

# Measurement of Rheologic Property of Blood by a Falling-Ball Blood Viscometer

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(Received 2 June 2007; accepted 28 January 2008; published online 8 February 2008)

**Abstract**—The viscosity of blood obtained by using a rotational viscometer decreases with the time elapsed from the beginning of measurement until it reaches a constant value determined by the magnitude of shear rate. It is not possible to obtain an initial value of viscosity at time  $t = 0$  that is considered to exhibit an intrinsic property of the fluid by this method. Therefore, we devised a new method by which one can obtain the viscosity of various fluids that are not affected by both the time elapsed from the beginning of measurement and the magnitude of shear rate by considering the balance of the forces acting on a solid spherical particle freely falling in a quiescent viscous fluid. By using the new method, we studied the rheologic behavior of corn syrups, carboxy-methyl cellulose, and human blood; and compared the results with those obtained with a cone-and-plate viscometer. It was found that in the case of corn syrups and washed red cell suspensions in which no red cell aggregate (rouleau) was formed, the viscosity obtained with the two different methods were almost the same. In contrast to this, in the case of the whole blood in which massive aggregates were formed, the viscosity obtained with a falling-ball viscometer was much larger than that obtained with a cone-plate viscometer.

**Keywords**—Human blood, Blood viscosity, Falling-ball viscometer, Power law model, Flow property, Rheologic constant, Rouleaux formation, Shear rate, Solid sphere.

## INTRODUCTION

The extensive studies carried out on the relationship between blood flow and various vascular diseases revealed that atherosclerosis and intimal hyperplasia develop preferentially in regions where blood flow is locally disturbed by the formation of slow secondary and recirculation flows and where wall shear stress is low.<sup>1,6,8</sup> In such a region where flow is extremely slow, since red cells form aggregates (rouleaux), it is expected

that blood exhibits a non-Newtonian behavior and the viscosity of blood is locally elevated. Especially in veins where flow is generally slow and even in arteries in which blood flow is decreased by the formation of severe stenoses due to the development of atherosclerosis, the higher the viscosity of blood is, the more it becomes difficult for blood to flow. It may result in the formation of thrombi and stoppage of blood flow in severe cases. Therefore, for patients suffering from such vascular diseases, it is necessary to accurately measure the viscosity of blood under low shear conditions, and if the values were abnormally high compared to those of normal subjects, it is necessary to improve blood flow by lowering the viscosity of blood by taking appropriate measures such as defibrinogenation, plasmapheresis to remove excessive amount of plasma proteins, and hemodilution to reduce the number of red cells.

Presently, to measure the viscosity of various fluids, rotational apparatuses such as a cone-plate and coaxial-cylinder viscometers are widely used. However, in the case of an inhomogeneous fluid such as blood and suspensions of polymer materials, since the fluid is in flow and constantly subjected to shear stresses, the viscosity measured by using these apparatuses that are based on a steady flow decreases with the time elapsed from the beginning of measurement until it reaches a constant value determined by the magnitude of shear rate applied to the fluid. Therefore, it is not possible to obtain an initial value of viscosity at time  $t = 0$  that is considered to exhibit an intrinsic property of the fluid. To solve the problem and obtain the intrinsic property of various fluids, we devised a new method by which one can obtain the viscosity of various fluids that is not affected by both the time elapsed from the beginning of measurement and the magnitude of shear rate by considering the balance of forces acting on a solid spherical particle freely falling in a quiescent viscous fluid. By using the new method, we studied the rheologic behavior of corn syrups, dilute solutions of

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carboxy-methyl cellulose (CMC), and human blood. The results were compared with those obtained with a cone-plate viscometer.

The ultimate goal of the present study is to establish the new method as a standard method to measure and detect the abnormality of the viscosity of blood with high sensitivity and use clinically as a substitute for the measurement of erythrocyte sedimentation rate (ESR) presently used for screening of patients.

## MATERIALS AND METHODS

### *Theoretical Background*

The principle of our falling-ball viscometry is based on the theoretical analysis carried out by Fararoui and Kintner in 1961, although they did not use the results to obtain the viscosity of the fluid they were studying.<sup>4</sup>

