Computation of the Coefficients of the Power law model for Whole Blood and Their Correlation with Blood Parameters

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Abstract

This study introduces a quantitative analysis of the coefficients of the power law model, which is used to describe the non-Newtonian behavior of blood. Twenty blood samples from healthy donors were used to measure the whole blood viscosity under different values of the shear rates, which are between 2.25 and 450.0 s^{-1}. The shear rate viscosity curves were used to calculate n (flow index) and m (the consistency of the fluid) according to the power law model. Strong correlations ($R^2 > 0.5$) between m and the hematocrit (HCT %), hemoglobin (Hb), erythrocytes count (RBC), mean corpuscle volume (MCV), and mean corpuscle hemoglobin concentration (MCHC) were obtained. Strong correlations ($R^2 > 0.5$) between n and the RBC, MCV, and MCHC were achieved. The relation obtained between the power law coefficients and the blood parameters in the present investigation provides new parameters that can be used to evaluate the flow state of blood besides blood viscosity. In addition, these parameters may be used to examine blood under pathological conditions, representing a new tool for the diagnosis of blood abnormal conditions.

Keywords: Blood, Viscosity, Power law, HCT, Hb, RBC, MCV, MCHC

1. Introduction

Blood is a heterogeneous multi-phase mixture of solid corpuscles (red blood cells, white blood cells, and platelets) suspended in liquid plasma, which is an aqueous solution of proteins, organic molecules, and minerals. The rheological characteristics of blood are determined by the properties of these components and their interaction with each other as well as with the surrounding structures. Blood rheology is also affected by external physical conditions, such as temperature; however, in living organisms, in general, and in large mammals, in particular, these conditions are regulated, and hence, they are subject to minor variations that cannot significantly affect the general properties (Bodnar, 2011). Other physical properties, such as the mass density, may also play a role in determining the overall blood rheological conduct. The rheological properties of blood and blood vessels are affected by the intake of fluids, nutrients, and medications, although in most cases, these effects are not substantial, except possibly over short periods of time, and normally do not have lasting consequence (Breithaupt-Grogler et al., 1997; Vlastos et al., 2003; Marcinkowska Gapinska et al., 2007; Tripette et al., 2010).

Plasma behaves as a Newtonian fluid, whereas whole blood has non-Newtonian properties. In large vessels, where shear the rates are high, it is reasonable to assume that blood has a constant viscosity and a Newtonian behavior. However, in smaller vessels, or in some disease conditions, the presence of cell induces a low shear rate and whole blood exhibits remarkable non-Newtonian characteristics, such as shear-thinning viscosity, thixotropy, viscoelasticity and possibly a yield stress. This is largely due to the behavior of RBCs, namely, their ability to aggregate into microstructures (*rouleau*) at low shear rates, their deformability into an infinite variety of shapes without changing volume and their tendency to align with the flow field at high shear rates (Chien et al., 1970; Schmid-Schöenbein & Wells, 1969). An understanding of the coupling between the blood composition and the physical properties of blood is essential to develop suitable constitutive models to describe blood behavior (see the recent reviews) (Robertson et al., 2009; Robertson et al., 2008).

Many models have been developed to describe blood viscosity. One of the most widely used forms of the general non-Newtonian constitutive relation is a power-law model, which can be described as (Bird et al., 1987):

$$\tau = m\gamma^n \tag{1}$$

Where τ is shear stress, γ is shear rate and m, n are power-law model constants. The constant m is a measure of the consistency of the fluid: the higher the value of m, the more viscous the fluid is. n is a measure of the degree of non-Newtonian behavior: the greater the departure from the unity, the more pronounced the non-Newtonian properties of the fluid are. Viscosity for the power-law fluid can be expressed as (Bird R B. et al., 1987):

$$\eta = m\gamma^{n-1} \tag{2}$$

where η is the non-Newtonian apparent viscosity. If $n < 1$, then a shear thinning fluid is obtained; such a fluid is characterized by a progressively decreasing apparent viscosity with an increasing shear rate (Bird et al., 1987).

The present work aims to compute n and m for whole blood and test their relationship with the physiological properties of blood. In addition, this work explores whether these power-law model constants reflect the state of the internal structure and the interaction between blood contents.

