Relationship between power law coefficients and major blood constituents affecting the whole blood viscosity

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The present work concerns a quantitative analysis of parameters that affect apparent blood viscosity at different low shear rates, i.e, between 1 s^{-1} and, 100 s^{-1}. Viscosity profile of a large number of blood samples from thromboembolic stroke cases and age and sex matched healthy controls were studied which confirmed non-Newtonian power law behaviour of blood. The power law coefficients, n and k, which are unique to each blood sample, were related with blood viscosity parameters in the form of a mathematical equation by performing non-linear regression analysis. It was possible to calculate n and k of power law model by supplying the values of major blood constituents in the equation obtained for stroke and controls. The calculation of n and k of a blood sample using the equation obtained, provided a quick information on its apparent viscosity values at any given shear rate without viscometry. The calculated and the experimental viscosity were found in good agreement within a permissible error range. The relation obtained between power law coefficients and major blood constituents in the present investigation would give a quantification of different blood viscosity parameters contributing to the resistance to flow of blood. Such an analysis may be considered as a scientific basis for the study of blood fluidity in different disease conditions.

1. Introduction

Mathematically the inverse of blood fluidity is known as the whole blood viscosity. Viscosity is that property of fluid by virtue of which it offers resistance to flow or shear. The viscosity of whole blood is influenced by a number of blood constituents like haematocrit (% packed red cell volume), plasma proteins, temperature and shear rates. The dependence of blood viscosity on the shear rate or the non-Newtonian nature of blood has been reported by many workers. For instance, the viscosity of blood increases with decrease in shear rates and vice versa showing that blood behaves as a non-Newtonian fluid (Charm and Kurland 1974; Cokelet 1972; Dintenfass 1972; Merill 1969).

1.1 *Power law model*

The apparent whole blood viscosity, which is the ratio of shear stress to shear rate at a particular rate of shear, can be expressed as:

$$\tau/(du/dy) = \mu_a, \tag{1}$$

where, μ_a = apparent viscosity or structural viscosity.

In case of Newtonian fluid: $\mu_a = \mu$.

The apparent blood viscosity is computed as the ratio of the measured shear stress existing at a given shear rate, to the shear rate itself as

$$\mu_a = k(du/dy)^{(n-1)}. \tag{2}$$

Taking logarithm on both sides of equation (2), we have

$$\log \mu_a = \log k + (n-1)\log(du/dy), \tag{3}$$

when $k = 1$ is substituted in equation (3) then $\log k = 0$, and equation (3) changes to

$$\log \mu_a = (n-1)\log(du/dy). \tag{4}$$

The slope $(n-1)$ is calculated from equation (4). By substituting the value of n obtained, intercept k is found from equation (3).

Keywords. Cerebrovascular accidents (CVA); blood viscosity; power law; haematocrit; fibrinogen; cholesterol

Thus by plotting the log μ_a and log(du/dy) it is possible to obtain n and k for each blood samples by linear least square regression method reported at length elsewhere (Hussain *et al* 1994).

1.2 *Physiological meaning of n and k*

The parameters n and k are the power law coefficients and represent resistance to flow of the blood. The n is defined as non-Newtonian behaviour index and is a dimensionless quantity, while k is described as flow consistency index and its' unit is mPa.S^n. They explain more explicitly, the behaviour of blood over a range of shear rates (Hussain *et al* 1994).

1.3 *Genesis of the problem*

Although there are recommendations of International Committee for Measurements of Blood Viscosity (ICSH, 1986), the interpretation and comparison of clinical whole blood viscosity data are not satisfactory. This is because workers in this field generally, while reporting viscosity values have used one or two different particular shear rates (Walker *et al* 1985; Lechner *et al* 1986; Ott *et al* 1986; Caimi *et al* 1987; Ernst *et al* 1987; Fisher *et al* 1987). There has been no agreement about the shear rates at which the viscosity should be compared between two given samples (Inglis *et al* 1981). Therefore, the consideration of a range of shear rates and averaging out the resulting viscosity values by finding the best fit for the data was tried out in the past. Charm and Kurland (1962) suggested that shear rate versus apparent blood viscosity data followed power law. This was supported by Benis *et al* (1971). Bernasconi *et al* (1986, 1989, 1991) and Kar *et al* (1991) have shown that power law regression method is suitable for blood viscosity quantification. Bernasconi *et al* (1986, 1989, 1991) conducted their series of experiment taking exclusively normal blood samples while Kar *et al* (1991) and later Hussain *et al* (1994) of the same research group have conclusively proved that not only normal blood but other pathological blood also follow power law model. The results obtained are extremely useful for understanding rheological behaviour of blood.