When a solid sphere with a diameter  $d$  and density  $\rho_s$  is falling slowly under the influence of gravity in a quiescent liquid having density  $\rho_l$ , the inertial force acting on the sphere is given as a sum of the gravitational force acting downward and the buoyancy and drag force acting upward. However, as the falling velocity of the sphere increases, the drag force also increases. Therefore eventually, the inertial force becomes zero since the gravitational force is balanced with the buoyancy and the drag force, making the sphere fall with a constant velocity  $U_\infty$ . Here, if we express the apparent viscosity of the fluid by  $\mu_a$  and extend the law of Stokes to be applicable to all the fluid including non-Newtonian fluids, the drag force acting on the sphere is expressed by  $D = 3\pi d\mu_a U_\infty$  and the terminal velocity of the falling sphere is given by  $U_\infty = gd^2(\rho_s - \rho_l)/18\mu_a$ . Here the shear stress (mean-value) acting on the surface of the sphere due to the viscous nature of the fluid is calculated to be  $\tau = D/\pi d^2$ . By using the above relationship, the shear stress can be rewritten as  $\tau = gd(\rho_s - \rho_l)/6$ . Furthermore, since there is a relationship that  $\tau = \mu_a\gamma$  between the shear stress  $\tau$  acting on the surface of the sphere and the shear rate  $\gamma$ , the shear rate (mean value) can be given by  $\gamma = 3U_\infty/d$  by using the above relationship. Therefore, it is possible to obtain flow property of a fluid by dropping several solid spheres having different diameter or density in a fluid, measuring their terminal velocities, and plotting the values of  $\tau$  and  $\gamma$  calculated by using the measured velocities of the spheres together with the physical values such as the densities of the fluid and the spheres, and the diameters of the spheres by taking the shear rate,  $\gamma = 3U_\infty/d$ , on the abscissa and the shear stress,  $\tau = gd(\rho_s - \rho_l)/6$ , on the ordinate of a logarithmic graph paper. The apparent viscosity of a fluid  $\mu_a$  can be obtained from the relationship  $\tau = \mu_a\gamma$  or more specifically  $gd(\rho_s - \rho_l)/6 = \mu_a(3U_\infty/d)$ .

Here it should be noted that since the present method is based on the law of Stokes, it can be used only in a range where the Reynolds number calculated for a sphere,  $Re = dU_\infty\rho_l/\mu_a$ , is smaller than 1, that is, in a range of relatively low shear rates.

In the present method, since the sphere falling slowly in a quiescent liquid comes in contact or interacts with only limited number of fluid elements existing around it and only in short times, the fluid elements are subjected to shear stress which is very low and only very short times compared to the case of rotational viscometers that are based on a steady flow. Therefore, the rheologic constant or viscosity obtained by this new method is regarded to correspond to the viscosity of a fluid at time  $t = 0$  as measured by using a rotational viscometer and it could be regarded as an intrinsic property of the fluid that is not affected by both the time elapsed from the beginning of measurement and the magnitude of shear rate.

### *Experimental Apparatus*

Figure 1 is a schematic drawing of the falling ball blood viscometer that was designed and constructed especially for the present study. The most important part of the apparatus is composed of an ultrasound echo probe (5 MHz: NDT-88910, Panametrics Co. Ltd.) that was used to detect the position of an invisible solid sphere falling freely in blood, an amplifier, and an oscilloscope. It was designed to detect the position of a solid spherical particle falling freely in a quiescent liquid sample as a function of time by means of an ultrasound echo, and then calculate the velocity of the particle based on it.

### *Materials*

The fluids used were corn syrups, aqueous solutions of CMC, and human blood. Human whole blood was obtained from 20- to 50-year-old healthy

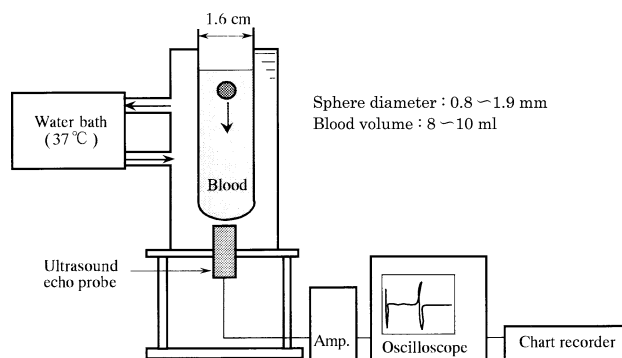


FIGURE 1. Schematic drawing of the falling-ball blood viscometer designed and constructed in the present study.

donors of both gender by using sodium citrate as an anticoagulant. Blood was taken from donors by a nurse at the outpatient clinic of Hokkaido University Hospital.

The whole blood and washed red cell suspensions with various hematocrit were prepared by centrifuging the whole blood and re-suspending red cells in serum or a Tyrodes-albumin solution, respectively. As the solid spheres used to measure falling velocities, polystyrene spheres with diameters of 0.8–2.0 mm, and density of 1.05–1.11 g/cm<sup>3</sup> were used as they were or by coating their surfaces with platinum–palladium by means of ion sputtering to make the densities of the spheres slightly greater than that of the liquid to be tested so that the spheres fall in the liquid very slowly. Here the maximum diameter of the sphere to be used was determined so that the falling velocity of the sphere was not affected by the presence of the wall of the test tube used as a container of blood by actually measuring the velocity of spheres having various diameters falling in a 70% CMC solution. The diameter of each sphere was measured under a light microscope by using a micrometer scale. The densities of the spheres and the liquids were measured by using a precision electronic chemical balance and a pycnometer, respectively.

