

Unusual Rheological Properties of Some Biomaterials and Biologic Materials

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ABSTRACT

In this review paper, the unusual rheological behaviors of some biomaterials and biological materials are presented, confronted with the theory for the behaviors presented by most materials.

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I. INTRODUCTION

Rheology of Polymeric Solutions and Gels

The properties of solutions obtained from association of high molecular weight polymeric molecules with low molecular weight solvent molecules is very differently from those solutions involving low molecular weight solids and liquids [1]. The higher the molecular weight of the polymer it is more probable their chains have entanglement points and ramifications. So, the rheological and flow properties of polymeric solutions are not simple at all.

The polymer molecular weight effect upon solution viscosity depends of the pair polymer-solvent, and is given by the power law relation like that proposed by Mark, Houwink and Sakurada, the famous MHS equation:

$$[\eta] = kMv^\alpha \quad (1)$$

Where, $[\eta]$ is the intrinsic viscosity, Mv the viscosimetric molecular weight, k and α constants related to the pair polymer-solvent.

The viscosity of the polymeric solutions also depends on the solvent nature. If the solvent is a good one, the solution viscosity will be higher than the viscosity of a solution formed with a poor solvent at the same polymer concentration [2]. Although polymer macromolecules do not interact with one another in very dilute polymer solutions, where they are sufficiently away from one another, such isolated macromolecules can have different conformations. If the macromolecule is flexible, it has the conformation of a random coil, which swells to a certain extent in the solvent, depending of the solvent nature and temperature. When the concentration of these solutions increases, the high molecular weight polymer molecules begin to come into contact with one another, so associates are formed. A good solvent does not allow these associated swell in big extent, and the most probable type of contact is polymer-solvent and the macromolecules remains linear. The resultant solution viscosity will be higher than that of the solutions when the contact is polymer-polymer due the poor action of the solvent. In the last case, a coil will be formed rather than extended molecules. So, the viscosity of the solution will be lower [1,2].

In general, polymeric gels obtained from solutions occur as a result of swelling of a linear, branched or three-dimensional polymeric molecule against a low molecular weight solvent. There are two type of gels. The gels of type 1 are polymer low molecular liquid systems in which the network is formed by chemical bonds between molecules. The bonds are not destroyed on heating, and such gels do not melt at any temperature. When such gels are heated to a temperature higher than a critical one, the entire system is irrecoverably destroyed thermally. Therefore, such gels are called thermally irrecoverable. The gels of type 2 are systems in which the network is formed by intermolecular bonds of a different nature. These bonds are stable under certain conditions, but they may rupture when conditions, like temperature and the low molecular liquid type, for example, change. In this case, a homogeneous true solution is formed and the gels are thermally recoverable [1].

Polymeric gels are cross-linked polymer network swollen with a solvent, ie, they are gels type 1. In rheological terms, the polymeric gels behave like solid and liquid, depending on the shear rate, frequency and temperature range [3] and the equilibrium swelling in a given solvent [2].

Hydrogels are water-swollen, crosslinked polymeric structures with covalent bonds from the reaction of one or more co-monomers, physical crosslinks from chain entanglements, and hydrogen bonds and van der Waals interactions between chains or crystallites combining macromolecular chains [4].

Chitosan Hydrogels Based on Certain Hydroxy Acids

Chitosan hydrogels are obtained by the interaction of chitosan with small acid molecules. Such a combination does not favor chitosan solubility, but is positive in terms of medical applications due to its biological activity and low toxicity.

As expected, chitosan hydrogels made with mandelic acid are characterized by higher viscosity values, as compared to hydrogels containing lactobionic acid due higher activity of the mandelic acid on the chitosan molecules.

Despite the mixed liquid-solid behavior presented by the gels, ie, they are viscoelastic, normally the gels, when in adequate shear ranges that allow the viscous flow, present themselves as Newtonian fluids or very rarely as pseudoplastic fluids without any internal “structure” that prevents them from flowing in such shear conditions. So, polymeric gels in the fluid range may be described by simple relations like

$$\tau = \mu \dot{\gamma} \quad (2)$$

If they present Newtonian behavior, or

$$\tau = k \dot{\gamma}^n \quad (3)$$

For pseudoplastic ones, where τ is the shear stress; $\dot{\gamma}$ is the shear rate; μ the viscosity, k the consistence index and n power-law index.

Zavyalova and co-workers [5] obtained chitosan solutions by dissolving lowmolecular-weight chitosan in solutions of lactobionic acid and mandelic acid. The gels were formed from different mechanisms. Dynamic viscosity ($\eta = \tau/\dot{\gamma}$) is the apparent viscosity for Non-Newtonian fluids) versus shear rate measurements were made. All the obtained hydrogels have high viscosity and these viscosities increase with time at rest.

In general, when pseudoplastic gels, by some process, have the initial value of dynamic viscosity increased, their sensitivity to shear is also increased, that is, they become more pseudoplastic and more unstable (See Figure 1). For pseudoplastic fluids, $0 < n < 1$. Shear sensibility increases as $n \rightarrow 0$. So, its apparent viscosity decreases with shear rate more quickly towards the Newtonian equilibrium value.