A few studies exist which find the correlation of power law coefficients with haematological and biochemical parameters in the form of constitutive equation (Walburn and Schneck 1976; Easthope and Brooks 1980). Easthope and Brooks (1980) have used a constitutive function first employed by Walburn and Schneck (1976) describing the flow properties of whole blood which relates the shear stress measured in a viscometer to the shear rate and haematocrit of the sample. In the present work, however, we have tried to find out a mathematical equation by performing non-linear regression analysis. Since the n of power law model is the non-Newtonian behaviour index and k is the flow consistency index of blood, they are naturally dependent on the constituents of blood such as haematocrit, fibrinogen, cholesterol etc. It is possible to have such relationship between power law coefficients and the above mentioned parameters in the form of a mathematical equation by using non-linear regression analysis. As a continuation of our previous studies (Hussain *et al* 1994, 1995) we have considered blood samples of cerebrovascular disease only along with normal controls for the present analysis.

2. Patients and methods

2.1 *Selection of patients and controls*

Patients admitted to a major hospital in Bombay with a fresh thromboembolic stroke (less than 24 h old at the time of the first blood collection) were included in this study. A total of 150 cerebrovascular accident (CVA) cases were studied. Apart from this, 109 healthy volunteers were also studied as control. All controls were age and sex-matched and are shown in table 1.

2.2 *Selection criteria*

2.2a *CVA cases:* Although it is not possible to distinguish reliably a cerebral haemorrhage from infarction on clinical grounds alone, the features usually associated with haemorrhage as explained by WHO were considered primarily to screen out haemorrhagic cases (WHO 1989). Over and above the WHO criteria, a CT scan was performed to rule out intracranial haemorrhage in the cases included in the analysis. A

Table1. Mean age (years) and sex composition of CVA cases and healthy controls.

	Men mean age ± SD	Women mean age ± SD	Total mean age ± SD
CVA	52 ± 16·10 (N = 109)	55 ± 13·77 (N = 41)	53 ± 15·54 (N = 150)
Normal	48 ± 7·74 (N = 95)	44 ± 5·91 (N = 39)	47 ± 7·43 (N = 134)

CVA = Cerebrovascular accidents.

detailed history was taken and a thorough clinical examination was done in the case of each patient. All patients were investigated with a haemogram, blood urea nitrogen, creatinine, fasting blood sugar (FBS) (Daniel 1983), plain chest X-ray and ECG. Patients with a BUN : serum creatinine ratio of 20 : 1, indicative of dehydration were excluded from the study.

2.2b *Healthy controls*: Clinically normal aged volunteers were included in this control group so as to match with the patient's age and also to nullify the well-known effect of age on the disease.

2.3 *Laboratory methods*

Different laboratory methods to evaluate patients and controls used in this study are mentioned below.

2.3a *Anticoagulant*: EDTA was used as an anticoagulant for all analyses.

2.3b *Haemorheological studies*

(i) *Whole blood viscosity*

Instrument used: Contraves, low shear 30 viscometer (Zurich, Switzerland): This instrument was used for the study of whole blood viscosity. A stationary bob within a rotating cup, produces shear force in sample fluid contained in the cup. The viscosity of the fluid generates resistance to the rotating cup proportional to the shear rate. Readings can be taken at different shear rates from 0·017 s^{-1} to 128·5 s^{-1}. Sample is kept at 37°C in a temperature bath. The amount of torque produced by the resistance is indicated on a digital display. This is easily converted into absolute centipoise units from precalculated range chart available with the instrument.

Method: Six ml of venous blood collected with a dry disposable syringe in an EDTA plastic bulb from patients and controls, were subjected to 7 different shear rates namely, 1·285/s, 3·23/s, 4·39/s, 8·11/s, 20·4/s, 51·2/s and 94·5/s and viscosity was calculated as described above.

(ii) *Method of viscometric data analysis*: Apparent blood viscosity values corresponding to above mentioned seven shear rates were plotted against these shear rates on log–log scale. Thus by plotting the $\log \mu_a$ and $\log(du/dy)$ it was possible to obtain n and k of power law for the blood samples by linear least square regression method and this has been reported elsewhere (Hussain *et al* 1994).

