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BIOLOGICAL DIELECTRICS- A REVIEW

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Abstract

The dielectric parameters of different types of tissues of skeletal muscle, heart, liver, kidney and brain reveal extensive variant, which is to be attributed to the level of hydration, molecular composition with respect to proteins and lipids. The structural constituents and molecular compositions of tissues have amalgamated commotion in influencing the dielectric properties of tissues. The dielectric properties of blood are imperative for practical application. Impedance techniques at audio frequencies are well well-known for the measurement of blood flow or other physiological parameters. Impedance methods can be used to screen blood flow through arteries, small impedance change can be pragmatic during the heart cycle, that replicate changes in blood volumes and flow induced charges in the conductivity of blood. A dielectric relaxation is present in the audio frequency range. Magnitude of the dielectric dispersion is significantly high in audio frequency range.

Keywords: Dielectric parameters, lipids, dielectric relaxation, dielectric dispersion.

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Introduction:

Blood is the fluid connective tissue, a medium for transport of nutrients, gases and waste products. The blood reaches to every part of the body with the assistance of blood vessels that in turn are connected to the heart. It is the heart that pumps the blood through the blood vessels. Blood often act as fluid as it supplies *oxygen* to various parts of the body from lungs and *Carbon dioxide* to lungs from various parts of the body. Cook (1952) compared the behaviour of pure water and human blood at microwave frequencies and estimated ionic conductivity of blood. Mario branca et al (1983) studied binding between human serum albumin and a spin labelled derivative of bilirubin was explored by circular dichroism, the corresponding circular dichroism measurement for the binding between spin labelled bilirubin and bovine serum albumin are also discussed. Ernesto Pollitt et al (1989) reported that deficiency of iron in the children impacts their educational treatment and IQ of the children. They have been classifiedinto three main groups iron depleted, iron replete, iron deficient anemia. The kaven progressive matrices were used to evaluate IQ and found that there is optimisticconnotation between IQ and iron status. Simon P.wolff et al (1991) reported that Hyperglycemia is the source of diabetic complications. Glycationstudies and browning of protein suggested a vital role for the processes of oxidation and different kinds of less molecular weight decreasing agents are seen in persons suffering from Type – II diabetes. Luis C. Ramirez et al (1991) reported that thehyperglycemia is essential for the progress of the micro – vascular complications of diabetes re of the micro vascular complications of diabetes. Capillary cellar membrane thickness is the hallmark of histological result in diabetic microangiopathy. Antonio Piccolo et al (1994) reported a new method for daily monitoring of the body fluid fluctuation in each patient without considering composition of body. The technique is based on the careful observation of the bivariate distribution of the impedance vector in normal persons who possess more body weight because of obesity or edema from renal disorder. Gabriel (1996) studied tissues dielectrically with respect to frequency using automatic swept-frequency network and impedance analyzers. Meyer and Schatz (1998) studied metabolic control of Type - I, Type-II in diabetic patients using laser Doppler anemometry and concluded that metabolic control is important aspect in Type –II diabetic patient. Ronald E Pelrine et al (1998) reported that the electrostriction of elastomeric polymer dielectrics with compliant electrodes was potentially useful as a small scale solid state actuator technology. The mechanism of electrostriction was shown to be the electrostatic attraction of free charges on the electrodes. Antonio Piccolo (1998) estimated body fluid changes in the body weight, which may not lead to correct findings. Recurring analysis of bio electrical impedance produced prejudiced estimates of fluids. This is because of assumption of continuous tissue hydration. Sanjay A. Desai et al (2000) studied that growth of the malarial parasites in human Erythrocytes. Parasites in human red blood cells, accompanied by an increased uptake of many solutes, the permeability of infected red blood cell is more when associated with uninfected red blood cells. Biju kumar et al (2001) reported the role played by microwaves for the treatment than diagnosis. Cavity resonators having rectangular shape are used to evaluate the complicated permittivity of person’s bile. The calculations are carried out in J and S bands. Rectangular cavity resonators were used to evaluate the complex permittivity of human bile. The measurements were carried out in S and J bands. It was detected that dielectric constant of gastric juice and ill bile altered from patient to patient. Peter Gascoyne et al (2002) studied dielectrophoretic of malaria infected cells from blood and found that *plasmodium falciparum* increases ionic permeability of membrane of infected erythrocytes. Emsri Pongponratn et al (2003) studied cerebral malaria which is a major cause of death in severe *Plasmodium falciparum* malaria and found that most of the parasitize RBC in cerebral micro vessels were significantly large in the brain of patients when compared with those in non-cerebral malaria. Nuutinen et al (2004) reported variation of water content of tissue in human skin and built non- invasive device for a local calculation and its variation with respect to water content of tissue in skin. LuanaPillon et al (2004) studied that shorter predialysisbio-impedance