Gels of chitosan in a mixture of acetic and maleic acids behave like shown in Figure 1. The zero shear viscosity, η_0 , of the gel increases with chitosan content, but the apparent viscosity decreases more quickly in the pseudoplastic region. In Figure 2 it is shown the variation of the zero shear rate and final equilibrium apparent relative viscosity, η_∞ , (see Eq. 4) with the chitosan content. As the gels become more pseudoplastic this relative difference tends toward unity.

$$\bar{\eta} = \frac{\eta(\dot{\gamma}) - \eta_\infty}{\eta_0} \quad (4)$$

All the chitosan gels used by Zavyalova co-workers [5] exhibited pseudoplastic behavior, but the increase of the shear sensibility were not observed, so the upper curves are just parallels to the lower ones (see Figure 3).

Based on the FTIR spectra, it was proved that both carboxyl and hydroxyl groups were involved in the interaction between chitosan and the molecules of the hydroxyl acids mentioned before. The viscosity increased over rest time due to progressive process of protonization of the amino groups resulting from the progressive dissociation of hydroxyl acids and the increasing number of bonds between chitosan and hydroxyl acids [5].

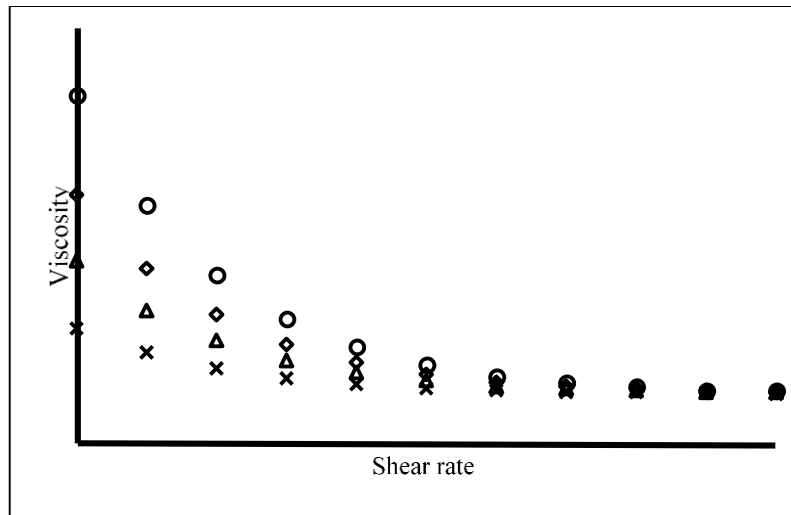


Figure 1. Usual rheological curves for pseudoplastic gels.

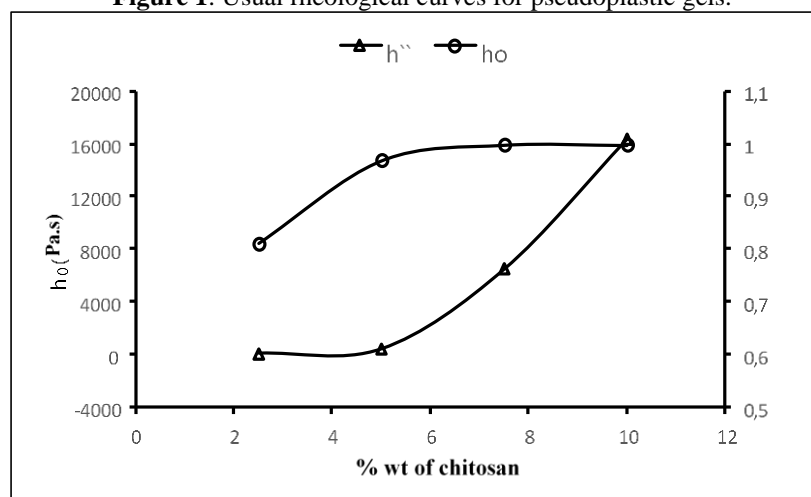


Figure 2. Pseudoplastic character of chitosan gels as a function of chitosan content. (Font: Certbio's Laboratory of Rheology).

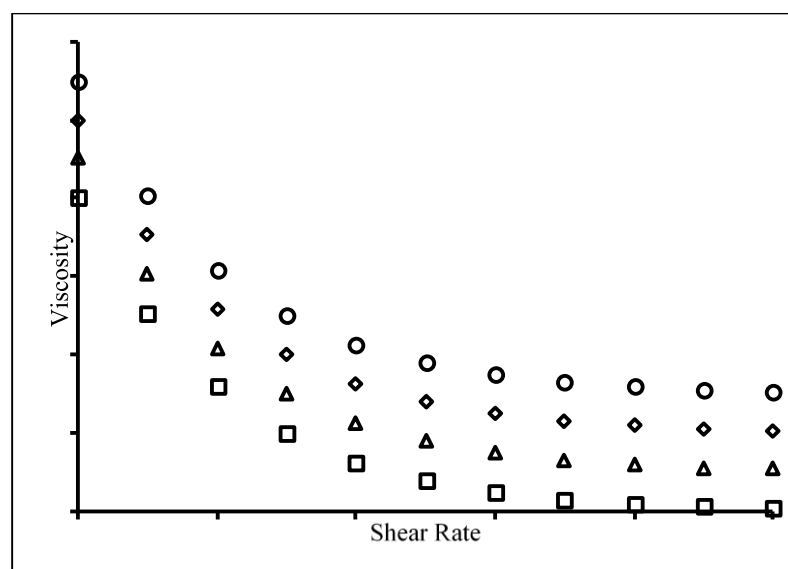


Figure 3. Rheological curves of chitosan hydrogels with certain hydroxy acid with different times of rest (adapted from [5]).