2.3c *Haematocrit and biochemical parameters*: Haematocrit was estimated using capillary haematocrit method at 17,000 rpm (Micro Centrifuge, RM 12, Remi). Fibrinogen and cholesterol were estimated using routine laboratory methods.

2.4 *Quantification of blood viscosity parameters using n and k of power law*

As we have proposed in the present work n and k may be related in the form of an equation and may be estimated as functions of blood viscosity parameters (blood constituents) mainly haematocrit, fibrinogen and cholesterol. The reason for selecting these three parameters are discussed in § 4.
We can write,

$$k = \alpha(\text{Hct, Chol, Fibrn, . . .}). \tag{5}$$

Similarly,

$$n = \beta(\text{Hct, Chol, Fibrn, . . .}). \tag{6}$$

Fibrinogen and chololesterol are measured in mg/dl, while k has a unit mPa.s^n. Haematocrit is represented in per cent. As can be seen, the equations (5 and 6) are dimensionally inconsistent. Since any equation, which is physically true should also be dimensionally consistent so Raleigh's method (Maurice 1961) can be applied according to which equations (5 and 6) are written as follows:

$$k = \alpha(\text{Hct}^{a1}\ \text{Chol}^{a2}\ \text{Fibrn}^{a3} \ldots) \tag{7}$$

and

$$n = \beta(\text{Hct}^{b1}\ \text{Chol}^{b2}\ \text{Fibrn}^{b3} \ldots). \tag{8}$$

In order to make parameters on both the sides dimension-less they are divided by a constant value of healthy subjects. For example,

$$K = k/k_n$$

where, k_n is average value of flow consistency index of healthy controls. The average value taken is 17·0 mPa.s^n for k_n in order to make k a dimensionless quantity denoted as K by taking ratio of $k : k_n$. Similarly fibrinogen and cholesterol are made dimensionless by taking constant values in the normal range as follows:

$$\text{Fibrn}' = \text{Fibrn}/\text{Fibrn}_n \text{where } \text{Fibrn}_n = 200 \text{ mg/dl}$$

$$\text{Chol}' = \text{Chol}/\text{Chol}_n \text{where } \text{Chol}_n = 150 \text{ mg/dl}.$$

Now the equations (7 and 8) can be written as,

$$k/k_n = \alpha\{\text{Hct, (Chol/Chol}_n\text{), (Fibrn/Fibrn}_n\text{), . . .}\} \tag{9}$$

$$n = \beta\{\text{Hct, (Chol/Chol}_n\text{), (Fibrn/Fibrn}_n\text{), . . .}\}. \tag{10}$$

These can also be written as follows:

$$K = \alpha\ (\ \text{Hct}^{a1}\ \text{Chol}'^{\,a2}\ \text{Fibrn}'^{\,a3} \ldots) \tag{11}$$

and

$$n = \beta\,(\mathrm{Hct}^{b1}\,\mathrm{Chol}'^{\,b2}\,\mathrm{Fibrn}'^{\,b3}\ldots). \quad (12)$$

Coefficient and exponents of equations (11 and 12) is obtained using nonlinear regression method for a particular set of experimental data of patients and controls as follows.

2.5 *Calculation of coefficient and exponents*

The subroutine RNLIN of IMSL (International Mathematical and Statistical Library) is used to calculate coefficient and exponents in the present analysis through optimization technique (IMSL 1987a). The n, K and corresponding Hct, Chol', Fibrn' data from 150 CVA cases and 134 normal subjects were used to find the best fit equation viz., equations (11 and 12), and the values of coefficients and exponents involved therein. The obtained values of coefficient and exponents was used to calculate the n and K values of fresh blood samples by feeding Hct, Chol', Fibrn' data from CVA and normal control as mentioned below.

2.5a *Reliability of the analysis*: To check the reliability of the present analysis and uniqueness of the coefficient and exponents, fresh samples of CVA cases ($N = 43$) as well as healthy controls ($N = 36$) were estimated for Hct, Fibrn and Chol. Dimension-less values of these blood viscosity parameters e.g., Hct, Fibrn', Chol' were supplied in the equation and using respective coefficients and exponents of CVA group of patients and healthy control group, n and K were calculated. These samples were also experimentally analysed using viscometer and n and K were estimated directly to check the reliability of our analysis.