vectors, representinglarger hydration of soft tissue, which are related with grim existence of hemodialysis patients. Suresh (2006) reported that any modifications in the cytoskeletal and membrane molecular edifice of the human RBC could be infectious diseases such as hereditary disorders and *Plasmodium falciparum* malaria. Zibeman-Kravtis et al (2006)) studied red blood cell agreeability in Type-I and Type-II diabetic mellitus developed a new approach based on the dielectric properties of disperse system. They reported that electric method had a significantly higher sensitivity to detect enhanced red blood cells aggregation than other methods. Maureen Johns et al (2005) investigated the interaction between light and tissue by using small source - detector separation, in order to characterize the optical properties of the tissue. Myungsakang et al (2005) identified dantrolene as a novel inhibitor of the plasmodial surface anion channel which was used as a high therapeutic index and a compound for antimalarial development. Louis Schofield and Georges E Grau (2005) studied the essential and immune adaptive mechanisms which can cause or prevent malaria, leading to design of vaccine. Maciejzborowski et al (2006) measured power attenuation in tissue representative of clinical applications. The results provided important insights regarding physical mechanism of weak power dissipation in tissues. ZongxiuNie et al (2007) made high pace mass analysis of mass spectrometry of ion trap charge detection quadrapole and concluded that there was variation in red blood cell size. Maria A stuchly (2007) reported reflection methods of coaxial line in order to measure dielectric properties at microwave and radio frequencies of biological material. Ronald Pethig (2007) studied mammalian tissues dielectrically frequency ranging from 1 Hz to 10 G Hz and alsothe influence of magnetic and electric field on biomaterials and the outcome is discussed considerably. Foster et al (2007) reported thermal mechanisms of interaction between radio frequency fields and biological systems with relevance to modify the exposure guidelines. Dean et al (2008) applied the technique of spectroscopy of electrical impedance by using Solarton 1290 impedance analyzer and studied rat lung, other tissues (vivo) electrical impedance properties. Gabriel Y H lee, Chwee T lim (2007) investigated nano-biomechanics, at the cellular and molecular levels, of some human diseases, and provided vital information for early detection of the diseases such as malaria, sickle cell anemia and cancer. Prasad et al (2008) investigated electrical properties of high bilirubin gall stone by employing the complex impedance spectroscopic method. The dielectric relaxation observed to be non-Debye type. Eckhardt et al (2008) reported that overweight women and non-overweight women need iron. The intake of other micro nutrients might also be insufficient. Diet quality remains an important issue even among with sufficient energy intakes. Carlos Edurada, Ferrante Amarai and Benhard wolf (2008) reported that painless control of blood glycemia levels expands life quality of diabetes patients from hyper tohypoglycaemia and explained treatment algorithms useful for multi variable analysis. Omar S. Desouky et al (2009) reported β - thalassemia RBC's biophysical characterization and estimated early screening technique for β - thalassemia. HulyaHalis (2009) investigated that children who suffers from iron deficiency anemia with certain variations with regard to iron replacement of hemo – rheological parameters, concluded that Iron treatment reverses the systems of anemia and contribute to regulate blood flow. Aryehshander (2009) reported that the quantity of iron in the body should be regulated as it increases the risks of chronic transfusion therapy. Omar S. Desouky et al (2009) studied the β - thalassemia RBC's biophysical classification. They compared normal hemolysis percentage along with osmotic fragility test and turbidity test, in addition to rheological properties besides dielectric properties, the dielectric loss, relative permittivity and found that alternating RBC's conductivity get decreases when compared with normal samples. HulyaHalis et al (2009) studied iron deficiency anemia and found that due to decrease in RBC aggregation, deformability, plasma and returns to normal values. After supplementation therapy of iron, hematological parameters and levels of serum ferritin tends to increase after treatment. Anil Lonappan et al (2009) made calculation of dielectric properties in analyzing vitro bile at microwave frequency. The rectangular cavity perturbation technique was used at the S-band of microwave frequency with various bile samples. Clotilde Ribout et al (2009) reported that human erythrocytes are occupied by plasmodium falciparum and induces significant changes in the host cell using red blood cell altered electrode to make electrochemical impedance spectroscopy which is helpful in determining growth of the parasite. Cedric Pemetier et al (2010) reported that majority of malarial death is due to *Anopheles gambiae.* Also, presented frequency matching of different tones formed in the nonlinear variations of the antenna by the collective flight tones of pair of mosquitoes. Harvey N. Mayrovitz (2010) measured dielectric constant of skin that decreased with age, Body Mass Index (BMI) status. Tissue dielectric constants were affected differentially by BMI and age in a depth dependent manner. Abdalla et al (2010) studied the effects of the blood microstructure on two correlated properties i.e.,electrical and mechanical properties, using micro fluidic device operating between 10 kHz and 1 MHz at room temperature. Andra Tura et al (2010) studied glucose induced dielectric property by introducing electromagnetic sensors which was considered as a new methodfor non – contact glucose monitoring and non - invasive.