The usefulness of the combination of the chitosan, which has unique properties, with bioactive hydroxyl acids for medical application is still better with the rheological properties showed by obtained gels. The shear rate stability at any dynamic viscosity provides application without change necessity of the apparatus used with others chitosan-based hydrogels and that the injected gel, for example, will be at desired application point.

Rheology of Suspensions

Many important industrial, pharmaceutical and biologic fluids are suspensions that has a fluid as dispersion media and solids particles as dispersed phase. Once solid can be considered a fluid with infinite viscosity, the suspension viscosity is very dependent of the solid content, and, even with infinitesimal content of solids, almost all suspensions show Non-Newtonian behavior. The simplest model for a suspension is the system idealized by Einstein. In this system, solid spherical and rigid particles are dispersed in a Newtonian fluid, forming a very dilute suspension where the volumetric fraction of solids particles, ϕ , tends to zero. It is assumed that there isn't any contact between particles. So, the motion of one particle not depends of the motion of another particle. For this idealized model, the viscosity of the suspension, η_s , is given by

$$\eta_s = \eta_{DM}(1 + 2,5\phi) \quad (5)$$

Where η_{DM} is the dispersion media viscosity.

So, the higher the solid concentration the higher is the suspension viscosity in a monotonic and linear way. But as the solid concentration increases, the probability that arise contact between the particles also increases. Thus the Einsteinian model is rarely useful for most of the existent suspension and there is a necessity to determine the critical point to the solid content from which the suspension can't be considered dilute and becomes concentrated. At this critical concentration, the hydrodynamic motion of the suspended particles is very dependent one another and frequently clusters of particles are formed. As a result, the suspension viscosity increases dramatically. Above critical concentration, several Now-Newtonian behaviors arise and some suspensions do not flow as a simple liquid and some behave as a solid in the limit case. So there is to be stated the maximum content of suspended particles for the suspension still be considered a fluid.

Vinogradov & Malkin [6] proposed that this maximum concentration should be given by

$$\Phi = \frac{2,5\phi}{1 - \frac{\phi}{\varphi}} \quad (6)$$

Where Φ is the maximum concentration and φ is the packaging factor of the particles agglomerate with values between 0,5 and 0,7 and $\phi \rightarrow 0, \Phi \rightarrow 2,5 \phi$ [2].

It is obvious that φ and also Φ depend of the particle's shape. Non-spherical particles will form clusters more easily than spherical ones and its hydrodynamic motion will be more difficult as well. So Φ for a suspension of rodlike particles is lower than that for spherical ones, for example.

In the literature one can find a lot of equations that use the maximum particles content concept [2]. For a suspension with a very dilute polymer solution as dispersion media, the suspension viscosity is given by

$$\eta_s = \eta_{DM} \left(1 - \frac{\phi}{\Phi}\right)^{-[\eta]\Phi} \quad (7)$$

Where $[\eta]$ is the intrinsic viscosity of the polymer in the solution.

Suspensions based on non-spherical particles exhibit non-Newtonian behavior even in very dilute cases. This occurs due de hydrodynamic effects caused by nonsymmetrical form of the particles. In the literature [2], there are a lot of rheological models related to these suspensions. For dilute suspensions of elliptical particles, the Fedors's Model, that uses de maximum charger concept in terms of packaging factor, φ , is the most utilized.

$$\eta_s = \eta_{DM} \left(1 + \frac{1,25\phi}{\varphi - \phi}\right)^2 \quad (8)$$

Rheological Properties of PMMA Based-Cement

Among several rheological properties, polymeric suspensions based on powder spherical particles dispersed in the curable polymers have a complex viscosity that arises with time. In cement-particle systems,

there are two trends. The first one is, of course, the increasing of the complex viscosity (η^*) with time, which can be explained by several common rheological model, as the Krieger-Dougherty equation for concentrated suspensions (eq. 7). Unfortunately, this model just works for Newtonian suspensions. In models like this, is very clear the viscosity dependence with particles diameter and concentration.

In systems containing PMMA, at the initial stage of mixing of the cement (PMMA beads + particles powder) there is an increasing of the viscosity of the system. This increasing is due the swelling of the PMMA beads in the cement powder. As a result, as the time of mixing increases, the maximum packing fraction of the particles powder and the intrinsic viscosity of the fluid medium are decreased.

By the way, the second trend shows an uncommon [7]. The measured complex viscosity of this system is extremely higher the those expected for similar systems.

As preconized in the literature, there is an inverse relationship between the maximum temperature of curing (T_C^M) of cement and the polymeric matrix beads overall mean diameter (D_{bom}). So, there was expected that the PMMA + powder system with low D_{bom} should have high MTC but low value for time at the onset of the cement cure (t_{oc}). It was a very important problem during bone implant procedure.

Why the problem above mentioned occurs? During curing procedure, the small polymeric beads are completely dissolved by the liquid monomer that are not still polymerized and that the biggest ones survive for much time in the mixing processing. By this point of view, the higher proportion of polymeric matrix beads of small diameter (d_{sz}) ($0 < d < 40\mu m$) in the powder the higher the cement MTC, and that the higher proportion of polymeric matrix beads of big diameter (d_{bz}) ($d > 75\mu m$) the higher is the T_C^M .