2.5b *Justification for the IMSL subroutine RNLIN used in the present investigation*: The method of simulation is primarily selected on the basis of degree of accuracy and reliability of the solution obtained. In the first attempt IMSL subroutine RNLIN which involves nonlinear regression using least square method was used and coefficients were obtained. Now to check the reliability and accuracy of the solution two other methods were used. One was IMSL subroutine UMPOL, which used simplex optimization routine (IMSL 1987a) and another subroutine used was DFPMIN (William 1986), which is based on Broyden–Fletcher–Goldfarb–Shanno variant of Davidon–Fletcher–Powell minimization. However both the methods yielded identical results with those given by IMSL's RNLIN subroutine. All simulations to calculate coefficients and exponents were done using subroutine RNLIN because of easy handling of IMSL package. In other words, the simplicity of RNLIN over UMPOL favoured the use of former subroutine.

3. Results and discussion

The parameters n and k represent resistance to flow of blood. They explain more explicitly, the cumulative behaviour of blood constituents over a range of shear rates. We have selected mainly three blood viscosity parameters to be correlated with n and k in the present study. These blood viscosity parameters are haematocrit, fibrinogen and cholesterol and, are estimated routinely in clinical laboratories. Haematocrit is nothing but the percentage packed volume of red blood cells and a major contribution to whole blood viscosity comes from it. This parameter includes not only the effect of packed cell volume of red blood cells but, also other important physical parameters namely, aggregability, filterability/deformability and rigidity or internal viscosity of red blood cells. These physical parameters in turn are affected by the alteration in the concentration of biochemical factors in plasma or plasmatic factors. For instance, red blood cell aggregability which is induced by fibrinogen, is well documented. Similarly, red blood cell filterability/deformability and rigidity are not only influenced by external and internal constituents of red blood cells but to a larger extent by the membrane characteristics (Lange *et al* 1982; Garnier *et al* 1985; Annapurna *et al* 1990). A red cell has a semipermeable membrane whose chemical composition mainly constitutes cholesterol and phospholipid. Any alteration in cholesterol concentration in plasma may effect the ratio of cholesterol: phospholipid in the lipid bilayer and the lipid bilayered matrix depending upon this ratio may influence the red cell deformational properties (Lange *et al* 1982; Garnier *et al* 1985; Annapurna *et al* 1990). Hence, we have selected fibrinogen and cholesterol along with haematocrit as major factors contributing to blood viscosity. Our study focuses on the quantification of these three parameters and, has shown their contributions to blood viscosity as values of their exponents in the equation relating to n and K (tables 2 and 3).

The table 1 presents the mean age and sex composition of CVA cases ($N = 150$) and normal controls ($N = 134$) considered for the calculation of coefficients and exponents involved in the equations (11 and 12) as shown in the tables (2 and 3). This is apparent from the tables (2 and 3) that the two populations, viz., normal control and CVA cases differ by their respective coefficients and exponents involved in the equations (11 and 12) relating n and K with haematocrit and biochemical factors. The most significant contribution in the calculation of both n and K comes actually from haematocrit. The normalized flow consistency index K, in case of healthy controls depends on haematocrit raised to a power of almost double to that of haematocrit power in case of CVA cases. This may relate to deformable normal red cells' ability to consistently contribute to flow consistency with increasing shear rate, while a less deformable, rigid red cells as in CVA cases contribute to a lower degree to flow consistency index. Cholesterol shows its contribution more in CVA cases, which may be attributed indirectly to red cell rigidity as a result of disturbed cholesterol and phospholipid ratio in the red cell membrane (Annapurna *et al* 1990).

The tables (4 and 5) show the comparison of experimentally obtained n and K values with that of the theoretically calculated n and K values, in CVA cases and

Table 2. The value of coefficient and exponents involved in the equation $K = \alpha Hct^{a1}$ Chol' ^{a2} Fibrn' ^{a3} as estimated by using subroutine RNLIN of ISML through optimization technique.

Coefficient and exponents	Healthy control	CVA cases
α	0·0022	0·0435
a1	1·5963	0·8495
a2	0·1545	0·3181
a3	0·0527	0·0234

α, Coefficient; a1, a2, a3, exponents; Hct, haematocrit; Chol, cholesterol; Fibrn, Fibrinogen; *K*, normalized flow consistency index.

Table 3. The value of coefficient and exponents involved in the equation $n = \beta Hct^{b1}$ Chol' ^{b2} Fibrn' ^{b3} as estimated by using subroutine RNLIN of ISML through optimization technique.