Anjum Qureshi et al (2010) constructed an innovative capacitive bio sensor depends on inter digital gold nano diamond electrode for the detection of C- reactive protein antigen. The C- reactive proteindielectric constant measurement performed antigen detection. Wolf et al (2011) applied broad band dielectric spectroscopy on human blood and evaluated γ- relaxation beyond 1 GHz. Burhan Davarcioglu (2011) studied physical characterization of electromagnetic energy absorption by human body tissues at frequency ranging from 3 kHz to 300 GHz and stated that rate and distribution of radio frequency energy absorption depends on frequency. Janak Prasad et al (2011) developed flourmetric cholesterol biosensors works on self – assembled alginate mesoporous silica microsphere. The prepared cholesterol biosensors showed prodigious potential in curing of hyper cholesterolemia. Suresh K. Alla et al (2011) studied the constitutionaljaundice and prepared an algorithm using wavelet transform to analyse the image design of grey scales and concluded that their algorithm produced more accurate result than clinical treatment. Ivanov et al (2012) investigated polarization of spectrin-actin under membrane skeleton of red blood cell by impedance spectroscopy and concluded that heat could be selectively deposited in the plasma membrane. FarzanehAhmadi et al (2012) reported that low frequency ultrasound (20 Hz -100 kHz) had a diverse set of industrial and medical applications. Lonappan et al (2012) made vitro analysis of urine by evaluating dielectrically, using rectangular cavity perturbation technique at microwave frequencies. Cludin et al (2012) suggested that if proper glycemia control is not achieved it may lead to critical chronic complications like heart diseases etc. They discussed the consequences of the clinical management of the patients suffering from diabetes. Naresh Madepalli et al (2013) developed microneedle and iontophoresis mediated delivery of iron through transdermal path as a treatment for controlled transdermal delivery of iron may become safe, effective alternative therapy of iron. Sandra March et al (2013) reported plasmodium liver stage for the development of anti-malarial drugs vaccines which could provide a chance to interrupt the life cycle of the parasite at a critical early stage. Hence, it was the significant drug which can save the human life at the early stage of the disease. Heidi Hopkins (2013) developed new device called *Malaria lamp* which was used to identify low density infections of malaria and provided a new tool for diagnosis, surveillance, screening in elimination strategies. The malarial lamp is significantly important in improvising the detection of malaria. Ross D. Peterson et al (2014) reported that iron deficiency anemia afflicts one in individuals mostly women and children. He further presented a novel application, using iron oxide nano particles and photonic crystals optical bio sensors, as an immune diagnostic platform for the detection of serum ferritin as a biomarker for iron deficiency. Antonio Piccoli (2014) reported that both multiple as well as single frequency are accurately equal in calculating body's total water content and intracellular fluid. The vector analysis of bio electrical impedance serves as a comparison of the real body impedance with respect to reference population. Adeel Ahmad and Kaleem Ahmed Jaleeli (2014) reported that erythrocytes are disease detectors. They adopted dynamic dielectrophoretic technique and concluded that diseased erythrocytes were less dielectric when compared with normal erythrocytes, which could be attributed to the perturbation of erythrocyte membrane due to the disease. Douglas B. Kell and Etheresia Pretorius (2014) reported that iron storage protein is not synthesized in serum, but they arose from damaged cells. Serum levels represent cell stress and damage. Ateeba et al (2015) calculated excess permittivity (Ke) of RBC anemicpatients (iron deficiency) and dielectrodynamic collection rate was also evaluated by using non-uniform electric field method is employed suffering from iron deficiency anemia. The calculations were made in the frequency range of 1 – 10 MHz at constant applied voltage.The Kedata was related with that of normal RBC. The $K_e$spectra shows peaks at about 5 MHz in the case ofanemia, while 4 MHz in the case of normal blood. Ateeba et al (2015) observed yield or dielectrodynamic collection rate of erythrocytes depends on frequency at persistent voltage, elapsed time and cell concentration. Excess permittivity of erythrocytes was computed, knowing yield and micro polar parameter. The data was compared with that of normal erythrocytes. The study suggests that diabetic erythrocytes are less dielectric compared to normal erythrocytes. Francesco Farsaci et al (2016) reported a new method of calculating complex conductivity and dielectric constant, applied to human erythrocyte suspension for metabolic deductions. Stuchly (2016) evaluated dielectric properties such as dielectric constant and dielectric loss of biological materials in the frequency range 10 kHz – 10 GHz and tabulated and approximated the result clinically. Shen