#### Experimental Procedures

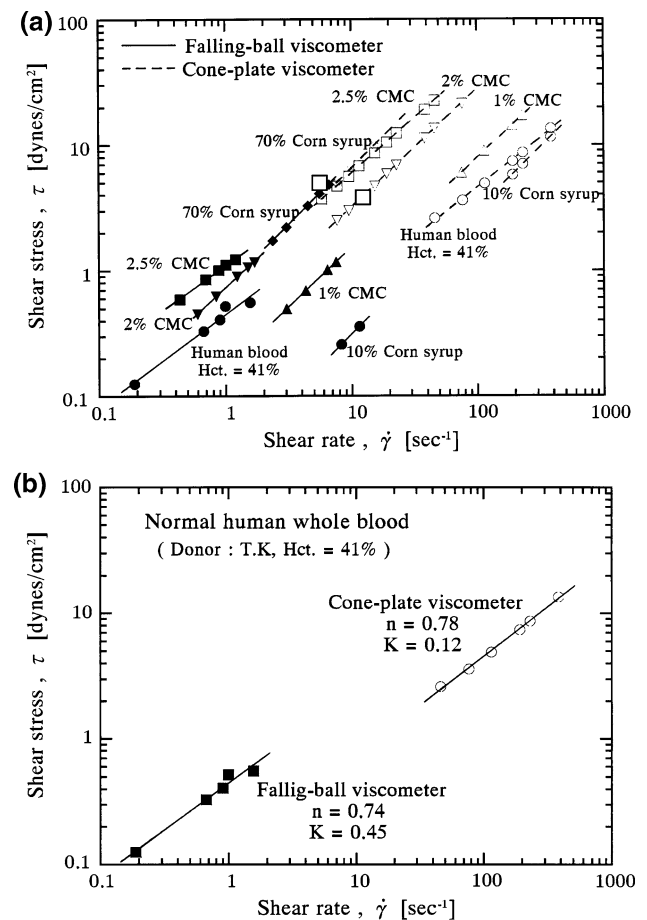
Measurements of the viscosity or flow property of various liquids were carried out as follows. A plastic test tube having a diameter of 1.6 cm and length of 10 cm was filled with 8–10 mL of liquid to be tested and left stand still until the temperature of the liquid reached a desired value that was the body temperature of 37 °C. Then after stirring the liquid gently and leaving stand still for 20 s, a solid spherical particle whose surface was prewetted with the same liquid was carefully introduced into the liquid from the center of the test tube by using a forceps so that no air bubble attached to the particle, and the position of the falling particle was detected as a function of time by an ultrasound echo probe located at the bottom of the test tube. From these data, the terminal velocity of the sphere  $U_{\infty}$  was calculated. Measurement was repeated at least eight times for one particle, and a mean value was obtained.

By using the terminal velocities obtained with several spheres together with the densities of the liquid and the spheres, and the diameters of the spheres, the value of shear stress  $\tau$  and shear rate  $\dot{\gamma}$  acting on each sphere were calculated and plotted one by one on a logarithmic graph paper to obtain flow property of the liquid tested.

Measurements of viscosity or flow property of a liquid were all ways carried out by both the falling-ball viscometer constructed in the present study and a cone-plate viscometer, and by comparing the values obtained by these two different apparatuses, we investigated the relationship between them.

## RESULTS

Figure 2a shows the flow property of corn syrups, CMC solutions, and human whole blood obtained by using our newly constructed falling-ball viscometer and a conventional cone-plate viscometer. As evident



**FIGURE 2.** (a) Flow property of various liquids obtained with the falling-ball viscometer and a cone-plate viscometer. Note that, in all the cases, measured values are aligned on a straight line with a slope of 45° or less, suggesting that the flow property of these liquids could be expressed by a power law model. (b) Flow property of human whole blood obtained with the falling-ball viscometer and a cone-plate viscometer. The values of rheologic constants  $n$  and  $K$  calculated by approximating the measured values with straight lines and expressing by a power law model are also shown in the figure. Note that, the value of  $K$  obtained with a cone-plate viscometer is much smaller than that obtained with the falling-ball viscometer.

from the figure, in all the cases, measured values were aligned on one straight line with a slope  $\leq 45^\circ$ , suggesting that the flow property of these liquids could be expressed by a power law model as  $\tau = K\gamma^n$  where  $\tau$  is shear stress,  $\gamma$  is shear rate, and  $K$  and  $n$  are constants. This made it possible to obtain the values of the rheologic constants  $n$  and  $K$  that are not affected by both the time elapsed from the beginning of measurement and the magnitude of shear rate and exhibit an intrinsic property of the fluid from the slope of the straight line and the intersection at  $\log \gamma = 1$ , respectively. Table 1 shows the summary of the rheologic constants obtained for all the liquids by the method described above. From these results, it was made clear that in the case of corn syrups,  $n = 1.00$ , indicating that it is a Newtonian fluid. In the case of CMC solutions and human whole blood,  $n < 1.00$ , showing that they are non-Newtonian fluids. The value of  $n$  for these fluids became smaller with increasing the concentration, indicating that non-Newtonian behavior was enhanced with increasing the concentration. It was also found by comparing the values obtained with our falling-ball viscometer with those obtained with a

cone-plate viscometer that in the case of cone syrups that was found to be Newtonian fluids, the values of rheologic constants obtained by both methods were the same, while in the cases of CMC solutions and human whole blood that were found to be non-Newtonian fluids, the values of  $n$  and  $K$  were, respectively, always smaller and larger than those obtained with the cone-plate viscometer.

