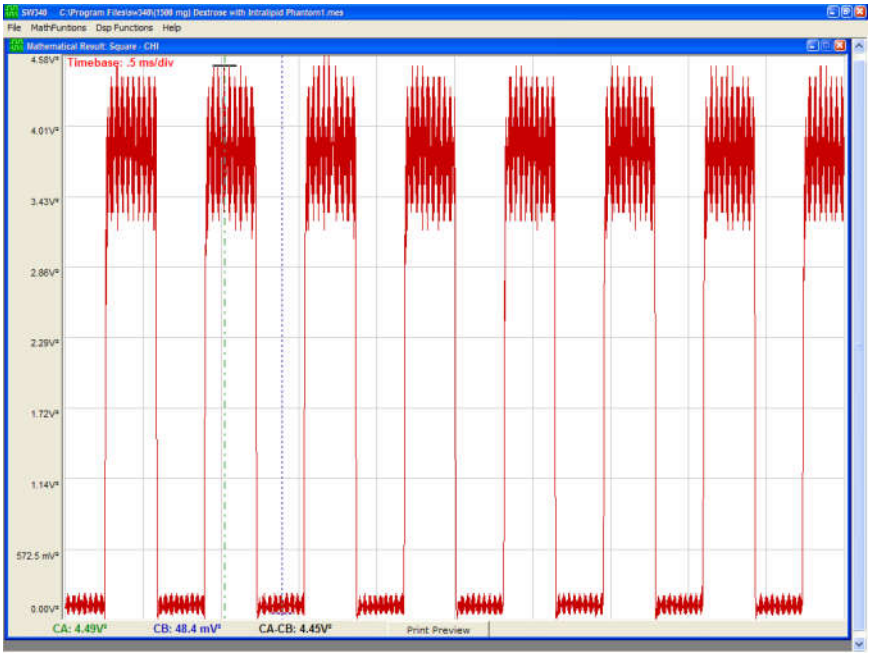

Figure 4.9: Shows mathematical function of square value (1500 mg) dextrose with Intralipid™ phantom (tissue based).

Table 4.2: Showing mathematical function values of blank with Intralipid™ phantom (tissue based).

Peak-to-peak amplitude calculation of Dextrose (0 mg) Intralipid™ phantom (tissue based)	**Time & Frequency (dt: 0.27ms,1/dt: 3.774 kHz)**		
Mathematical Function	**S_{max}**	**S_{min}**	**$S = S_{max} - S_{min}$**
Absolute Value	1.36 V	200.0 mV	1.16 V
Square Value	1.85 V^2	40.0 mV^2	1.81 V^2

Table 4.3: Showing mathematical function values of 500 mg dextrose with Intralipid™ phantom (tissue based).

Peak-to-peak amplitude calculation of Dextrose (500 mg) Intralipid™ phantom (tissue based)	**Time & Frequency (dt: 0.28ms,1/dt: 3.604 kHz)**		
Mathematical Function	**S_{max}**	**S_{min}**	**$S = S_{max} - S_{min}$**
Absolute Value	1.38 V	200.0 mV	1.18 V
Square Value	1.90 V^2	40.0 mV^2	1.86 V^2

Table 4.4: Showing mathematical function values of 1000 mg dextrose with Intralipid™ phantom (tissue based).

Peak-to-peak amplitude calculation of Dextrose (1000 mg) Intralipid™ phantom (tissue based)	**Time & Frequency (dt: 0.32ms,1/dt: 3.175 kHz)**		
Mathematical Function	**S_{max}**	**S_{min}**	**$S = S_{max} - S_{min}$**
Absolute Value	1.52 V	120.0 mV	1.40 V
Square Value	2.31 V^2	19.6 mV^2	2.29 V^2

Table 4.5: Showing mathematical function values of 1500 mg dextrose with Intralipid™ phantom (tissue based).

Peak-to-peak amplitude calculation of Dextrose (1500 mg) Intralipid™ phantom (tissue based)	**Time & Frequency (dt: 0.28ms,1/dt: 3.604 kHz)**		
Mathematical Function	**S_{max}**	**S_{min}**	**$S = S_{max} - S_{min}$**
Absolute Value	2.12 V	220.0mV	1.90 V
Square Value	4.49 V^2	48.4 mV^2	4.45 V^2