Peck Mun et al (2016) studied dielectric properties of urine of the patients suffering from chronic kidney disease andhealthy individuals at microwave frequency ranging between 1 GHz and 50 GHz using support vector machine. Mehrishi and Angela Risso (2016) reported that sialic and acid residues are important components that play a role in determining cell structure, survival, chemical and electrical properties and developed quantitative rapid tests on micro samples of blood for monitoring the physiology and surface markers of red blood cells to be applied to the clinical monitoring of disorders in blood. Vijaya Ushasreeet al (2016) reported IR spectroscopic data on human blood and its elements. IR analysis was also done on whole blood, serum and plasma. The distinctive spectral bands pertaining to hemoglobin, fibrinogen, and lipids of erythrocyte membrane were identified. They concluded that IR spectroscopy can be used in analyzing the diseases. Vijaya Ushasree and Adeel Ahmad (2017) measured concentration of glucose using FTIR Spectroscopy. The FT-IRspectra of human blood serum samples were recorded using liquid cell in Mid IR region 4000-400 cm. The normal blood serum was treated with glucose at different concentrations viz2, 4, 6, 8 and 10gm/dl and the FT-IR spectra were recorded, which confirmed the specific peak for glucose. A graph between concentration of glucose and intensity of absorption showed a linear relation. Vijaya Ushasree and Adeel Ahmad (2017)reported IR spectroscopic data on blood of patients suffering from *Diabetes mellitus*. They made IR analysis on whole blood, plasma and serum and identified characteristic spectral bands pertaining to glucose in the medium of blood. Vijaya Ushasree and Adeel Ahmad (2017) presented spectroscopic data on human blood of groups A, B, AB and O. IR analysis was made on 90% packed erythrocytes and discussed the characteristic spectral bands pertaining to antigens. They explored the possibility of identification of blood antigens spectroscopically. AteebaShazi et al (2017) reported dielectrophoretic data on erythrocytes of blood of patients suffering from Jaundice. Dielectrophoretic collection rate (DCR) or yield was measured suspending the red cells in isotonic medium of glycine–glucose and non-uniform electric field (NUEF) is applied by using pin –pin electrode configuration. The content of bilirubin inblood samples was in the range of 1 to 18 %. DCR decreased with the bilirubin content in blood samples. DCR spectrum revealed *two* relaxations at 4 MHz and 7 MHZ. Data was compared with normal blood samples. There was a shift in the dielectrophoretic relaxation time when compared with normal erythrocytes. Mohammed Ibraheem Altaf and Adeel Ahmad (2017) investigated dielectric properties of anemic blood and its 90% packed cells and plasma. Electrical conductivity, dielectric loss and dielectric constant were measured at 1 kHz. It was observed that the values of Electrical conductivity, dielectric loss and dielectric constant were low in 90% packed erythrocytes, high in plasma and in between whole blood. The study revealed that there was a substantial change in dielectric parameters, possibly because of a change in hemoglobin percentage and cellular concentration. Mohammed Ibraheem Altaf and Adeel Ahmad (2017) reported dielectric properties of malaria parasite infected human blood. The malaria parasites studied were *Plasmodium vivax* and *Plasmodium falciparum*. Dielectric loss,electrical conductivity and dielectric constant of malaria infected blood were calculated in vitro at 1000 Hertz. It was observed that the values of electrical conductivity, dielectric loss and dielectric constant are higher in malaria parasite infected blood, when compared to normal blood.