Figure 2b and Table 2 show, respectively, the flow property of human whole blood obtained with the falling-ball viscometer and a cone-plate viscometer and the values of rheologic constants obtained from nine healthy donors.

Here, since the equation which describes the flow property of power law model fluids can be rewritten as  $\tau = K\gamma^n = K\gamma^{n-1}(\gamma) = \mu_a\gamma$ , if we know the values of the rheologic constants  $n$  and  $K$ , it is possible to obtain apparent viscosity of the fluid at any shear rate from  $\mu_a = K\gamma^{n-1}$ .

Table 3 shows a portion of raw data on physical properties of the sphere and blood, and various measured and calculated values used to obtain the rheologic constants and apparent viscosity of blood. The values of apparent viscosity of whole blood calculated by using the mean values of  $n$  and  $K$  obtained for blood of nine healthy donors (cf. Tables 2 and 3) by the falling-ball viscometer and a cone-plate viscometer are plotted as a function of shear rate in Fig. 3a. Here, the thick lines are the mean values of nine subjects, and the upper limit and lower limit of shaded areas indicate, respectively, the highest and the lowest values obtained for blood of nine donors. As evident from the figure, the apparent viscosity of blood obtained with the falling-ball viscometer is much higher than that obtained with a cone-plate viscometer. Here comparison of the mean values of rheologic constants for blood of healthy donors shown in Table 3 and Fig. 3a shows that variation of the values of  $K$  obtained with the falling-ball viscometer is much greater than that

**TABLE 1. Comparison of rheologic constants of various fluids obtained with a cone-plate viscometer and a falling-ball viscometer.**

Fluids	Viscometer			
	Cone-plate viscometer		Falling-ball viscometer	
	$n$	$K$	$n$	$K$
10% Corn syrup	1.00	0.030	1.00	0.031
70% Corn syrup	1.00	0.72	1.00	0.73
1.0% CMC	0.95	0.09	0.95	0.17
2.0% CMC	0.94	0.36	0.92	0.72
2.5% CMC	0.88	0.78	0.73	1.09
Human blood (Hct. 44%)	0.81	0.13	0.74	0.70

**TABLE 2. Comparison of the values of rheologic constants of human whole blood obtained with a cone-plate viscometer and a falling-ball viscometer.**

Blood donor	Hct. (%)	Cone-plate viscometer		Falling-ball viscometer	
		$n$	$k$	$n$	$k$
A	41	0.78	0.12	0.74	0.45
B	33	0.87	0.08	0.72	0.50
C	37	0.81	0.11	0.73	0.63
D	40	0.78	0.17	0.70	0.83
E	50	0.83	0.13	0.75	0.81
F	52	0.81	0.17	0.78	0.83
G	46	0.83	0.13	0.74	0.66
H	50	0.84	0.11	0.75	0.76
I	48	0.77	0.19	0.75	0.83
Mean $\pm$ SD	44 $\pm$ 6.2	0.81 $\pm$ 0.03	0.13 $\pm$ 0.03	0.74 $\pm$ 0.02	0.70 $\pm$ 0.14

**TABLE 3. Physical properties, measured values and calculated rheologic constants of normal human whole blood.**

Blood donor	Hct. (%)	Sphere diameter $d$ (cm)	Sphere density $\rho_s$ (g/cm <sup>3</sup> )	Blood density $\rho_b$ (g/cm <sup>3</sup> )	Distance $L$ (cm)	Time $t$ (s)	Shear stress $\tau$ (dynes/cm <sup>2</sup> )	Velocity $U_\infty$ (cm/s)	Shear rate $3U_\infty/d$ (1/s)	$\mu_a$ (cP)	Rheologic constants
S.W	40	0.167	1.092	1.065	1.037	19.94	0.736	0.052	0.934	77	$K = 0.83 \quad n = 0.70$
		0.161	1.098		1.037	17.88	0.868	0.058	1.081	80	
		0.181	1.076		0.593	32.41	0.333	0.016	0.265	127	
		0.185	1.108		1.037	6.60	1.300	0.108	1.751	74	
		0.192	1.081		1.037	33.45	0.502	0.031	0.484	103	
Y.K	37	0.176	1.080	1.055	1.043	15.12	0.719	0.069	1.176	61	$K = 0.63 \quad n = 0.73$
		0.121	1.078		1.043	41.72	0.455	0.025	0.620	73	
		0.130	1.081		1.043	28.19	0.552	0.037	0.854	65	
		0.166	1.080		1.043	17.38	0.678	0.060	1.084	63	
		0.126	1.081		1.043	31.61	0.535	0.033	0.786	67	
T.K	41	0.161	1.068	1.047	0.903	10.80	0.552	0.084	1.560	35	$K = 0.45 \quad n = 0.74$
		0.0959	1.073		0.516	17.98	0.407	0.029	0.898	45	
		0.233	1.050		0.645	43.60	0.125	0.015	0.189	66	
		0.167	1.066		0.516	9.32	0.518	0.055	0.995	51	
		0.155	1.060		0.516	15.00	0.329	0.034	0.667	46	
J.S	50	0.167	1.066	1.056	1.037	76.25	0.282	0.014	0.246	115	$K = 0.81 \quad n = 0.75$
		0.161	1.073		1.037	45.09	0.447	0.023	0.429	105	
		0.181	1.062		0.593	65.11	0.177	0.009	0.151	123	
		0.185	1.086		1.037	13.74	0.907	0.076	1.224	74	
		0.192	1.067		1.037	54.29	0.345	0.019	0.298	118	
T.I	48	0.161	1.068	1.052	0.506	24.18	0.421	0.021	0.392	107	$K = 0.83 \quad n = 0.75$
		0.167	1.066		0.633	37.30	0.382	0.017	0.305	117	
		0.155	1.062		0.506	42.55	0.253	0.012	0.231	114	
		0.0959	1.073		0.506	56.32	0.329	0.009	0.281	117	
		0.181	1.067		0.506	17.93	0.444	0.029	0.468	96	