Coefficient and exponents	Healthy control	CVA cases
β	2.1750	0·9969
b1	− 0·2940	− 0·0915
b2	− 0·0095	− 0·0188
b3	− 0·0161	− 0·0083

β, Coefficient; a1, a2, a3, exponents; Hct, haematocrit; Chol, cholesterol; Fibrn, fibrinogen; *n*, non-Newtonian behaviour index.

normal controls respectively. The standard deviation and the percentage error of the difference between experimentally estimated *n*, *K* values and theoretically calculated *n*, *K* values are found within permissible error range (tables 4 and 5).

Although shear rates less than 1 s^{-1} and higher than 100 s^{-1} are very important for any clinical study, we have not selected them because the power law model does not allow investigation on these ranges of shear rates. However, the present consideration of the range of shear rates, between 1 s^{-1} and 100 s^{-1} do have prognostic importance in early detection of the episode. Moreover, it serves our purpose to make investigation on the relationship between power law coefficients and blood viscosity parameters based on group study of a particular type of disease or population. This type of relation would allow the calculation of *n* and *k* of power law of any fresh blood sample falling in a particular group. Major routine biochemical parameters and haematological values can be supplied in the relation obtained, in order to calculate *n* and *k* of the power law. Once *n* and *k* become known, the apparent viscosity may be calculated at any desired shear rate, thus providing quick information about apparent whole blood viscosity at a particular shear rate without viscometry. This is demonstrated and discussed in the following section.

3.1 *Calculation of viscosity without viscometry*

The calculated *n* and *K* are obtained by supplying Hct, Fibrn' and Chol' values in the equations (11 and 12) for five fresh

Table 4. Average and standard deviation of calculated *K* of fresh blood samples with respect to its experimental values.

	Average		Difference	
Groups	*K* (experimental)	*K* (calculated)	SD	Error (%)
Healthy control ($N = 36$)	0·980	0·995	0·106	9·138
CVA cases ($N = 43$)	1·029	1·054	0·210	15·650

K, Normalized flow consistency index; SD, standard deviation of the difference between experimental and calculated values.

Table 5. Average and standard deviation of calculated *n* of fresh blood samples with respect to its experimental values.

	Average		Difference	
Groups	*n* (experimental)	*n* (calculated)	SD	Error (%)
Healthy control ($N = 36$)	0·708	0·713	0·025	3·030
CVA cases ($N = 43$)	0·703	0·707	0·027	2.978

n, Non-Newtonian behaviour index; SD, standard deviation of the difference between experimental and calculated values.