Survey of Literature reveals extensive research work on biological, chemical, biochemical and physical properties of normal and diseased blood. Also, reports are available on various techniques employed for the diagnosis and early detection of the diseases. In the literature, some articles are found on dielectric properties of human blood studied at radio and microwave frequency ranges. The present study is an attempt to understand dielectric behaviour of normal and diseased blood in the audio frequency range.

Discussion:

The dielectric properties of blood are important for practical application. Impedance techniques at audio frequencies are well established for the measurement of blood flow or other physiological parameters. For example, impedance methods can be used to monitor blood flow through arteries, small impedance changes can be observed during the heart cycle, that reflect changes in blood volumes and flow induced charges in the conductivity of blood.

The basis of the dielectric spectroscopy is the interface of electric field with the dipole moments of the substance. The frequency range of the electric field is from 10^{-6} Hz to 10^{10} Hz. Above 10^{10} Hz in the infrared, optical and ultraviolet regions, the absorption and emissions of radiation is due to variations in the induced dipole moments, which are reliant on polarizability of the atom and molecules. At lower frequencies, the contribution of the induced dipole moments becomes small in contrast with that of the permanent dipole moments of the system. Consequently, the dielectric spectroscopy is useful for studying polar molecules in solution, where absorption of radiation is mainly due to the reorientation of permanent dipoles. This method, introduced by Debye in 1931, has been used since then, to determine molecule dipole moments of liquids and solids.

The dielectric spectroscopy was extended to biological cell suspensions to understand their distinct frequency dependencies, which permits identification of several entirely different mechanisms responsible for their characteristics.

From the literature, it is evident that dielectric properties of cells, tissues are most unusual because of the large quantity of water in cells and soft tissues.

The dielectric parameters of diverse types of tissues of skeletal muscle, heart, liver, kidney and brain reveal substantial variation, which is to be ascribed to the extent of hydration, molecular composition with respect to proteins and lipids (Basharath Ali 1991). The structural constituents and molecular compositions of tissues have unified activity in influencing the dielectric properties of tissues. The values of dielectric constant and dielectric loss are comparatively low in hard tissues, like bone and integuments (Rama Rao, 1989) and in marine molluscan shells (Annapurna, 1991) due to the presence of inorganic material in large quantities and also due to lack of free water.

When the constitution of blood is examined, the blood is a complex fluid tissue which contains 55% plasma and a solid cellular portion of 45% of formed elements (erythrocytes, leucocytes and thrombocytes) suspended in the plasma.

The results of the present investigation on dielectric parameters such as dielectric constant, dielectric loss and conductivity of plasma, whole blood and 90% packed RBC of blood of different groups A, B, AB and O, measured at the frequency of l kHz, reveal that dielectric constant and electrical conductivity are high in plasma, low in 90% packed cells and in between in whole blood irrespective of blood group. But situation is opposite in the case of dielectric loss as it is low in plasma, high is in 90% packed cells and in between in whole blood.

$$\varepsilon'_P > \varepsilon'_{WB} > \varepsilon'_E$$

$$K_P > K_{WB} > K_E$$

$$\varepsilon''_P < \varepsilon''_{WB} < \varepsilon''_E$$

It is obvious that substantial variation in dielectric parameters could be ascribed to the cellular concentration. The results, further, can be explained, considering the structure of erythrocyte membrane (Fig. 5. 1.).