2. Materials and Method

2.1 Sample Collection

Twenty blood samples were collected from donors of the same age and gender. All blood samples were collected after overnight fasting in a quiet environment at normal ambient temperature. Blood was withdrawn after a 10 minute resting period and in a seated position. Blood was collected from the antecubital vein 90 s after application of a tourniquet and without removing it to avoid the effect of pressure on the blood samples (Baskurt et al., 2009). EDTA (1.5 mg/ml) was used as an anticoagulant. Two milliliters from each sample was sent to the clinical laboratory to measure the hematocrit (HCT %), hemoglobin (Hb), erythrocytes count (RBC), mean corpuscle volume (MCV), and mean corpuscle hemoglobin concentration (MCHC) using a hematology auto analyzer.

2.2 Blood Viscosity Measurement

Viscosity measurements were performed at 37 ℃ using a rotational viscometer fitted with a small sample cup and a temperature controller (Brookfield Digital LVTD viscometer). The viscometer was calibrated according to the manufacturer's explicit, step-by-step instructions. Proper calibration and operation were verified through the measurement of the viscosity of the standard solution for both Newtonian and non-Newtonian fluids.

The viscosities were measured at the different shear rates specified on a Brookfield viscometer: 2.25, 4.50, 11.25, 22.5, 45.0, 90.0, 225.0 and 450.0 sec^{-1}. A volume of 0.5 ml of a whole blood sample was added to the viscometer. For each test, the measurement was repeated ten times, and then, the average of the readings was taken. Each test was performed on a new sample. The cone, cup, and spindle assembly were rinsed and carefully dried between each trial.

2.3 Power Law Model's Coefficient Calculations

The relationship between $\log \eta$ and $\log \gamma$ was a straight line according to the power law model. $\log \eta$ was the y-axis and $\log \gamma$ was the x-axis. n and m were calculated graphically. n was calculated from the slope of the line ($slope = n - 1$). m was calculated from the intercept of the line with the y-axis ($\log m = intercept\ from\ y - axis$). Microsoft Excel 2010 was used to calculate both n and m. Linear regression was used after the relationship between $\log \eta$ and $\log \gamma$ was plotted. The equation of the linear trend line was used to compute n and m, as mentioned above.

2.4 Statistical Analysis

The results are presented as the mean ± SD unless otherwise noted. Correlations were made using Pearson's coefficient. Pearson's R^2 can range from -1 to 1. A R^2 of -1 indicates a perfect negative linear relationship between variables, a R^2 of 0 indicates no linear relationship between variables, and a R^2 of 1 indicates a perfect positive linear relationship between variables. The data within each group were analyzed using Microsoft Excel 2010.

3. Results

The viscosity data revealed the non-Newtonian behavior of normal human blood over the given range of shear rates (Figure 1). Shear thinning of whole blood was viewed through the relationship between η and γ (Figure 1). A sharp decrease in η was observed between 2.25 and 450.0 sec^{-1}. The measured values of η were 12.5 mPa.s at a low shear rate (2.25 sec^{-1}), 4.89 mPa.s at 45 sec^{-1}, and 2.38 mPa.s at a high shear rate (450.0 sec^{-1}).

The logarithmic relationship between η and γ was represented as a straight line that intercepted the y-axis (Figure 2). This relation was used to compute the values of m and n. n was in the range of 0.7163 ± 0.00145 to 0.6672 ± 0.00178, and m was in the range of 16.24 ± 0.0064 mPa.s^n to 16.101 ± 0.003 mPa.s^n

n was found to be strongly correlated with RBC and MCV ($R^2>0.5$). A positive correlation was indicated for the relationship between n and RBC. By contrast, negative correlations were indicated for the relation between n and HTC and MCV (Figure 3). A moderate positive correlation was found between n and MCHC ($R^2=0.5$). A positive weak correlation was found between n and Hb ($R^2<0.5$). By contrast, a negative weak correlation was found between n and HTC (Figure 3).