obtained with a cone-plate viscometer. However, this is not due to the errors caused by the measurement since the same flow property (a straight line) shown in Fig. 2 was obtained for all the blood samples. It is likely that differences in concentration and aggregability of red cells are responsible for this. Therefore we tested the effects of hematocrit and removal of plasma proteins that cause aggregation of red cells on flow property and the values of rheologic constants  $n$  and  $K$ .

Figure 3b and Table 4 show, respectively, the flow properties of whole blood of one donor, and the values of rheologic constants of whole blood of 10 donors obtained with the falling-ball viscometer by varying its hematocrit between 10 and 60%. As evident from these figure and Table,  $n$  takes values smaller than 1.00 that corresponds to a Newtonian fluid, and it becomes smaller with increasing hematocrit, indicating that non-Newtonian behavior is enhanced with increasing hematocrit. Regarding the value of  $K$ , it increased with increasing the hematocrit, implying that apparent viscosity of blood is determined mainly by the value of  $K$ .

Figure 3c shows the effect of shear rate on apparent viscosity of human whole blood with various hematocrits. Here the values of apparent viscosity for blood with various hematocrits were calculated by using the mean values of  $n$  and  $K$  given in Table 4 for blood obtained from 10 healthy donors. It was found that the

apparent viscosity of blood increases with increasing hematocrit, and it increased exponentially with going to low shear rate region.

From the results presented hitherto, it was made clear that if we compare the values of rheologic constants obtained with a cone-plate viscometer with those obtained with the falling-ball viscometer, the value of  $n$  is larger and the value of  $K$  is smaller. As a possible cause of that, it was considered that as described earlier, in the case of a cone-plate viscometer, since blood is in flow and always subjected to shear stress, the red cells that are forming rouleaux in plasma are gradually disaggregated and dispersed one by one with increasing shear rate, and because of that the value of  $n$  approaches to 1.00 which corresponds to the value for Newtonian fluids. Therefore to confirm it, we prepared blood samples (washed red cell suspension) in which plasma proteins such as fibrinogen and globulin were removed by washing red cells with Tyrodes-albumin solution so that no aggregate (rouleau) formed, and obtained rheologic constants with both the falling-ball viscometer and a cone-plate viscometer and compared the results.

Figure 4a and Table 5 show, respectively, the flow property of a 50% washed red cell suspension prepared from blood of one donor and mean values of rheologic constants obtained for four samples by the two