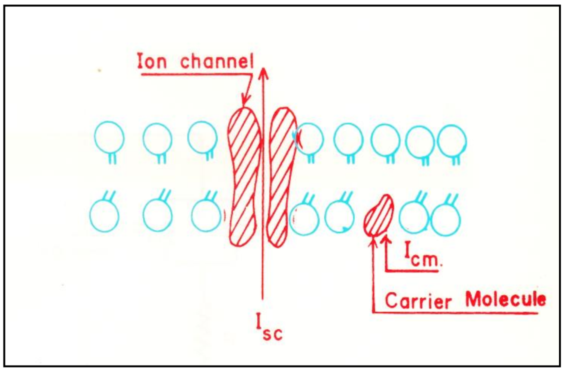
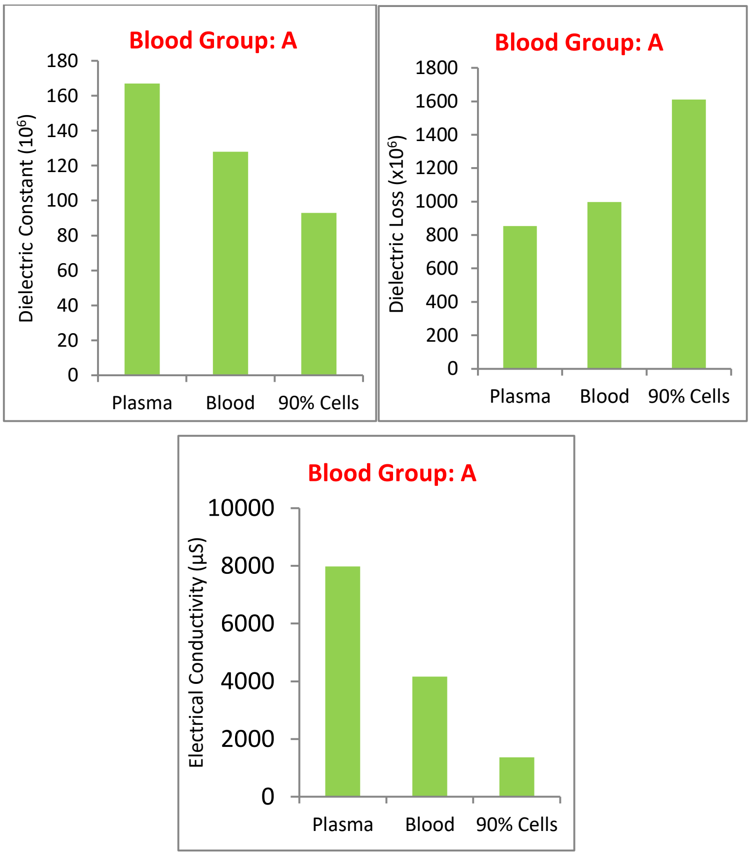
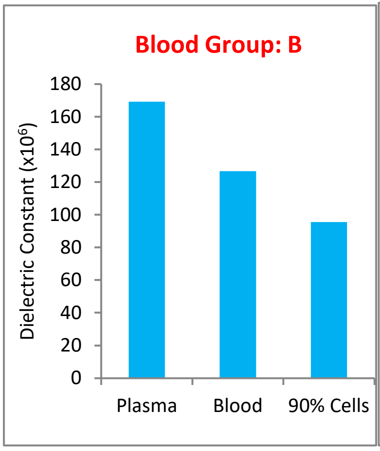
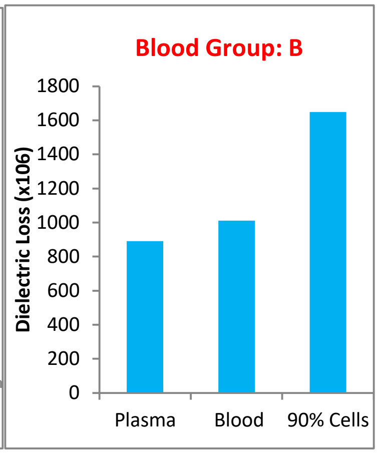