As the results obtained by [7] are very statistically significant, so it can be understand that a cement's rheological properties during curing should be based on d_{sz} and d_{bz} than as were made by D_{bom} .

So, it has to be developed a correct method to manipulating the cement powder particle size distribution in order to obtain the optimum rheological behavior of the polymeric dough including the maximum curing temperature and complex viscosity.

Rheology of Blood

Ordinary fluids and elastic solids obey universal laws, namely Navier-Stokes and Hooke-Lamé laws. Contrariwise, complex fluids still continue to escape a universal description (if any). Complex fluids are ubiquitous in nature.

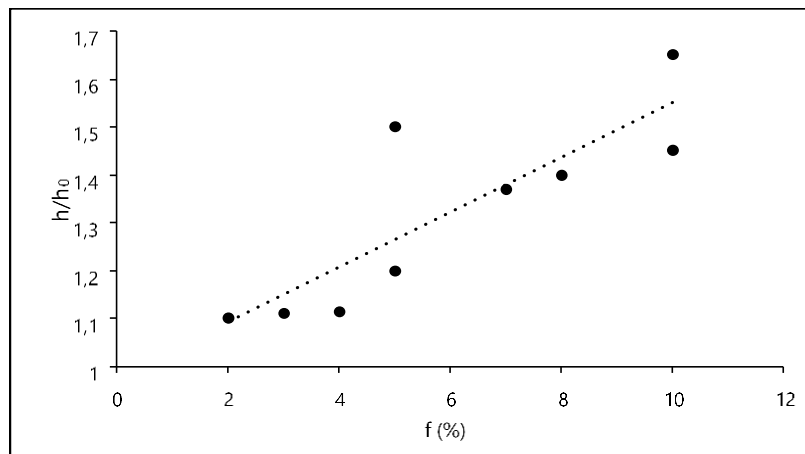


Figure 4. Viscosity (relative to solvent viscosity) vs volume fraction for suspensions of red blood cells in phosphate buffer saline buffer. (adapted from [8])

Normal blood is a prominent example of a complex fluid and consists of highly deformable particles (red blood cells (RBC) or erythrocytes), white blood cells (leukocytes), and platelets suspended in aqueous Newtonian solution of proteins and salts (plasma). As the other particulate constituents of blood (white blood cells and platelets) usually occupy only less than 1% of the total volume of blood cells in normal human blood, thus the RBC govern the flow properties of blood. Freely suspended, without external stress, a mature human red cell normally takes the form of a "biconcave" disk, about $8\mu m$ in diameter and $2\mu m$ thick, with a concavity in each face. It has no nucleus, and its interior is filled with a concentrated hemoglobin solution, an incompressible viscous fluid. This is surrounded by a flexible viscoelastic membrane, which consists of a lipid bilayer and a cytoskeleton (a network of protein molecules adjacent to and projecting through the bilayer) [9]. In blood, the RBC move and deform over time scales during flow, so the macroscopic constitutive law should carry information on the dynamics of the suspended entities, even if the law is averaged.

Blood in Capillary Flow

Vitkova et al [8] studied several red blood cells suspensions and do not observed a non-linear relationship between suspension relative viscosity and blood cells for concentrations up to 10% (see Figure 4), which is an unexpected result due the suspension behaved as a one of the rigid spherical particles even though the red blood cells don't be spherical but elliptical. The behavior expected is similar to that shown in Figure 2). This occurs due the particles to orients steadily itself in parallel to the flow direction like vesicles suspension. So, its hydrodynamic effect is not as high as expected for common elliptical particles suspended in a Newtonian fluid. the rheology of RBC suspension can be described by vesicle theory even though it is a simpler object, which seems to capture the essence of RBC dynamics under flow, as far as rheology is concerned. On the other hand, in [10] it can be seen that blood disorders strongly affect the deformability of erythrocytes as well as their dynamics in the blood stream leading in some cases to dramatic physiological consequences for the organism. It is known that some diseases (ex. anemia) and social behavior (ex. chronic alcoholism) modify the mechanical and rheological behavior of the blood. Since the rheological measurements are sensitive to the physical properties of the cells, they can be used to capture pathological deviations in the shape, the reduced volume, and/or rigidity of cells by such macroscopic assay of suspension rheology.

As seen before, RBC are non-spherical and deformable particles that flow in veins, arteries and capillaries. Capillaries are the smallest and most numerous blood vessels in the circulatory system, with diameters ranging from about 3 μm to 10 μm in mammals. Since the diameter of a freely suspended RBC exceeds the diameter of many capillaries, red cells must undergo large deformations in order to pass through capillaries. Nonetheless, red cells pass through even very small capillaries with relative ease, as a result of the fluid nature of their interiors and the flexibility of their membranes [9].

Observed red blood cell shapes in capillaries are generally not axisymmetric. The question arises whether departures from axisymmetry significantly affect rheological parameters such as apparent viscosity given by Eq. 9 (see Figure 5). If the cell is not symmetric, asymmetric external fluid forces are generated. Since the cell has a fluid interior and a flexible membrane, these forces can drive a continuous motion of the membrane around the cell. This phenomenon, known as tank treading, was observed in capillary tubes [11,12].

$$\eta = \eta_{DM}(1 + K_T H_T) \quad (9)$$

Where, K_T is the apparent intrinsic viscosity of blood in cylindrical tubes with near-minimal diameters, H_T is the local tube hematocrit in capillaries.