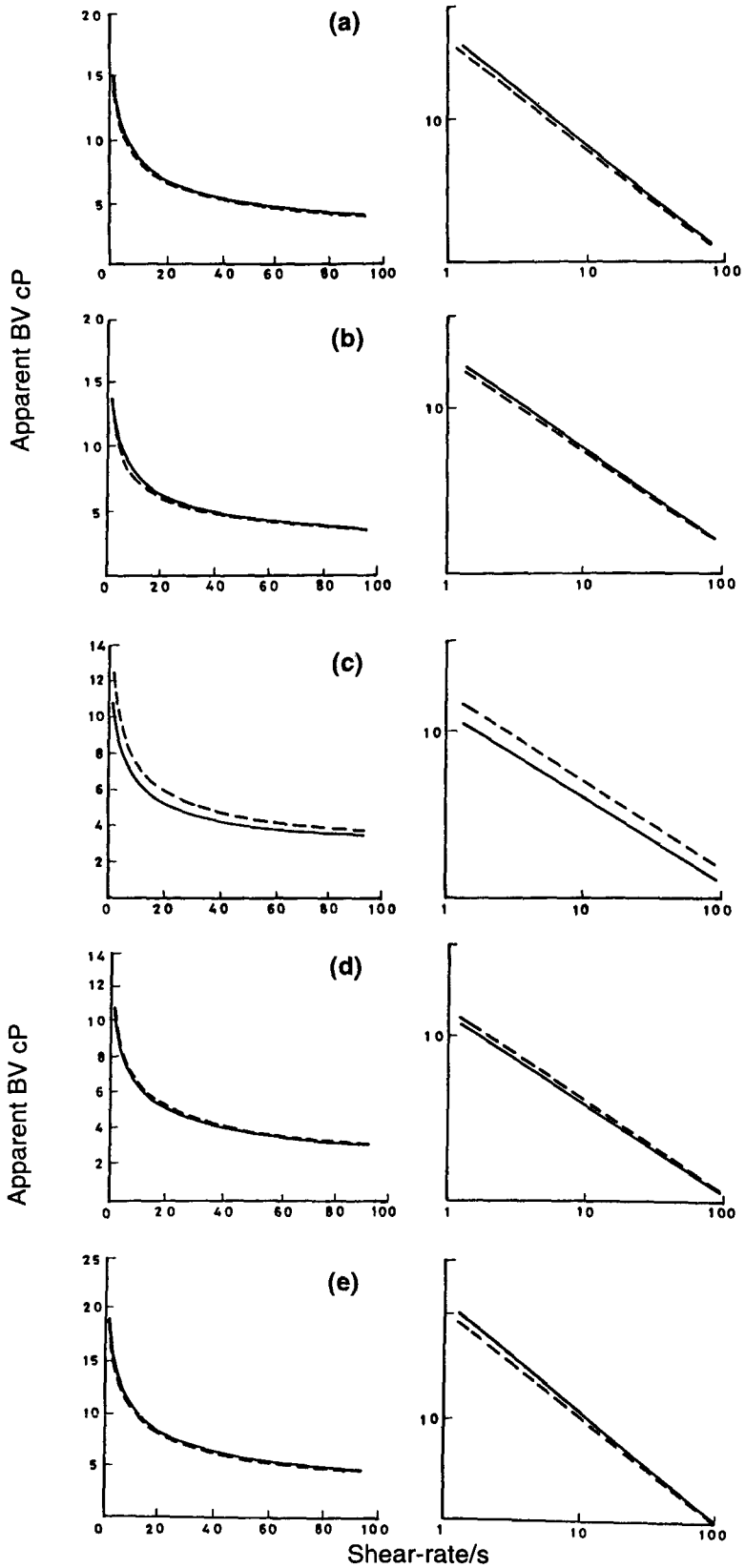

Figure 1. Linear and log–log plot of experimental values of BV versus shear rate (SR), superimposed with theoretical values of BV and SR of five fresh CVA cases. (——), Experimental curve; (– – –), theoretical curve.