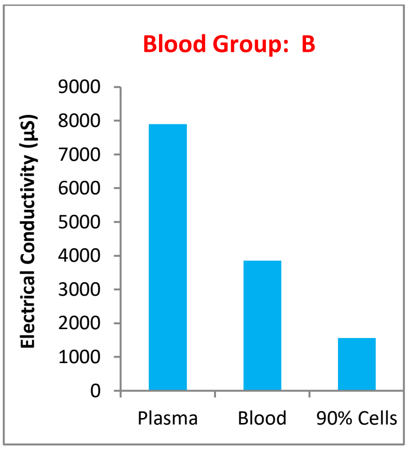
Fig. 5. 1. Model of biological membrane

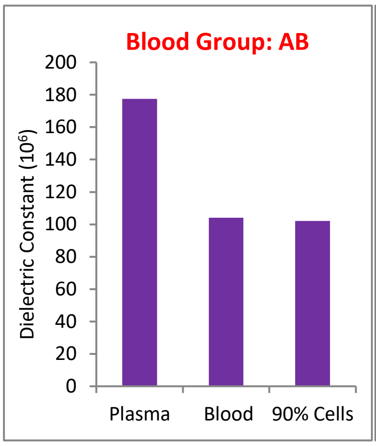
The main constituent of membrane is lipids. Lipids are arranged in two layers and make a bilayer. Also, the lipids are aligned in such a way that their headgroups directed outward in both lipid monolayers. Globular proteins are embedded in the bilayer. The proteins and hydrocarbons together act as ion channels. As a result, ions, water molecules and other small molecules pass through the membrane. Hence, one can draw the conclusion that blood contains protein solutions, ionic solutions and suspended cells in a large number. There is another component known as lipid bilayer membrane of erythrocytes, which splits the cell interior (hemoglobin) and cell exterior (plasma). This membrane acts as an electrical insulator due to the presence of lipids. Because of this fact, dielectric constant and electrical conductivity of plasma decreases with the increase in concentration erythrocytes, in which membrane is an insulator (Fig. 5. 2.).

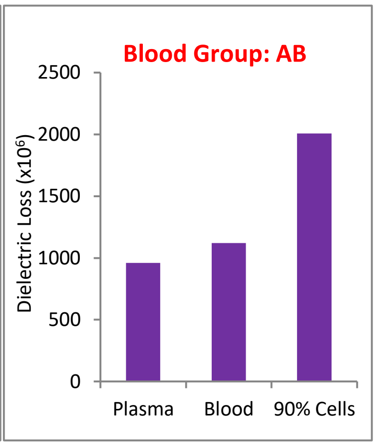


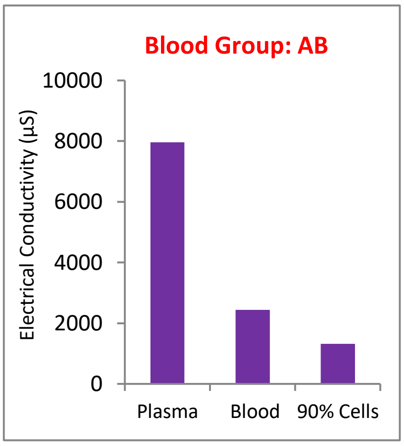

Blood Group: B
Dielectric Constant (x10^6)
0
20
40
60
80
100
120
140
160
180
Plasma
Blood
90% Cells


Blood Group: B
Dielectric Loss (x106)
0
200
400
600
800
1000
1200
1400
1600
1800
Plasma
Blood
90% Cells


Blood Group: B
Electrical Conductivity (µS)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
Plasma
Blood
90% Cells


Blood Group: AB
Dielectric Constant (10^6)
0
20
40
60
80
100
120
140
160
180
200
Plasma
Blood
90% Cells


Blood Group: AB
Dielectric Loss (x10^6)
0
500
1000
1500
2000
2500
Plasma
Blood
90% Cells