In capillaries, red blood cells often flow in single file, particularly if the diameter is about 6 μm or less. In such cases, it is reasonable to neglect interactions between red cells and to obtain estimates of rheological parameters by analyzing the motion and deformation of an individual red cell and the surrounding plasma in a capillary. In an excellent review, Secomb [9] presents several reasons for this remarkable behavior of RBC.

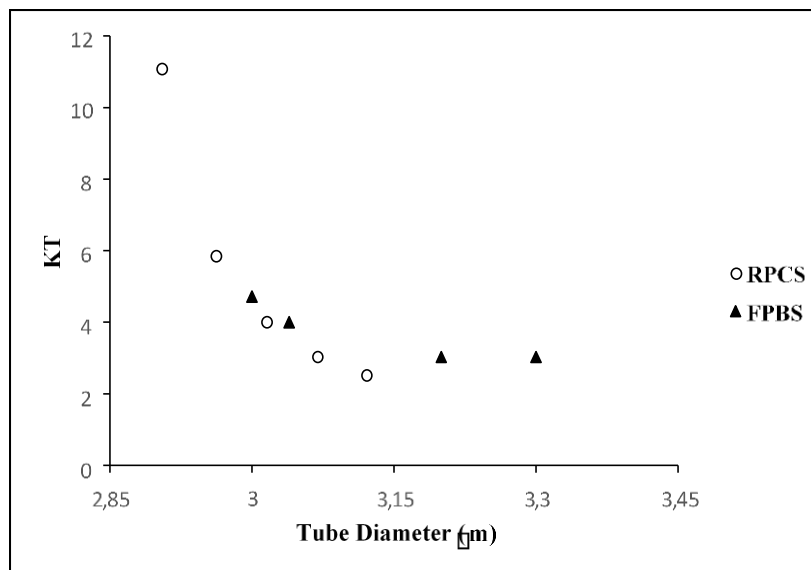


Figure 5. K_T as a function of tube diameter. Cell velocity is 0.01 cm/s. (RPCS = rigid particle with critical shape, and FPBS = flexible particle with bending and shear) Adapted from [9]).

For single-file flow of red cells, axisymmetric models using lubrication theory yield predictions of the apparent viscosity of blood that are in reasonable agreement with available experimental data from measurements made in glass tubes with appropriate diameters. Except at very low flow velocities, the apparent viscosity of blood in capillaries is substantially lower than the bulk viscosity of blood. Observed red cell shapes are not axisymmetric, and cell asymmetry results in tank-treading motion of the cell membrane around the cell. However, cell asymmetry and tank-treading have little influence on apparent viscosity in single file flow and in two-file zipper-type flow. Thus, once a RBC has entered a capillary, its ability to deform continuously in tank-treading motion seems to be of secondary importance. However, red cell deformability is, of course, essential to enable the cells to enter capillaries of $8\mu\text{m}$ or smaller diameter in the first place. Also, cells must be deformable in order to negotiate the diameter changes and other irregularities they encounter as they move along real capillaries in vivo [9].

Blood Flow in Large Arteries

The arterial blood flow is more complex than capillary one. The arterial blood flow in the human body is typically a multiphase non-Newtonian pulsatile flow in a tapered elastic duct with the terminal side and/or small branches. The pulsatile flow is an unsteady flow in which resultant flow is composed of a mean and a periodically varying time dependent component. Pulsatile flow is responsible for submissive effect on time-dependent viscoelastic and thixotropy behavior of blood [13]. The aggregatable and deformable nature of the red RBCs plays significant roles in blood rheology. RBC aggregation causes a large increase in viscosity at low shear rates. The size of RBC aggregation is a function of RBC concentration and shear rate [14]. The existence of aggregation also depends on the presence of fibrinogen and globulin proteins in plasma [15]. When shear rate tends to zero, RBCs become one big aggregate, which then behaves like a solid. As the shear rate increases, RBCs aggregates tend to be broken up and the structure becomes a suspension of a cluster of RBCs aggregates in plasma. These aggregates are in turn formed from smaller units called rouleaux as shown in Figure 6. As the shear rate more increases, the average number of RBCs in each rouleaux decreases. If the shear rate is larger than a certain critical value, the rouleaux are broken up into individual cells. At subcritical shear rates, the RBCs in each rouleaux maintain their rest-state equilibrium shape, biconcave discoid shape. If the shear rate is supercritical, the RBCs are dispersed in plasma separately and tend to become elongated and line up with the streamlines [16].