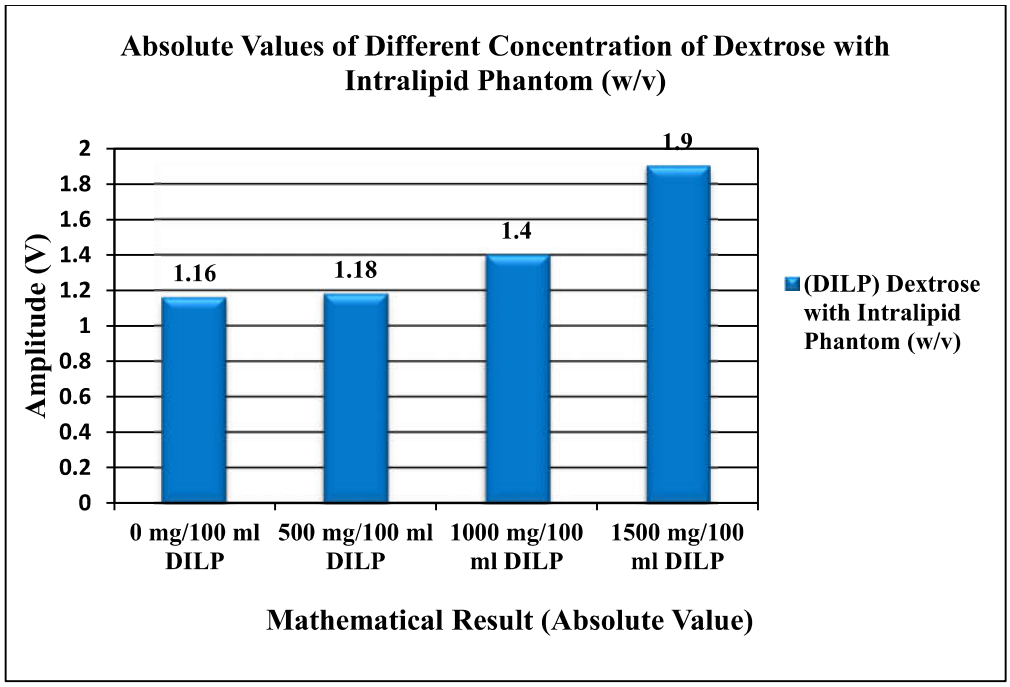

Figure 4.10: Shows mathematical function of absolute values of different concentration of dextrose with Intralipid™ phantom (tissue based) (w/v).

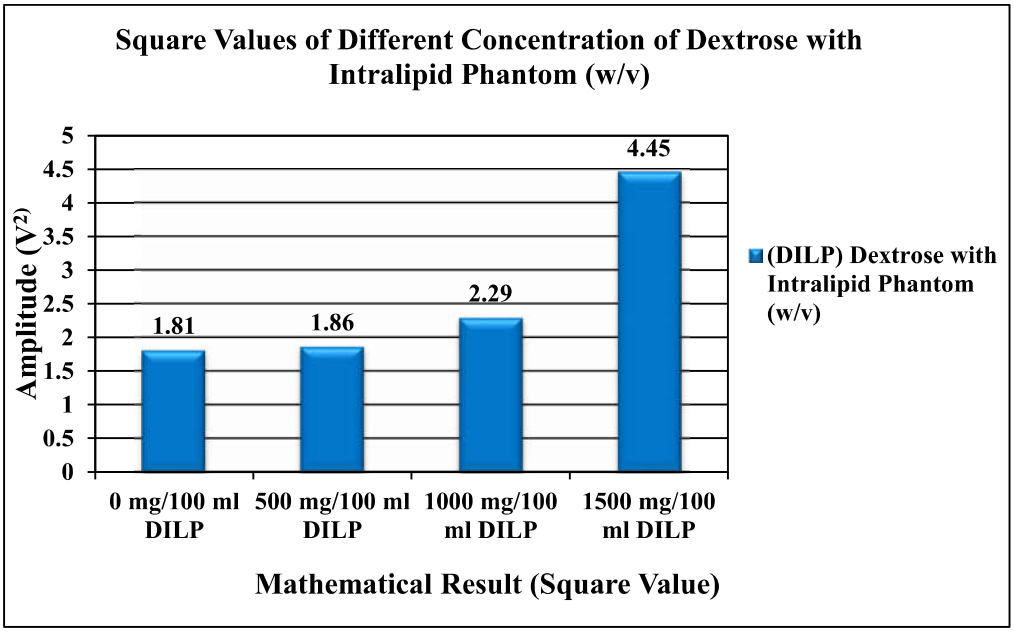

Figure 4.11: Shows mathematical function of square values of different concentration of dextrose with Intralipid™ phantom (tissue based) (w/v).