m was strongly correlated to RBC, Hb, HCT, MCV, and MCHC ($R^2>0.5$). The relationships between n and the RBC, Hb, and MCHC were inversely proportional, whereas n and HCT and MCV were directly proportional.
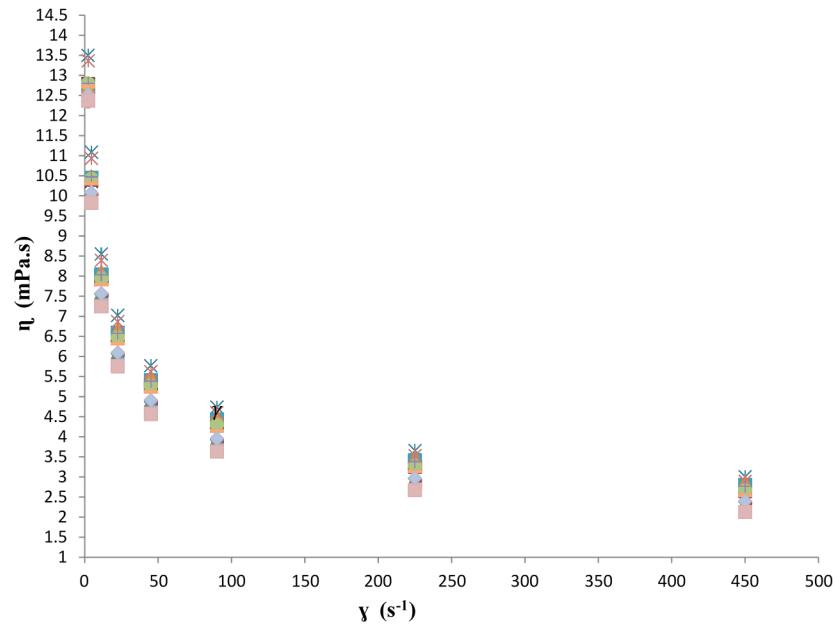

Figure 1. Whole blood viscosity as a function of the shear rate shows non-Newtonian behavior. Whole blood shear thinning over the range of shear rates from 2.25 to 450 sec^{-1}
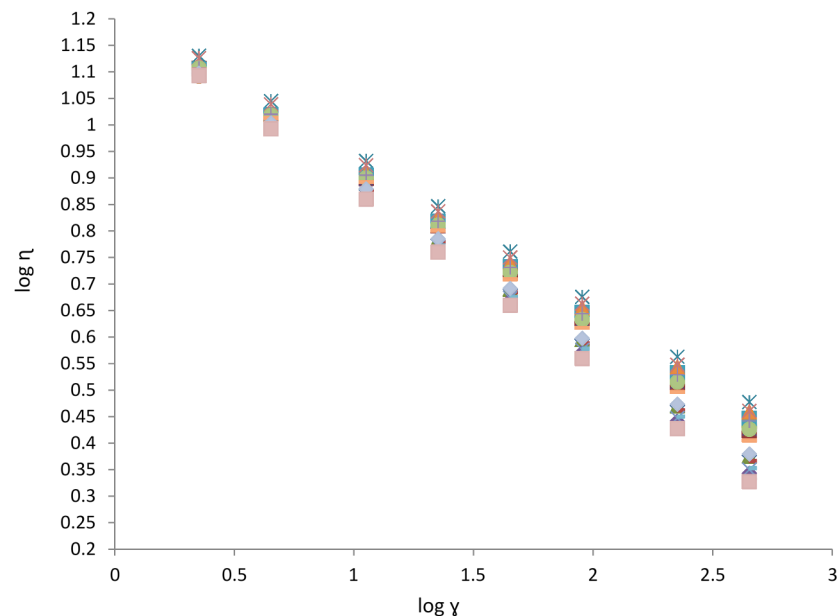