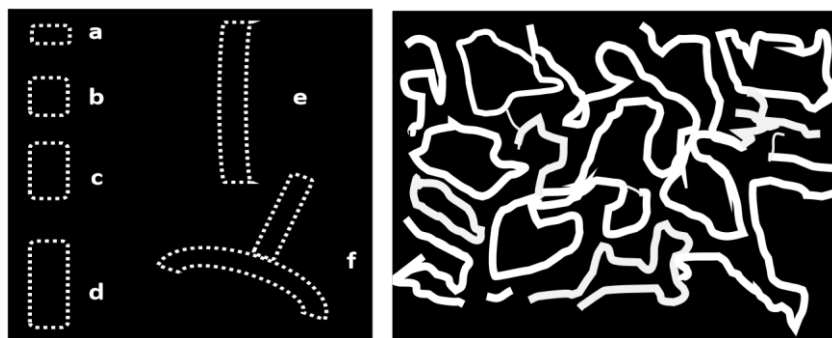


Figure 6. Rouleaux of human red cells in an idealized form showing single linear and branched aggregates (left part) and a network (right part). The number of cells in linear array are 2, 4, 9, 15, and 36 in a, b, c, d, f, respectively. Adapted from [15].

The studies related with RBC behaviors in the microcirculation, in the venous and in the general have shown that the mechanisms of RBC aggregation are figured out by the balance of aggregation and disaggregation force. Disaggregation forces mainly consist of mechanical shear force, repulsive force, and elastic energy of RBC membrane. However, the mechanism of aggregation force is unclear. As mentioned in Baumler et al [17], the bridging, due to the adsorption of macromolecules onto adjacent cell surfaces, and the depletion, due to the osmotic gradient arising from the exclusion of macromolecules near the cell surface, molecular models are presently used to describe aggregation behaviors [13].

It can be easily understanding from the studies directed on the structure of blood that the blood viscosity is dependent on the physiological flow conditions of blood and the blood composition properties such as hematocrit, temperature, shear rate, cell aggregation, cell shape, cell deformation and orientation. In a critical and large review, Yamaz & Gundogdu [13] present several viscosity models relating to blood viscosity, 28 for relative viscosity based on concentration dependence of dispersions and 13 time-independent non-Newtonian viscosity models. Unfortunately, none of these models works with desired efficacy, once the effects of cell aggregation, cell shape, cell deformation, and cell orientation have not clearly reflected in these models, although these models considers the effects of hematocrit or cell concentration, shear rate, and temperature. However, numerical studies

on RBC behaviors give a hope for transferring available knowledge of microscopic hemodynamic and hemorheological behaviors to a blood viscosity model. In spite of there is a large number of studies on both Newtonian and non-Newtonian blood viscosity models in literature, there have been a variation on the critical value of limiting shear rate used for addressing the transition from non-Newtonian to Newtonian viscosity character of blood. Hematocrit dependence of this limiting shear rate value should be investigated for evaluating the proper application of both non-Newtonian to Newtonian viscosity models in studies on blood flow.

Temperature Effect on Viscosity

The viscosity, μ , of materials is markedly affected by the effects of temperature variation, and can vary by up to 10% for a simple variation of 1°C in temperature. While low-density gases increase in viscosity with increasing temperature, most liquids' viscosity drops exponentially with increasing temperature. For this type of fluid, the most common way to represent the dependence $\mu(T)$ is through an Arrhenius-type equation, as proposed by Eyring for Newtonian fluids [2]:

$$\mu(T) = A * \exp\left(\frac{\bar{E}}{RT}\right) \quad (10)$$

where μ is Newtonian or absolute viscosity, R is the gas constant, T is the temperature in K , \bar{E} is the activation energy of the viscous flow, and A is a constant.

Viscous Flow Activation Energy

The energy \bar{E} indicates that there is a barrier to be overcome for viscous flow to occur. Thus, it constitutes the main quantity to be determined for the measurement of $\mu(T)$. The WLF model, known as the Williams, Landel & Ferry equation, assumes a constant value for E for any fluid at high temperatures. For polymers at these temperatures, however, \bar{E} takes on different values for each polymer under consideration and strongly depends on the composition of the polymer chain and its ramifications [18]. As for the side groups or branches, \bar{E} can grow markedly with the molar volume of the small branches attached to the main chain, except in the case of poly-1-olefins for which there is a critical value for this molar volume, from which \bar{E} or remains constant or falls with future increases in molar volume.

For low molecular weight materials, \bar{E} , increases with their melting temperature, T_m , due to molecular interrelationships that make the relative motion of the fluid layers more difficult. However, for some polyolefins, \bar{E} may fall with increasing T_m . Due to the various controversial behaviors in the relation $\bar{E}(T)$, other theories began to be developed to better configure the dependence $\mu(T)$ [2].

Wang & Porter Theory

For simple fluids, Dootile [2] proposed

$$\mu(T) = C \exp\left(\frac{B \cdot V_0}{V - V_0}\right) \quad (11)$$

where C and B are empirical constants ($B \sim 1.0$), V is the observed specific volume and V_0 is the specific volume for the state of free volume equal to zero. Eq. 11 is consistent with the fact that molecular transport only occurs when local micro voids exceed a certain critical volume. If f is a temperature-dependent fractional free volume and given by

$$f = \frac{V - V_0}{V} \cong \frac{V - V_0}{V_0} \quad (12)$$

the Eq. 11 takes the following form

$$\mu(T) = C \exp\left(\frac{B}{f}\right) \quad (13)$$

in $T = T_g$

$$f(T_g) = f_g = \alpha_L \cdot T_g = 0.164$$

For a temperature T_2 , at which the dependence $f(T)$ is more acute than at absolute zero, Ferry (1980) proposes

$$f_g = \alpha_L \cdot (T - T_2)$$

so, Eq. 11 becomes

$$\mu(T) = C \exp \left(\frac{B}{\alpha_L \cdot (T - T_2)} \right) \quad (14)$$

Vogel [2] proposed a similar relationship for $\mu(T)$

$$\mu(T) = K \exp \left(\frac{D}{(T - T_0)} \right) \quad (15)$$

where D , K and T_0 are three parameters that should be used to fit experimental data.

