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Significance of the cell membrane study; materialistic approach, mechanical behaviour and the future of its research

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Abstract: The cell membrane, composed of proteins and lipids protects the integrity of the interior of the cell. It undergoes certain mechanical properties; the ability of the cell to adopt a wide variety of shapes reversibly is a function of its unique shape, which provides the membrane, area in excess of that required to contain a constant volume. The area of the membrane is constant and it possesses a very high degree of one-directional deformability combined with a high resistance to two-dimensional stretch. Cellular structure, stress-stretch relationship, stiffness/elasticity, etc., of the membrane can be studied. The membrane can withstand a wide variety of tensions. Thus the cell exhibits material properties which pave a way into Nano-Biomaterials research.

Key words: Cellular structure, viscosity, human Red Blood Cells

Introduction

Red Blood Cells (RBCs) play an essential role in transporting oxygen from lungs to tissues and carbon dioxide from tissues to lungs. They are mechanically soft and flexible that, large deformations appear from low stresses. The mechanical deformation and characteristics are known to influence strongly with their chemical and biological functions and causes number of human diseases such as malaria reducing Red Blood Cells [1-3]. The factors that influence the mechanical properties of the cell are: the level of oxygenation, cell shape and the concentration of hemoglobin [4]. Human RBCs or erythrocytes have remarkable deformability; upon external forces, RBCs undergo large mechanical deformation without rupture, and they restore to original shapes when released [5].

Viscoelastic Properties of Blood:

Blood is a complex fluid whose flow properties are significantly affected by the arrangement, orientation and deformability of red blood cells. Viscoelasticity is a rheological parameter that describes the flow properties of blood. There are two components to the viscoelasticity, the viscosity and the elasticity. The viscosity is related to the energy dissipated during flow, primarily due to sliding and deformation of red blood cells and red blood cell aggregates. It is shown that elasticity is related to the energy stored during flow due to orientation and deformation of red blood cells [6]. Though RBC membrane is very much deformable, the membrane is much resistant to two-dimensional strain. The elastic modulus and viscosity of the membrane are significantly higher for the hereditary elliptocytosis RBCs than for the control cells [7]. The rheological properties of the membrane can undergo dynamic changes depending on the extent and duration of deformation, reflecting molecular rearrangement in response to membrane strain [8,9]. Under mechanical stress the volume of human Red Blood Cells rapidly exchanges with external medium which is not reversible [10].

When large forces are exerted by the suspending fluid on the red cell membrane it shows liquid behavior, i.e., it behaves similar to a liquid drop where its interior participates in flow. This behaviour is due to the fact that the cytoplasm of the red cell is liquid and contains no cell skeleton. When the forces are small the red cell behaves as a solid body. It may rotate in flow but its shape is the same as in the absence of external forces. The reason for this solid behaviour is the shear stiffness of the membrane and the fact that its relaxed shape is not spherical [11].

Stress-Strain Relationship

The stress-free red cell membrane has the bioconcave shape and the sphere shape of the same surface area [12]. We find three types of stretching: whole cell stretching, the stretching of a red cell evagination, and tether (long, thin membrane process) stretching. Tethers appear to possess both fluid and elastic properties [13]. Stretching is maximal in the normal red cell and lower in the sphered erythrocyte because the stretching of the cell membrane is probably caused by a surface tension between plasma and cell surface [14]. Spectrin (semiflexible filaments) tethers are flexible; the elasticity of the spectrin network can mostly account for the area compression modulus at physiological osmolality, suggesting that the lipid bilayer has significant excess area [15]. As the cell swells, the elastic contribution from the tensed lipid membrane becomes dominant [16]. Several researchers like Ademiloye, R P Rand, etc., concluded that the elastic and mechanical properties of the membrane vary with increase in area and volume constraint coefficients. Also that these elastic and mechanical properties are affected by temperature and membrane microstructure parameters, which inturn influence the response of the membrane under various loading conditions [4,17-22].

Effect of Nanoparticles

The membrane fluctuations of the red cell are governed by bending modulus, membrane tension, and cytosolic viscosity, with little or no dependence on the presence or absence of ATP [23]. Oxidative stress plays an important role in damaging the Red Blood Cell membrane and impairing its deformability. Decreased deformability and the oxidative stress removes RBC's from circulation [24-26]. Erythrocytes also play an important role in organism anti-oxidative defence. Direct exposure to reactive oxygen species (ROS) results in shortening of their half-life. The presence of glucose is one of the factors that can have influence on the level of oxidative stress [27]. There are several ways nanoparticles damage cells; there is a proof that they create pores in the cell membranes that can lead to cellular toxicity and abnormality in the functioning [28,29]. Study of various physical parameters by Sreevani et.al, [30] shows that there is a notable variation in physical parameters of blood with the addition of nanoparticles to the blood samples and that the change in the physical properties is at the cellular level alone. Stress-strain curve is an interesting result of mechanical behavior of RBC. The result (theoretical and experimental) is shown in figure.1 [31].

RBCs are constantly exposed to highly reactive radicals during cellular gaseous exchange. Such exposure often exceeds the cells' innate anti-oxidant defense systems, leading to progressive damage and eventual senescence. One of the contributing factors to this process are alterations to hemoglobin conformation and globin binding to red cell cytoskeleton. However, in addition to the afore mentioned changes, it is possible that oxidative damage induces critical changes to the erythrocyte cytoskeleton and corresponding bio-mechanical and nano-structural properties of the red cell membrane [32]. When a red blood cell (RBC) is subjected to an external flow, it is deformed by the hydrodynamic forces acting on its membrane. The resulting elastic tensions in the membrane play a key role in mechanotransduction and due to the strain-hardening property of the membrane, the deformation is limited but the membrane tension increases [33 - 36]. Moreover the breaking open of red blood cells (RBCs) results from their excessive deformation when exposed to a high shear flow [37]. Shear forces effective above a certain magnitude under flow conditions cause damage in blood cells [38].

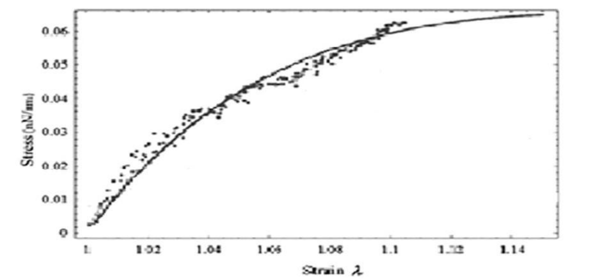

Fig1. Stress-strain relationship of RBC [see Ref. 31] Heavy line indicates theoretical result and the dots indicate experimental result

Significance of the Study

Writings of Rand et.al., and Evans et.al, [21,23] and many others [see all references], give a clear idea to the research of red blood cells and their membranes in the field of material science. Interaction studies of the cell membranes (model lipid membranes) with different chemicals/drugs (nanoparticles) have been very useful to predict pharmacokinetic properties of drugs and their efficacy [39]. Based on the structure and hydrophilicity of drug molecules, these interactions can also be used to study the transport mechanisms. Model lipid membranes are being explored to understand their mechanisms of interactions with peptides, polymers, and nanocarriers [40,41]. Membrane flickering study of RBC is one such means to understand the physicochemical interaction [42-45]. In certain disease conditions the lipid composition of cells and tissue may change and alter biophysical interactions, which may lead to the design of target-specific drugs and drug delivery systems [46]. Thus, the viscoeleastic and other physical properties of the cell (and its membrane) have entitled this tiny (nano) particle to be a part of material science and more specically, Nano-Biomaterials study, which has a scope of further research with interdisciplinary aspect.

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