Blood Group: AB
Electrical Conductivity (µS)
0
2000
4000
6000
8000
10000
Plasma
Blood
90% Cells

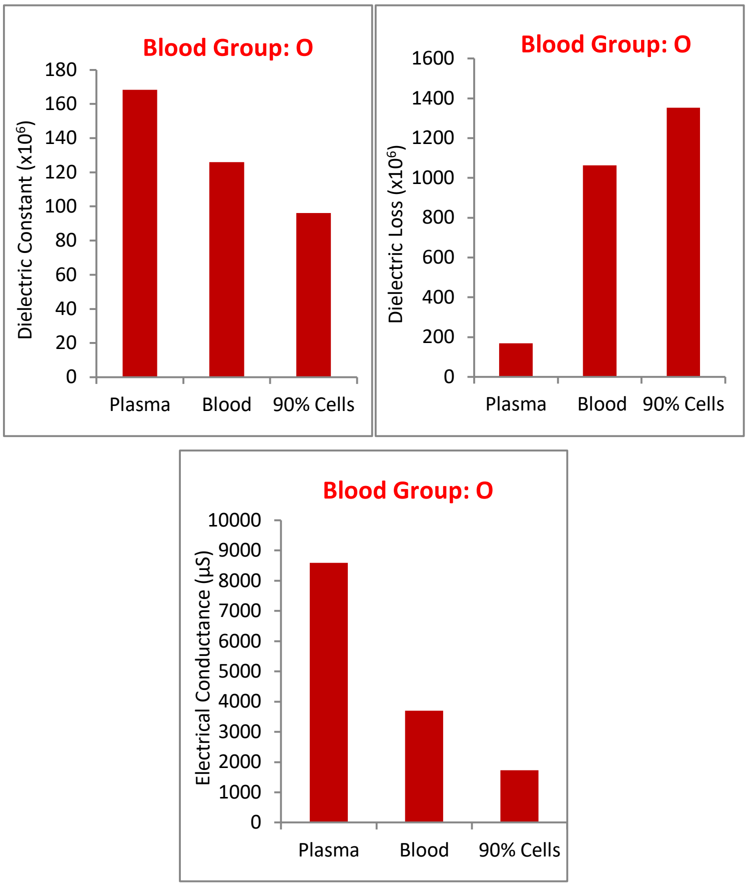


Fig. 5. 2. A comparison on ε', ε" and K of plasma, whole blood and 90% cells

The dielectric loss of plasma decreases with the increase in the concentration of erythrocytes, suspended in plasma. This observation can be explained, when the structure of erythrocyte membrane is examined. A cell membrane separates charges on both sides on it. The interior (intercellular) of the cell membrane possesses low dielectric medium, while the medium outside (exterior) the membrane is high dielectric one. Thus, the membrane acts as an insulator with conducting media on both sides. This arrangement makes the membrane equivalent to *Leaky Capacitor* and hence dielectric loss of increases with the presence of erythrocytes (Fig. 5. 2.). One can conclude that the presence of erythrocytes membrane causes significant variation in dielectric properties of human blood. Further, it is interesting to note that in the case of biological soft tissues, specially blood tissue; *high dielectric constant is coupled with high dielectric loss*, in contrast to non-biological material. Hence, biological tissues are lossy dielectrics. To understand the dielectric behaviour of human blood and its constituents (Plasma and erythrocytes) in terms of dielectric relaxations, operated by different types of polarization mechanisms, dielectric constant (ε'), loss (ϵ") and conductivity (K) were measured as a function of frequency in the range 100Hz – 25kHz. The frequency dependence of dielectric constant and dielectric loss over an extended range of frequency, starting from 1 Hz to 10^{10} Hz, exhibits three distinct types of relaxations operated by polarization mechanism. First, counter ion relaxation in the audio frequency range concerned with membrane channels and intra cell structure; second, interfacial polarization i.e., Maxwell – Wagner polarization in the radio frequency region related to tissue structure; third, operating at microwave frequency pertaining to water (free, bound, adsorbed). These first, second and third types of relaxations are referred as α, β and γ relaxations respectively.

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