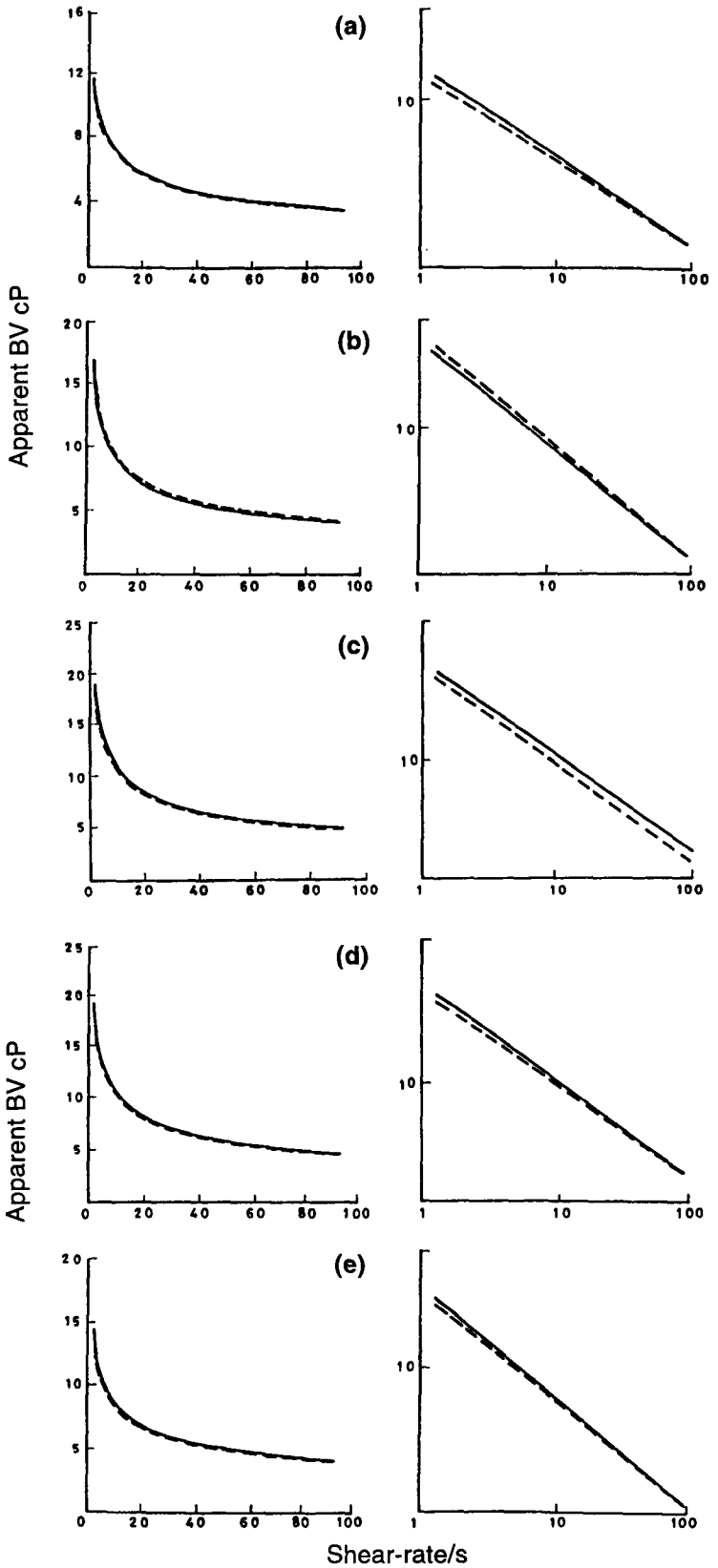

Figure 2. Linear and log–log plot of experimental values of BV versus SR, superimposed with theoretical values of BV and SR of five fresh healthy cases. (——), Experimental curve; (– – –), theoretical curve.

normal and five fresh CVA cases. The values of coefficients supplied to these equations are taken from respective tables (2 and 3) for normal and CVA cases. Apparent whole blood viscosity is calculated for these cases at 7 different shear rates using calculated n and K. Thus, theoretically calculated apparent whole blood viscosity, using proposed equation, matches with that of experimentally obtained value of the same subjects through viscometry.

Experimental values of apparent whole blood viscosity and shear-rates plot are superimposed on to the theoretically calculated values of apparent whole blood viscosity at 7 different shear rates for CVA cases and healthy controls as shown in figures 1a–e and 2a–e.

4. Conclusion

The present study concludes the following:

(i) All CVA and healthy blood samples behave as non-Newtonian power law fluid. The n and k are related with major blood constituents through equations (11 and 12) where, the coefficient and exponents involved are unique to the group of cases studied. These coefficient and exponents may be different in different disease conditions, which may be investigated.

(ii) The value of coefficients and exponents involved in the relation which are unique to the groups of cases studied gives a quantification of blood viscosity parameters considered in the present relation namely, fibrinogen, cholesterol and haematocrit. In other words the contribution to the resistance to flow of blood in CVA cases comes mainly from these three blood viscosity parameters. Such an analysis may be considered as a scientific basis for the study of blood fluidity in different disease conditions.

(iii) The quantitative relationship of n, k with blood constituents viz., Hct, Fibrn and Chol makes it possible to calculate apparent whole blood viscosity (BV) of a blood sample without viscometry.

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References

Annapurna V, Puniyani R R and Gupte R V 1990 Red cell deformability and erythrocyte lipids in hypertension; *Clin. Hemorheol.* **10** 95–101

Benis A M, Usami S and Chien S 1971 Determination of shear stress shear rate relation for blood by couette viscometry; *Biorheology* **8** 65–69

Bernasconi C, Del Santo A, Marralli F and Agostoni A 1989 Standardized correction of whole blood viscosity for the main determinants: a computerized system; *Clin. Hemorheol.* **9** 633–640

Bernasconi C, Del Santo A, Marralli F, Laffranchi M, Mitani S and Agostoni A 1991 Reference limits for blood viscosity influence of sex and age; *Clin. Hemorheol.* **11** 447–457

Bernasconi C, Ferraresi, Agostoni A 1986 Power law regression method for blood viscosity quantification; *Clin. Hemorheol.* **6** 541–551

Caimi G, Savettieri G, Fierro B, Catania A and Sarno A 1987 Multiple Sclerosis: Haemorheological Pattern; *Clin. Hemorheol.* **7** 695–698.