Figure 2. The logarithmic relationship between viscosity and the shear rate shows a high degree of linearity. The intercept with the y-axis is used to calculate m, and the slope of the line is used to calculate n
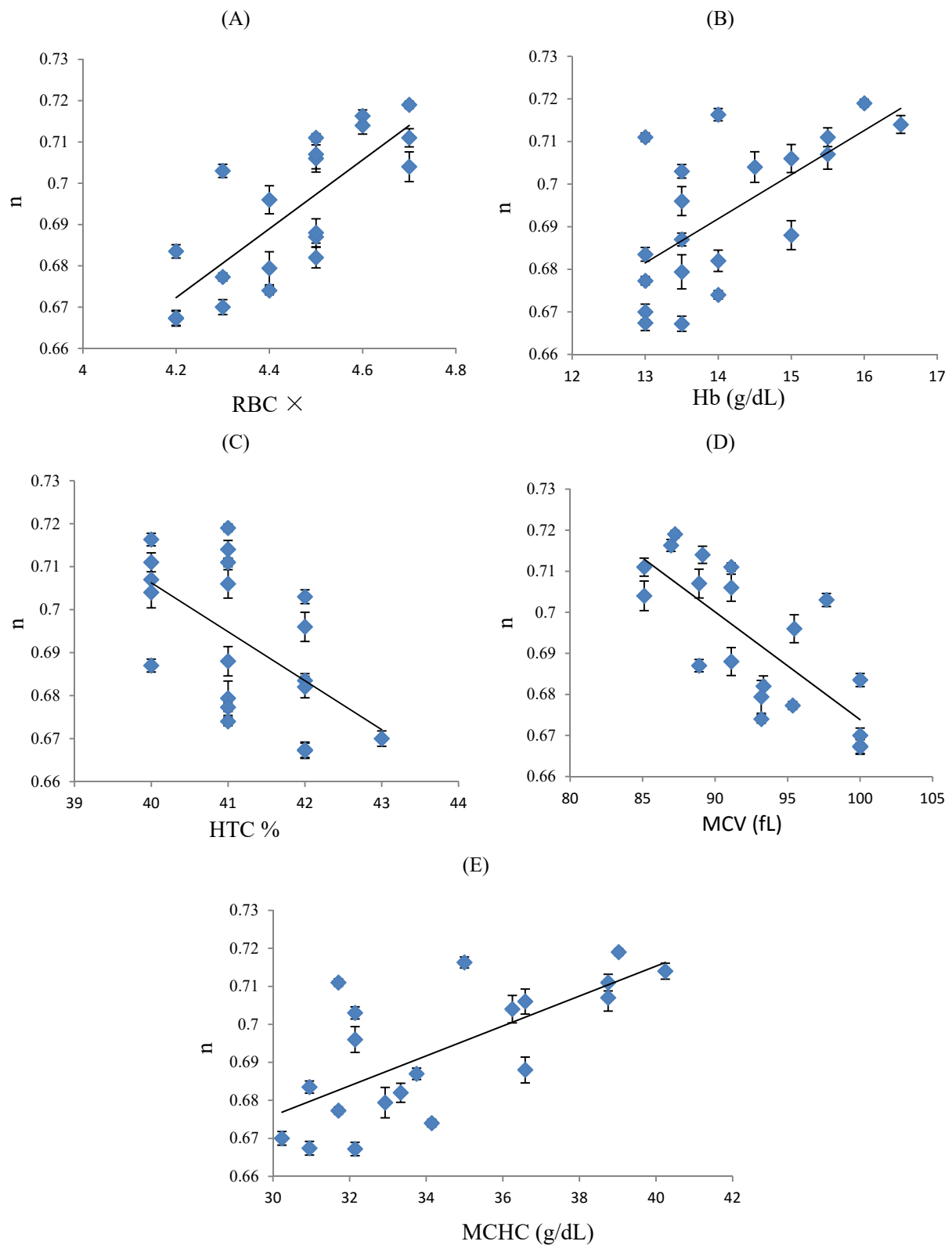
Figure 3. n correlates to some blood parameters. (A) The equation for the relationship between n and the RBC count is $n = 0.0834 \times RBC + 0.3218$ and $R^2 = 0.61$. (B) The equation for the relationship between n and Hb is $n = 0.0104 \times Hb + 0.5468$ and $R^2 = 0.42$. (C) The equation for the relationship between n and HTC is $n = -0.0114 \times HTC + 1.1617$ and $R^2 = 0.32$. (D) The equation for the relationship between n and MCV is $n = -0.0026 \times MCV + 0.9362$ and $R^2 = 0.6$. (E) The equation for the relationship between n and MCHC is $n = 0.0039 \times MCHC + 0.5579$ and $R^2 = 0.5$