If Eq. 14 is differentiated in relation to $1/T$, we obtain \bar{E} related to linear thermal expansion coefficient, α_L , and T_2 , that is,

$$\bar{E} = R \frac{d \ln \mu}{d(1/T)} = \frac{R \cdot B}{\alpha_L \left(1 - \frac{T_2}{T} \right)^2} \quad (16)$$

where T_3 is the temperature at which $f = 0$. Experimentally, it was determined that $T_3 = \beta T_g$, with β assuming a constant value equal to 0.77 regardless of whether there is variation in the molecular weight, structure and polarity of the polymer.

Defining \bar{E}_c as \bar{E} at a temperature $T > T_g = 150^\circ\text{C}$, with $B \sim 1.0$, then

$$\bar{E}_c = \frac{R}{\alpha_L} \left(\frac{T_g + 150}{0.23 T_g + 150} \right)^2 \quad (17)$$

The WLF Equation

Some polymers become unstable between $T > T_g + 100^\circ\text{C}$. In this case, the theory of Wang & Porter cannot be used, and equations such as the WLF (eq. 18) which is based on the theory of free volume are more recommended.

$$\log \frac{\mu(T)}{\mu(T_R)} = \log a_T = \frac{C_1(T - T_R)}{C_2((T - T_R))} \quad (18)$$

where C_1 and C_2 are constants, T_R a reference temperature and a_T a coefficient called the displacement factor.

According to Ferry [19], if T_g is taken as the reference temperature, the constants C_1 and C_2 assume universal values equal to -17.44 and 51.6, respectively. A few polymers have different values from these, so that Eq. 18 can safely be used to calculate the dependence $\mu(T)$, especially those whose graphical form is shown in Fig. 7. In general, the results presented by the various models for $\mu(T)$ are quite similar, but most researchers have given preference to the WLF (Eq. 18) and Vogel (Eq. 15) equations.

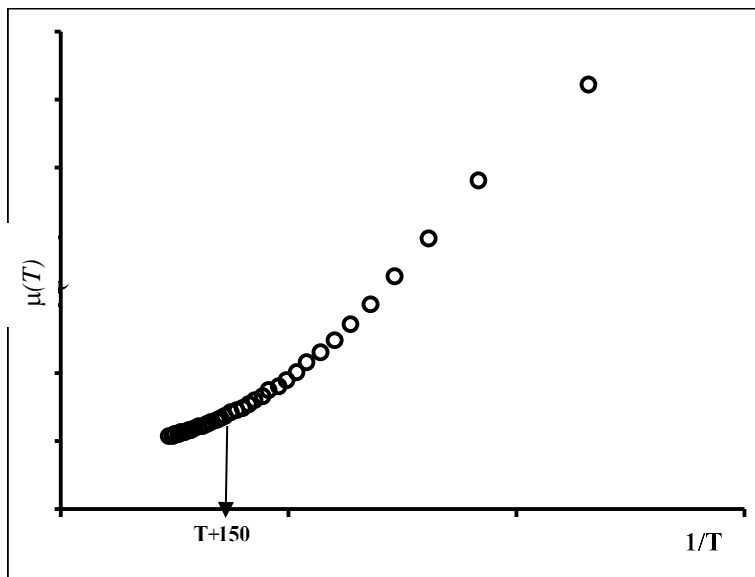


Figure 7. $\mu(T)$ dependence fitting with WLF equation.

Effect of Temperature on the Viscosity of Calcium Phosphate Paste

Due to population ageing, osteoporosis is becoming one of the severe medical problems. Osteoporosis leads to a remarkable increase of the incidence of bone fracture. The traditional operation with large surgical wound is being changed to the minimal invasive surgery. It has been showed that using minimally invasive bone cement injection for stabilizing osteoporosis or treating vertebral body fracture has significant clinical potential. Furthermore, with the development of noninvasive approaches such as percutaneous surgery, directly injectable biomaterials are in need. Calcium phosphate-based bone cement has been regarded as a promising material for bone defect repair because of its good biocompatibility, excellent bioactivity, self-setting characteristics, low setting temperature, adequate stiffness and shapeable for any complicated geometry [20].

As shown in Figure 8, with increasing of temperature the viscosity of the calcium phosphate paste increased significantly. This unusual behavior is because the dissolution-precipitation process is accelerated when temperature increase [21]. Note that in Figure 7, the viscosity is plotted against $1/T$. The viscosity changed just a little during hydration at room temperature or below (25°C and 20°C), and the viscosity increased quickly during hydration when the ambient temperature was higher (30°C and 35°C). This indicates that the pastes of the calcium phosphate paste can be prepared at room temperature with good fluidity for injection and, after injected into body, it will harden and become stiff in a short while. This performance makes it convenient for clinical applications.