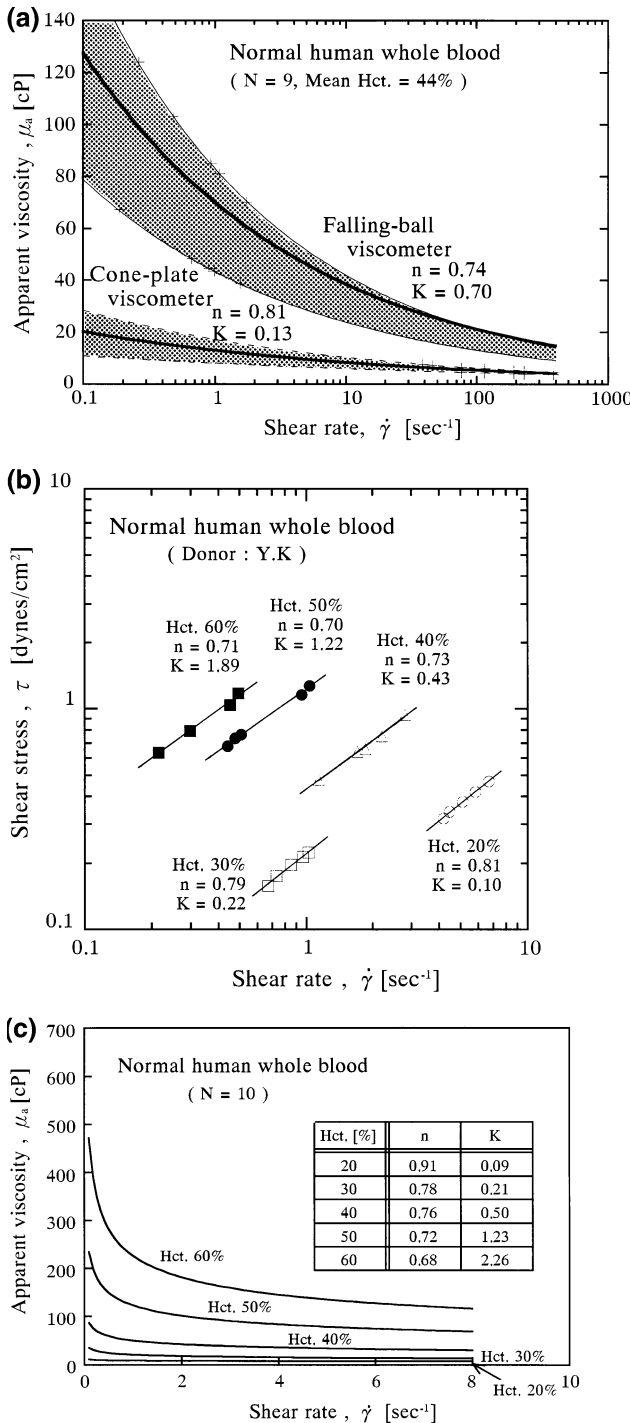
different apparatuses. As it is evident from the figure, in the case of a suspension of red cells from which plasma proteins were removed so that no rouleau formed, the values of rheologic constants obtained with the two different apparatuses were almost the same, indicating that the large difference in the value of  $K$  observed in whole blood was due to the formation of red cell aggregates (rouleaux). Therefore, it is pos-

sible to detect with high sensitivity the changes in viscosity caused by the formation of rouleaux by using the falling-ball viscometer.

Figure 4b shows the flow property and calculated rheologic constants of washed red cell suspensions having various hematocrits obtained with the falling-ball viscometer. Comparison of the results with those shown in Fig. 3b for whole blood shows that at any hematocrit, the value of  $K$  of washed red cell suspension is much smaller than that of whole blood, indicating that the presence of plasma proteins such as fibrinogen and globulin that are known to cause aggregation of red cells greatly affect the viscosity of whole blood.

Figure 5 shows the plot of mean values and standard deviations of rheologic constants  $n$  and  $K$  obtained with the falling-ball viscometer for whole blood and washed red cell suspensions with various hematocrits that were prepared from blood taken from four healthy donors as a function of the hematocrit. From the figure, it was found that the effect of plasma proteins on the value of  $n$  that indicates the degree of non-Newtonianity of the fluid appears mainly at low hematocrit, while its effect on the value of  $K$  that determines the magnitude of the viscosity of blood appears at high hematocrit and it becomes more prominent with increasing hematocrit.

In the present study, sodium citrate was used as an anticoagulant to take blood. However, in actual clinical practice, EDTA and heparin are used. Therefore, we also tested the effects of these anticoagulants on the flow property and the viscosity of blood. It was found that there was no statistically significant difference among the values of rheologic constants obtained with both the falling-ball viscometer and a cone-plate



◀ **FIGURE 3.** (a) Plot of apparent viscosity of human whole blood calculated by using the mean values of  $n$  and  $K$  obtained for blood of nine healthy donors with the falling-ball viscometer and a cone-plate viscometer as a function of shear rate. The thick lines are the mean values of nine subjects, and the upper limit and lower limit of shaded areas indicate, respectively, the highest and the lowest values obtained for blood of nine donors. As evident from the figure, the apparent viscosity of blood obtained with the falling-ball viscometer is much higher than that obtained with a cone-plate viscometer that uses a steady flow. (b) Flow property of human whole blood of one donor obtained with the falling-ball viscometer by varying its hematocrit between 10 and 60%. Note that  $n$  takes values smaller than 1.00 that corresponds to a Newtonian fluid, and it becomes smaller with increasing hematocrit, indicating that non-Newtonian behavior is enhanced with increasing hematocrit. The value of  $K$  increases with increasing the hematocrit, implying that apparent viscosity of blood is determined mainly by the value of  $K$ . (c) Plot of apparent viscosity of human whole blood calculated by using the mean values of  $n$  and  $K$  obtained for blood of 10 healthy donors with the falling-ball viscometer as a function of shear rate, showing the effects of hematocrit on apparent viscosity.

TABLE 4. Values of rheologic constants of normal human whole blood obtained with a falling-ball viscometer.