Charm S E and Kurland G S 1962 The flow behavior and shear stress, shear rate characteristics of canine blood; *Am. J. Physiol.* **203** 417–421

Charm S E and Kurland G S 1974 *Blood flow and microcirculation* (New York: Wiley)

Cokelet G R 1972 Its foundations and Objectives; in *Biomechanics* (eds) Y C Fung, N B Perrone and M Anlinker (Englewood Cliffs, New Jersey: Prentice Hall) pp 63–103

Daniel W F 1983 Diabetes mellitus; in *Harrison's principles of internal medicine* (eds) W T George, D A Raymond, B Eugene, K J Isselbacher and G P Robert (New York: McGraw-Hill Kogakusha Ltd: A Blakiston Publication) 8th edition, pp 661–678

Dintenfass L 1972 *Blood microrheology – Viscosity factors in blood flow, ischemia and thrombosis* (London: Butterworth)

Easthope P L and Brooks D E 1980 A Comparison of Rheological Constitutive Functions for Whole Human Blood; *Biorheology* **17** 235–247

Ernst E, Thies W, Matrai A, Seichert N, Schöps P, Magyarosy I, Kraft-Kupfer A and Schattenkirchner M 1987 Hemorheological Abnormalities in Rheumatoid Arthritis; *Clin. Hemorheol.* **7** 591–598

Fisher M, Giannotta S and Meiselman H J 1987 Hemorheological Alterations in Patients with Subarachnoid Hemorrhage; *Clin. Hemorheol.* **6** 611–618

Garnier M, Koutrsouris D and Hanss M 1985 On the membrane determinant of erythrocyte deformability; *Clin. Hemorheol.* **5** 401–409

Hussain M A, Puniyani R R and Kar S 1994 Quantification of blood viscosity using power law model in cerebrovascular accidents and high risk controls; *Clin. Hemorheol.* **14** 685–696

Hussain M A, Puniyani R R and Kar S 1995 Blood viscosity autoregulation factor in cerebrovascular accidents and high risk cases – A new approach; *Clin. Hemorheol.* **15** 61–71

ICSH (International Committee for Standardization in Haematology) 1986 Expert Panel on Blood Rheology, "Guidelines for measurement of blood viscosity and erythrocyte deformability"; *Clin. Hemorheol.* **6** 439–453

IMSL 1987a Problem-solving Software System, *MATH/LIBRARY: FORTRAN Subroutines for Statistical Analysis;* Softcover Edition (Control Data Corporation Publication Number 41621852, version 1·0 MALB-USM-PERFECT-1·0) pp 831–834

IMSL 1987b Problem-solving Software System, *STAT/LIBRARY: FORTRAN Subroutines for statistical analysis*; Softcover Edition (Control Data Corporation Publication Number 41621852, version 1·0 STLIB-USM-PERFECT-1·0) pp 239–247

Inglis T C, Carson P J and Sturat J 1981 Clinical measurement of whole blood viscosity at low shear rates; *Clin. Hemorheol.* **1** 167–177

Kar S, Mehta J and Sharma K 1991 Investigation on non-Newtonian behaviour of normal and leukemic blood, in *Proceeding of 13 Annual International Conference IEEE Engineering in Medicine and Biology* (Orlando, USA) vol. 13 (5), pp 1991–1992

Lange Y, Gouch A and Steck T L 1982 Role of the bi-layer in the shape of the isolated erythrocyte membrane; *J. Membr. Biol.* **69** 113–123

Lechner H, Ott E, Ossama N and Fazekas F 1986 Round table: Follow up studies of the haemorheologic profile in acute ischaemic strokes; *Clin. Hemorheol.* **6** 3–9

Maurice H 1961 Dimensional Analysis, in *Handbook of fluid dynamics*, First edition, (ed.) V L Streeter (New York: McGraw-Hill) pp 15.1–15.25

Merill E W 1969 Rheology of blood; *Physiol. Rev.* 49 863–888

Ott E, Niederkorn K, Fazekas F, Körner E, Ossama N and Lechner H 1986 The implication of hemorheologic abnormalities in cerebrovascular disease; *Clin. Hemorheol.* **6** 331–336

Walburn F J and Schneck D J 1976 A constitutive equation for whole human blood; *Biorheology* **13** 201–210

Walker T, Matrai A, Flute P T and Dormandy J A 1985 Hemorheological and functional changes in intermittent claudication following plasma exchange with haematocrit; *Clin. Hemorheol.* **5** 99–106

WHO 1989 Stroke prevention, diagnosis and therapy; *Stroke* **20** 1407–1434

William H P 1986 Minimization of Functions – The Broyden–Fletcher–Goldfarb Shanno variant of Davidson–Fletcher-Powell minimization; in *Numerical recipes; The Art of scientific computing* (eds) H P William, P F Brian, A T Saul and T V William (Cambridge: University Press) pp 310–311

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