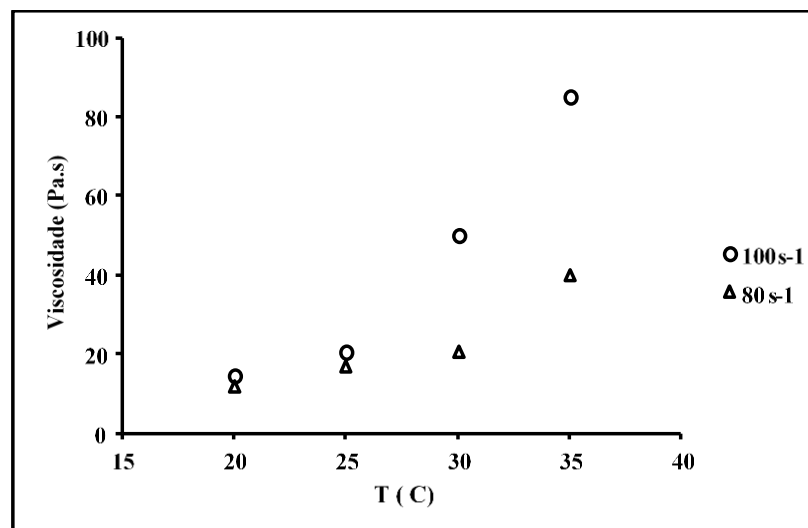


Figure 8. Effect of temperature on the viscosity of a paste of calcium phosphate with de-ionized water at a liquid/particle ratio of 0.5 ml/g. Adapted from [20].

Thixotropy

Thixotropy is a non-Newtonian time-dependent phenomenon characterized by a decreasing in the apparent viscosity of the material with time of application of a constant shear rate. This isothermal and reversible phenomenon is common to systems with a liquid, as a dispersion media, and a solid, as a dispersed phase and occurs due to the gradual destruction of some structure that has been created by the attraction of the particles of the dispersed phase and whose binding force does not resist the action of the imposed shear. This phenomenon is considered reversible because the structure is reconstructed after the imposed shear is removed [22].

The bond reconstruction process is slower than the destruction process, therefore, it takes a longer time for the initial apparent viscosity to be recovered. This time, called thixotropic relaxation time, τ , will be longer the longer the application time and the magnitude of the imposed shear.

Since the initial apparent viscosity of the fluid-solid system depends on the solid content, as seen in the Suspension Rheology section, there will be a greater number of structural bonds to be broken with increasing solids content. A greater number of bonds capable of being broken increases the thixotropic character of the system, as proposed by the Vinogradov & Malkin Structural Theory of Thixotropy (Navarro, 1997). Thus, the greater the concentration of solid particles, the greater the apparent viscosity of the system and the greater the drop from the resting value to a given time under the action of a constant shear rate.

If the degree of thixotropy is taken to be the difference between the initial apparent viscosity and viscosity at a given time of application of shear, normally a time after which there is no further change in apparent viscosity, called the stabilization time, a model as proposed at [23], see Eq. 19, can be used to adjust the dependence $\eta(t)$.

$$\eta(t) = a \cdot e^{-(t/\tau)} + \eta_{final} \quad (19)$$

Where η_{final} is the apparent viscosity of the system at the stabilization time.

By the Vinogradov & Malkin theory and rheological model like Eq. 19, as the solid content in a dispersed system is increased the system becomes more viscous and presented bigger thixotropic character. So the difference $\eta_0 - \eta_{final}$ tends to η_0 [24].

Suspension of Hydroxyapatite

Hydroxyapatite (HA or HAP) of biologic (coral, bovine or marine algaederived) or synthetic origin are currently used for bone repair and bone regeneration in the form of granules, blocks and scaffolds, by itself or as composite with polymers or other ceramics or as coatings on orthopedic or dental implants. They are commercially available for use in bone repair, substitution, and augmentation and as scaffolds in tissue engineering for bone regeneration. The rationale for its development as a bone substitute material is its similarity in composition to the bone mineral. HA is also used as abrasives to roughen metal implant surfaces and as source material for depositing bioactive coatings on orthopedic and dental implants. These materials can also be used as transfection agents, drug carriers, and percutaneous devices. HA- or HAP-based biomaterials with improved properties included substituted apatites [25].

Studies with hydroxyapatite suspensions containing dispersant [26] showed suspensions with higher apparent viscosity for higher solids contents, like most suspensions, but the apparent viscosity growth with solids content, although following the model proposed in Eq. 7, was higher in suspensions with higher concentration of dispersant. All suspensions studied showed anti-thixotropy. Those behaviors are completely contrary to that proposed in several works in the literature, in which the common behavior is thixotropy, whose character increases as the particles are more agglomerated at rest. The function of the dispersant is to keep particles away and thus lessen the impact of increasing solids content in the suspension. Navarro & Alsina [27] identified the time-independent, pseudoplastic behavior, and time-dependent, anti-thixotropy behavior, in alumina suspensions in PDMS. As observed in [26], suspensions have their apparent viscosity increased with application time of a given shear rate (anti-thixotropic behavior). However, upon reaching equilibrium, that is, when the apparent viscosity no longer varies with time at that shear rate, an increase in the shear rate causes an immediate decrease in the apparent viscosity (pseudoplastic behavior). This leads to the assumption that structures formed by the dispersed particles during application of shear rate do not withstand future increases in shear rate. Thus, the apparent viscosity of the suspension increases with time and decreases with shear rate.

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