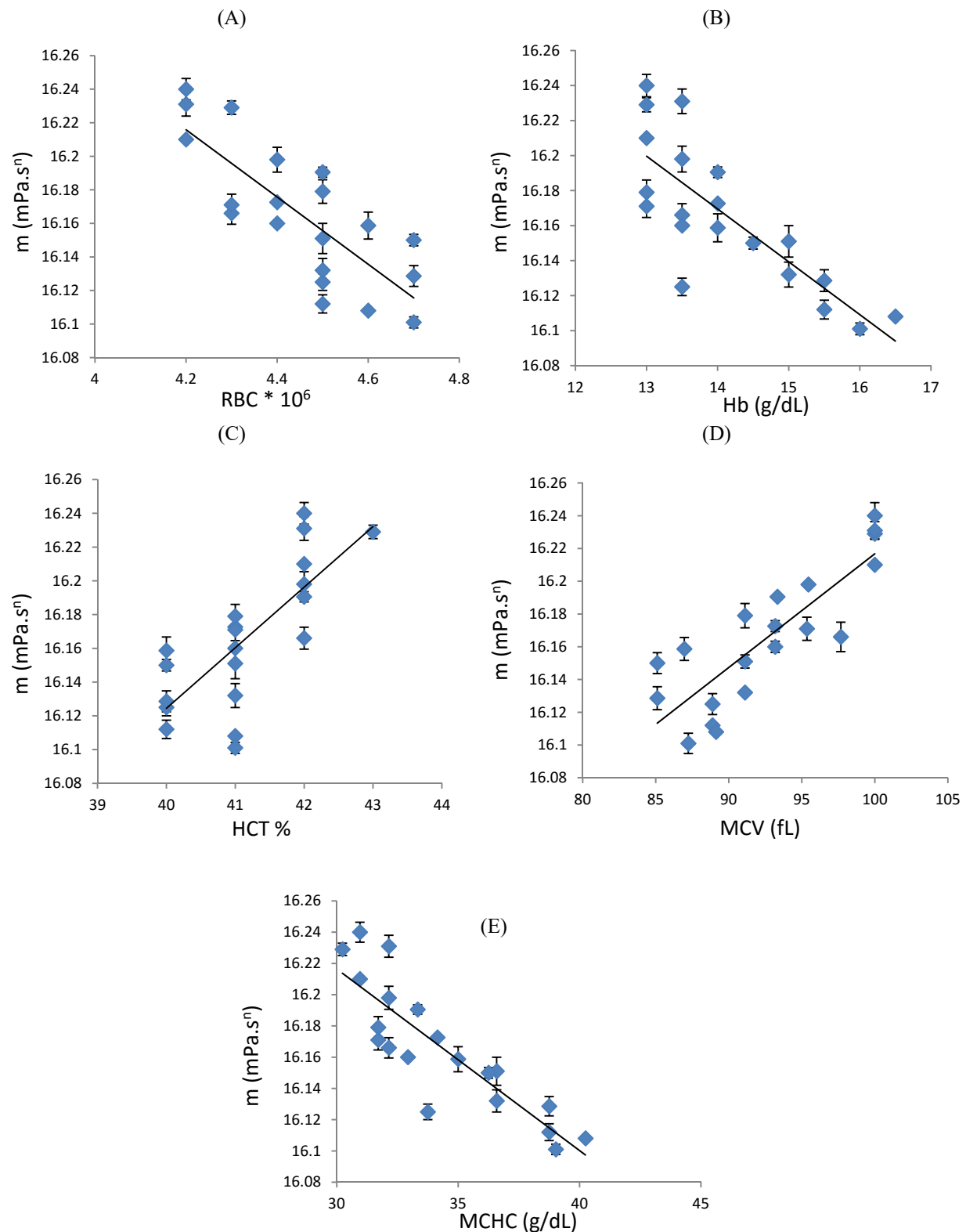
Figure 4. Correlation of *m* to some blood parameters. (A) The equation for the relationship between *m* and the RBC count is $m = -0.2006 \times RBC + 17.058$ and $R^2 = 0.63$. (B) The equation for the relationship between *m* and Hb is $m = -0.0302 \times Hb + 16.592$ and $R^2 = 0.64$. (C) The equation for the relationship between *m* and HTC is $m = 0.0359 \times HTC + 14.689$ and $R^2 = 0.6$. (D) The equation for the relationship between *m* and MCV is $m = 0.0069 \times MCV + 15.522$ and $R^2 = 0.71$. (E) The equation for the relationship between *m* and MCHC is $m = -0.0116 \times MCHC + 16.565$ and $R^2 = 0.75$