Blood donor	Hct. 20%		Hct. 30%		Hct. 40%		Hct. 50%		Hct. 60%	
	<i>N</i>	<i>K</i>	<i>n</i>	<i>K</i>	<i>n</i>	<i>K</i>	<i>n</i>	<i>K</i>	<i>n</i>	<i>K</i>
Y.E	0.89	0.09	0.79	0.18	0.76	0.45	0.75	0.95	—	—
S.W	0.90	0.10	0.76	0.22	0.76	0.57	0.71	1.98	—	—
K.S	0.91	0.13	0.75	0.22	0.76	0.43	0.73	1.27	0.70	1.96
N.G	0.92	0.09	0.75	0.18	0.75	0.48	0.74	1.17	0.71	1.58
T.K	0.97	0.05	0.80	0.23	0.78	0.46	0.70	1.28	0.69	2.45
T.N	—	0.07	0.82	0.16	0.72	0.71	0.69	1.31	0.66	2.74
M.T	0.90	—	—	—	0.79	0.51	0.75	0.97	0.70	1.61
T.I	0.90	0.08	0.76	0.23	0.75	0.43	0.72	1.11	0.64	2.80
H.S	0.96	0.07	0.80	0.25	0.76	0.56	0.69	1.06	0.64	3.08
Y.K	0.81	0.10	0.79	0.22	0.73	0.43	0.70	1.22	0.71	1.89
Mean ± SD	0.91 ± 0.04	0.09 ± 0.02	0.78 ± 0.03	0.21 ± 0.03	0.76 ± 0.02	0.50 ± 0.09	0.72 ± 0.02	1.23 ± 0.29	0.68 ± 0.03	2.26 ± 0.58

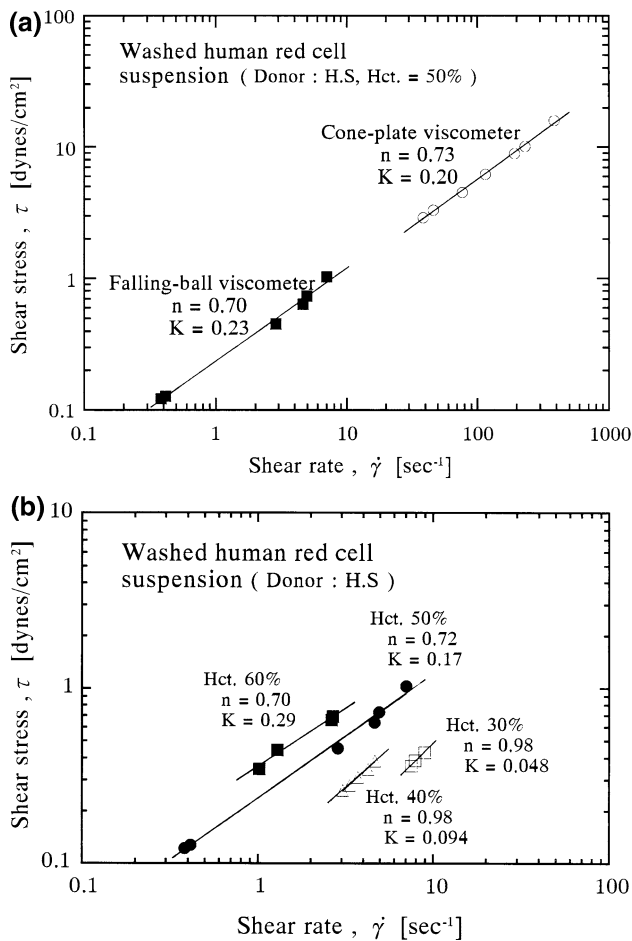


FIGURE 4. (a) Flow property of a 50% washed red cell suspension prepared from blood of one donor obtained with the falling-ball viscometer and a cone-plate viscometer. Note that the values of rheologic constants obtained with the two different apparatuses are almost the same, indicating that the large difference in the value of *K* observed in whole blood is due to the formation of red cell aggregates (rouleaux). (b) Flow property of washed red cell suspensions prepared from blood of one donor obtained with the falling-ball viscometer, showing the effect of hematocrit on the values of rheologic constants *n* and *K*.

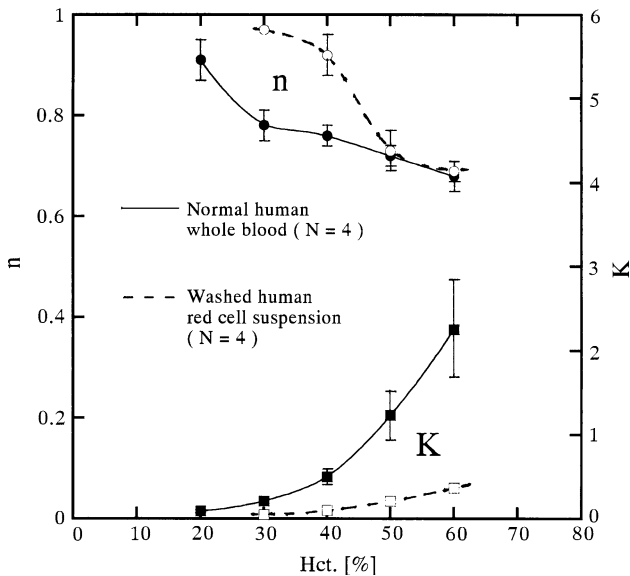
viscometer for blood anticoagulated with sodium citrate, EDTA, and heparin.