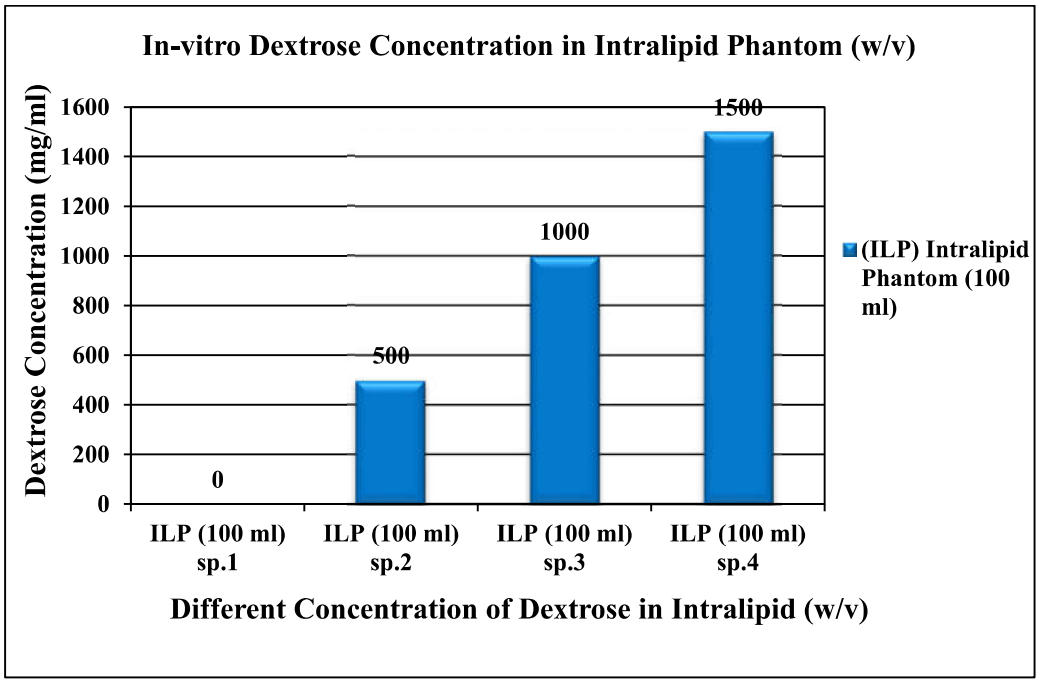

Figure 4.12: Shows *in-vitro* values of different concentration of dextrose with Intralipid™ phantom (tissue based) (w/v).

4.5 Discussion:

Zemansky (1968) studied the near-infrared absorption spectroscopy of glucose and established that the absorption coefficient of glucose differs approximately by ±20% from that of water at 905 nm and 1550 nm (0.007 mm^{-1} and 0.98 mm^{-1}, respectively). Kohl *et al.* (1994) described the experimental and theoretical investigations for the existence of glucose effects upon scattering media. The most significant of these effects was the modification of the reduced scattering coefficient and even this scattering effect was small. Glucose concentrations of an order of magnitude greater than physiological levels were needed to obtain measurable effects in tissue phantoms. It is hoped that the glucose effect in tissue is much greater than in these phantoms.

Bashkatov *et al.* (2009) discusses some aspects of tissue-like phantoms their optical properties, especially phantoms with a high concentration of scatterers, which corresponds to real tissues. Zhao *et al.* (2002)[a] proposed that photo acoustic apparatus could detect the minimal glucose concentration of 100 mg/dl in whole blood samples or in tissue phantoms. Decades of research indicate instrumentation with high specificity and sensitivity is required for non-invasive blood glucose determination.

This present work represents the importance of mathematical functions (Absolute and Square values) to observe the glucose induced optical clearing effects. Both the two parameter (absolute value and square value) provides significant results. The different concentration of dextrose such as (blank 0 mg, 500 mg, 1000 mg and 1500 mg) mixed with 100 ml of Intralipid™ phantom medium shows that the according to the concentration of dextrose the absolute and square values are increasing. The magnitude of both the parameters shows that the optical clearing effect increases with increase in dextrose concentration in Intralipid™ phantom samples (w/v).

Hence, this *in-vitro* study based on the light clearing effect in relation with glucose (dextrose) concentration mixed with Intralipid™ phantom samples by our modulated ultrasound and infrared technique proves to be efficient in developing the non-invasive blood glucometer.

4.6 Conclusion:

In this present work, we have used an Intralipid™ based tissue phantom to investigate the glucose induced optical clearing effect. A phantom that models the

tissue properties is needed to evaluate and optimize techniques and procedures for noninvasive measurement of glucose. Dextrose minimizes the refractive index dissimilarity between scatterers and their surrounding media, leading to a smaller scattering coefficient and consequently, a shorter optical path.

Our method utilizes amplitude-modulated ultrasound and Infrared light based techniques for detecting this optical clearing effect of dextrose in Intralipid^{TM} tissue phantoms based on two different mathematical parameters. Experimental results suggest that this optical phenomenon must be considered for noninvasive blood glucose measurement.

Henceforth, this proposed technique has been used principally for the design and development of non-invasive blood glucose meter prototype.