4. Discussion

Blood has previously been indicated to be a non-Newtonian fluid and exhibits a complex rheological behavior, such as shear-thinning viscosity and thixotropy, primarily due to the presence of and interaction between cellular elements, mainly red blood cells (RBCs), which are the most abundant component and whose mechanical properties are inherent to the microstructure characteristic of blood (Long et al., 2005; Gijsen et al., 1999; Thurston, 1972; Sousa et al., 2013). The non-Newtonian behavior of blood is mainly explained by three phenomena: the tendency of erythrocytes to form three-dimensional microstructures (rouleau) at low shear rates, their deformability (or breakup), and their tendency to align with the flow field at high shear rates. Chien et al. indicated that when blood is at rest or at low shear rates (below 1 s^{-1}), it seems to have a high apparent viscosity, whereas at high shear rates, there is a reduction in the blood's viscosity (Chien et al., 1967). The blood viscosity decreased with an increasing shear rate. For sufficiently high shear rates, the viscosity reached a plateau. Data (minimum of 132 data points) were fitted to a curve that decayed as a monotonic exponential in response to an increasing shear rate (David et al., 2000). The mean blood viscosity obtained by Robert S et al. at shear rates of 100, 50, and 1 s^{-1} were $3.26 \pm 0.43, 4.37 \pm 0.60$, and 5.46 ± 0.84 mPa.s, respectively (Robert et al., 1996). The blood viscosity was measured using a Coulter-Harkners viscometer at "high shear rates (over 300 s $^{-1}$). The normal controls correspond to blood viscosity values of 3.53 mPa.s and a corrected blood viscosity of 3.46 mPa.s (Lowe et al., 1993). Other studies reported that at low shear rates or shear stresses, the apparent viscosity was high, whereas the apparent viscosity decreased with increasing shear and approached a minimum value under high shear forces. At high shear rates above 100 to 200 sec^{-1}, the viscosity of normal blood measured at 37ºC is approximately 4 to 5 mPa.s and is relatively insensitive to further increases of shear. However, the viscosity becomes increasingly sensitive to shear rates below 100 s^{-1} and increases exponentially as the shear rate is decreased. Nominal values for the viscosity of normal blood are approximately 10 mPa.s at 10 s^{-1}, 20 mPa.s at 1 s^{-1}, and 100 mPa.s at 0.1 s^{-1}. Thus, at lower shear rates, the blood viscosity becomes extremely sensitive to the decrement in shear forces. At stasis, normal blood has a yield stress in the range of 2 to 4 mPa (Merrill EW, 1969; Rampling, 1988; Chien., 1975; Rand et al., 1964). Our results (Figure 1.), obtained using a rotational viscometer, are in good accord with the results obtained in the literature for both the non-Newtonian behavior of whole blood and for the values of the apparent blood viscosity in the given range of shear rates. The difference in the apparent viscosity at a specific shear rate, especially under low shear rates, from previous studies is due to the difference in the hematocrit percentages used in our study.

Experiments with the shear-rheometer in a Couette geometry (Behbahani et al., 2009) were used to accommodate the Parabolic model to obtain experimental data for the shear rate and shear stress. Six rheological measurements of human blood with 47 % hematocrit were analyzed, and the results for the Parabolic model are compared with the widely used Power law model. For the latter parameters, K (consistency index) and n (Flow index) were determined using the least-squares method (Marn & Ternik, 2003). The values of K were in the range of 1.568E-2 Pa.s to 1.8567E-2 Pa.s, and the values of n were between 7.4815E-1 and 7.18E-1. Bernasconi et al. and Kar et al. have shown that the power law regression method is suitable for blood viscosity quantification. Bernasconi et al. conducted their series of experiments on exclusively normal blood samples; Kar et al. and later Hussain et al., from the same research group, conclusively proved that not only normal blood but also other pathological blood types follow a power law model (Mohammad et al., 1990). The results obtained are extremely useful for understanding the rheological behavior of blood. A few studies determined the correlation of the power-law coefficients with the hematological and biochemical parameters in the form of the constitutive equation. Easthope and Brooks used a constitutive function that was first employed by Walburn and Schneck to describe the flow properties of whole blood that relate the shear stress measured in a viscometer to the shear rate and hematocrit of the sample (Walburn & Schneck, 1976; Easthope & Brooks, 1976). Hussain et al. reported that because *n* of the power law model is the non-Newtonian behavior index and k is the flow consistency index of blood, they are naturally dependent on the constituents of blood, such as hematocrit, fibrinogen, cholesterol, and so on. It is possible to have such a relationship between the power law coefficients and the above-mentioned parameters in the form of a mathematical equation by using non-linear regression analysis (Mohammad et al., 1990; Hussain et al., 1994; Hussain et al., 1995). Panagiotis used *m* = 14.67 mPa.s and *n* = 0.7755 for his simulation of blood flow; this simulation represented a typical behavior of blood flow according to the power law model (Panagiotis Neofytou, 2004). For healthy controls, Hussain et al. reported that the experimental value of *n* was 0.708 and the calculated value of *n* was 0.713, with 0.25 as the standard deviation of the difference between the experimental and calculated values. Alternatively, the value of normalized K for healthy controls (divided by 17.0 mPa.s^n) was 0.980 and 0.995 for the experimental and calculated values, respectively, with 0.106 as the standard deviation of the difference between the experimental and calculated values (Mohammad et al., 1990). The calculated *n* and K from the research of Hussain et al. were calculated as functions of hematocrit,