## DISCUSSION

The present work was carried out to develop a new method to obtain the flow property of non-Newtonian fluids such as blood and suspensions of polymer materials. By the development of the falling-ball viscometer based on a new principle of measurement that used ultrasound echo, it became possible to obtain rheologic constants that exhibit an intrinsic property of the fluid and calculate apparent viscosity of the fluid as a function of shear rate. Using the new apparatus, we obtained flow property of various liquids and compared the results with those obtained with a cone-plate viscometer that is based on a steady flow. It was found that the apparent viscosity of blood obtained with a cone-plate viscometer was much lower than that obtained with the falling-ball viscometer. It was considered that in the case of the falling-ball viscometer, since the sphere falling slowly in a quiescent liquid comes in contact or interacts with only limited number of fluid elements (blood cells and plasma) existing around it and only in short times, the fluid elements are subjected to shear stress which is very low and only during very short times compared with the case of rotational viscometers that are based on a steady flow. Therefore, the rheologic constant or viscosity obtained by this new method is regarded to correspond to the viscosity of a liquid at time  $t = 0$  as measured by using a rotational viscometer. By contrast, in the case of a cone-plate viscometer, the liquid is in flow and all the fluid elements are subjected to shear stresses. Therefore, it is considered that the rheologic constant or viscosity obtained by this method is the final value that reflects the equilibrium state of aggregation,

**TABLE 5. Comparison of the values of rheologic constants of washed human red cell suspensions obtained with cone-plate and falling-ball viscometer.**

Blood donor	Hct. (%)	Cone-plate viscometer		Falling-ball viscometer	
		<i>N</i>	<i>K</i>	<i>n</i>	<i>K</i>
Y.K	50	0.70	0.19	0.72	0.17
H.S	50	0.73	0.20	0.70	0.23
T.I	50	0.78	0.12	0.78	0.19
T.K	50	0.75	0.16	0.72	0.24
Mean $\pm$ SD	50	0.74 $\pm$ 0.03	0.17 $\pm$ 0.04	0.73 $\pm$ 0.04	0.21 $\pm$ 0.03



**FIGURE 5. Plot of the mean values and standard deviations of rheologic constants  $n$  and  $K$  obtained with the falling-ball viscometer for whole blood and washed red cell suspensions with various hematocrits that were prepared from blood taken from four healthy donors as a function of the hematocrit. Note that the effect of the presence of plasma proteins that cause aggregation of red cells on the value of  $n$  appears mainly at low hematocrit, while its effect on the value of  $K$  that determines the magnitude of the viscosity of blood appears at high hematocrit and it becomes more prominent with increasing hematocrit.**

deformation, orientation, and sedimentation of blood cells at time  $t = \infty$  under a certain shear rate applied. It was also found that the effect of the removal of plasma proteins such as fibrinogen and globulin that caused the formation of red cell aggregates (rouleaux) on the values of rheologic constants and apparent viscosity calculated for blood of healthy donors obtained with the falling-ball viscometer was much greater (especially the value of  $K$ ) than that obtained with a cone-plate viscometer. Therefore, it is possible to detect with high sensitivity the changes in blood viscosity caused by the formation and destruction of aggregates (rouleaux) of red cells depending on the increase or decrease of the concentration of fibrinogen and globulin by the falling-ball viscometer.

In our present study, we obtained rheologic constants and apparent viscosity for only blood of healthy volunteers whose viscosities measured with a cone-plate viscometer were relatively low. However, it has been reported that in some diseased states such as polycythemia, multiple myeloma, myocardial infarction, sickle cell disease, and acute stroke,<sup>2,3,5,7</sup> blood viscosity and ESR show abnormally high values due to the increase in the number of red cells, concentration of plasma proteins such as fibrinogen and globulin that cause aggregation of red cells, and deformability of red cells. Therefore, if we carry out measurements of rheologic constants and apparent viscosity for such blood obtained from patients with the falling-ball viscometer, we could detect the abnormality of blood more easily and sensitively than measuring with a rotational viscometer such as a cone-plate and coaxial-cylinder viscometers that are based on a steady flow. The new falling-ball blood viscometry could be used clinically as a substitute for the measurement of ESR presently used for screening of patients by detecting the abnormality of blood viscosity. It could be also used to study the effects of drug therapy and treatments such as defibrinogenation, plasmapheresis, and hemodilution on patients suffering from various diseases.

#### ACKNOWLEDGMENTS

The work was supported in part by The Suzuken Memorial Foundation. The authors thank Drs. Katsuyuki Yamamoto and Makoto Takahashi of the Graduate School of Information Engineering at Hokkaido University in Sapporo, Japan for their help in designing the falling-ball viscometer.

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