fibrinogen, and cholesterol; their results proved that n and K are correlated strongly with the selected blood parameters (Mohammad et al., 1990). Blood viscosity can be affected by various factors (e.g., hemospherine, glucose, and proteins), the most important of which is hematocrit, which denotes the percentage of blood volume that is occupied by red blood cells (Beatriz et al., 2006). Whole blood viscosity correlated with HCT ($r=0.63$, $p < 0.001$ at low shear and $r = 0.84$, $p < 0.001$ at high shear) (Craig et al., 2006). Karsheva et al. proved the dependence of the power law coefficients on both RBC and HCT (M. Karsheva et al., 2009). They obtained the value of $n<1$ and m between 0.9 to 1.3 $mPa.s^n$. A key feature of our study is to examine the correlations between m and n with the blood parameters that are mainly related to erythrocytes (such as HCT %, Hb, RBC, MCV, and MCHC) because erythrocytes play a major role in the non-Newtonian behavior of blood. The values of n and m obtained from our study are in a good agreement with previous studies. The correlations between n and both RBC and MCV were strong (Figure 3), in accordance with the dramatic dependence of the number and size of erythrocytes on the flow behavior of the whole blood. The correlations between n and other blood indices were moderate to weak (Figure 3) because the other blood parameters have stronger effects on the physiological and biochemical properties of whole blood than the macro-rheological behavior of whole blood.

RBC and their related indices are well known to affect viscosity (Chao-Hung, 2004). Chao-Hung found strong positive correlations between whole blood viscosity and the RBC count, Hb, and HCT. David M. et al. found that the blood viscosity increased with increasing hematocrit (David et al., 2000). M, which depends on the physiological parameters of blood, was strongly correlated to the blood indices considered in this study (Figure 4). HCT and Hg increase blood viscosity under different values of shears rates. This linear logarithmic relationship between viscosity and the shear rates corresponds to lines with higher slopes and increasing intercepts of the line, with the y-axis representing the shear rates. This leads to an increase of the value of blood indices with increasing m. From the dependence of m on the internal structure of the liquid under investigation, our results showed strong positive correlations with all of the blood indices.

5. Conclusion

From this study, we conclude that blood behaves as a non-Newtonian fluid, exhibiting a shear thinning behavior. Many models could be used to describe the non-Newtonian behavior of blood, the easiest of which is the power law model. Much information could be extracted from the power law model using an easy computational method. This information is related to the physiological parameters of blood; as a result, the extraction of information from the power law model is a powerful tool to evaluate blood under normal and abnormal conditions. The power law coefficients, n and m, used in this study and in previous studies showed promise as a method to describe the state of blood under investigation based on the correlations between the coefficients and blood parameters (such as HCT, Hb, RBC, MCV in this study and fibrinogen and cholesterol in other study). Further research should be performed to study the correlation between the power law coefficients and the blood physiological and chemical parameters under both normal and pathogenic conditions. In addition, research should be performed to evaluate the values of the power law model coefficients for blood at low shear rates.

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