Rheological properties of human blood plasma – A comparison of measurements with three different viscometers

C. Graf and J.-P. Barras*

Department of Physiology, University of Basel, Vesalgasse 1, CH-4051 Basel (Switzerland), 12 October 1978

Summary. Human plasma viscosity was measured in capillary tube, cone-plate and Couette viscometers. The measurement of the viscosity at very low shear rates showed that plasma is a non-Newtonian fluid with a pseudoplastic rheological behaviour. The importance of this phenomenon for the microcirculation is discussed.

Plasma viscosity is an important factor for the pressure-flow relationship in small blood vessels and especially in capillaries[1,2], where the relative viscosity (whole blood viscosity/plasma viscosity) approaches 1.0 (Fahraeus-Lindqvist effect[3]). For this reason, studies of rheological properties of blood plasma are very important to elucidate the flow dynamics of microcirculation.

Many authors consider plasma to behave as a Newtonian fluid[4-6] which is characterized by a constant viscosity being independent of the shear stresses prevailing. This assumption is partly based on the fact that many of the available viscometers do not produce shear rates low enough to detect variations of viscosity as a function of shear rate. Furthermore, some of the viscometers used have a markedly reduced accuracy at low levels of viscosity such as that of plasma[7]. Recently it has been discussed that plasma cannot be considered to be a Newtonian fluid[8,9]. Actually, this could be predicted by the fact that plasma is a heterogenous fluid, and that it has viscoelastic properties[8] and therefore its viscosity should be 'anomalous'.

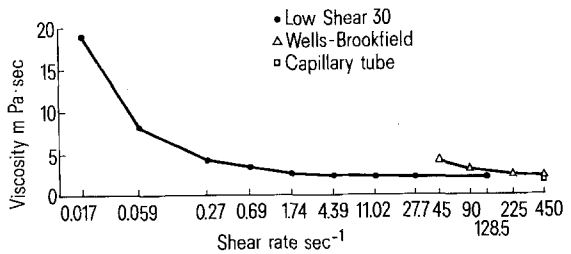
In order to demonstrate the non-Newtonian rheological behaviour of plasma, we have used a recently developed Couette viscometer (Contraves Low Shear 30) which allows viscosity measurements at especially low shear rates. Charm and Kurland have observed discrepancies in measuring whole blood viscosity with Couette, cone-plate and capillary tube viscometers[10]. Since blood plasma, like whole blood, is a heterogenous non-Newtonian fluid, it is important to compare the values of plasma viscosity obtained by measurements with these 3 different types of viscometers. In the present study we have measured the variation of plasma viscosity as a function of a large range of shear rates using various types of viscometers.

Material and methods. Plasma samples of 13 normal male subjects aged 20–39 were measured with 3 different viscometers, covering a shear range from 450 sec^{-1} down to 0.017 sec^{-1}. Approximately 20 ml of blood were withdrawn by venipuncture in the morning after at least 12 h of fasting, and measurements were made within the following 6 h. Anticoagulation was assured by Heparin 50 U-USP per ml whole blood. The viscometers used allow measurements of plasma viscosity at the different laminar shearings: 1. A telescopic shearing occurring in natural flow with a capillary tube viscometer[11]. The length of the capillary was 20 cm and its diameter 0.099 cm. 2. A torsional shearing in cone-plate flow with a LVT Wells-Brookfield Micro Viscometer (0.8° cone, 0.5 cm^3 sample). 3. A rotational shearing in Couette flow with a Contraves Low Shear 30 viscometer with a MGW Lauda RC 3 thermostabilisator which held the temperature constant within ±0.01 °C.

All measurements were performed at a temperature of 20 °C. To obtain a steady state of flow, the time for the initially measured shear rate of 450 sec^{-1} in the Wells-Brookfield viscometer was 2 min, then 45 sec for every lower level. In the Low Shear 30 we started at the lowest shear rate of 0.017 sec^{-1}. The measuring times were for 0.017 sec^{-1}: 90 min, for 0.059 sec^{-1}: 45 min, for 0.27 sec^{-1}: 15 min, for 0.69 sec^{-1}: 2 min, and for the others 30 sec. The measuring cup of the instrument was filled with plasma up to the rim to minimize influences of surface tension[1,8].

Results. The table contains the values of the viscosities obtained at various shear rates measured with the three different viscometers described. The figure shows graphically the variation of viscosity as a function of the shear rate. The increase of viscosity is evident at shear rates from 10 sec^{-1} downwards (measurements in the Low Shear 30). As shown in table and figure, the viscosity readings at 450 sec^{-1} in the cone-plate viscometer were 20% higher than in the capillary tube viscometer. The mean value of the viscosity in Couette Low Shear 30 at 125 sec^{-1} is 15% higher than those of capillary tube at 450 sec^{-1}. This comparison was made at high shear rates, where viscosity is constant over a large range of shear.

Discussion. Chmiel[9] has demonstrated that human plasma behaves like a typical non-Newtonian fluid under turbulent flow conditions. According to the present results, plasma cannot be considered to be a Newtonian fluid even under laminary flow conditions, the plasma viscosity not being a material constant. On the contrary, plasma shows a pseudo-



Plasma viscosity (m Pa·sec) as a function of shear rate (sec^{-1}), measured with 3 different viscometers: capillary tube viscometer (□), cone-plate Wells-Brookfield Micro Viscometer (△) and Contraves Low Shear 30 Couette Viscometer (●).

Mean value of plasma viscosity at different shear rates, measured with different viscosimeters. Temperature = 20 °C, n = 13

Shear rates in sec^{-1}	Mean values ± SD in m Pa · sec (=cP)
Capillary tube	
450	1.84± 0.09
Wells-Brookfield	
450	2.23± 0.13
225	2.46± 0.28
90	3.06± 0.70
45	4.13± 1.38
Low Shear 30	
128	2.14± 0.11
27.7	2.14± 0.11
11.02	2.19± 0.12
4.39	2.34± 0.14
1.74	2.60± 0.20
0.69	3.38± 0.64
0.27	4.35± 0.83
0.059	8.16± 3.17
0.017	19.15±12.71

plastic behaviour; its viscosity decreases as the shear rate increases (anomalous viscosity). Furthermore, the non-Newtonian behaviour may explain the different values of viscosity obtained with measurements using different flow patterns. Therefore it is important to determine exactly the flow patterns and the shear rates when values of plasma viscosity measurements are compared and interpreted.

The results obtained with the Wells-Brookfield cone-plate viscometer show the poor accuracy of this type of viscometer at low viscosity levels[7,12]. Although care has been taken in our investigations to minimize the influence of surface tension, which might affect the readings in Low Shear 30[4,8], there is a considerable standard deviation at the lowest shear rates (0.017 and 0.059 sec^{-1}) which might be due to the particular viscoelastic properties of the macromolecules in plasma. In order to characterize the rheological properties of plasma, it is necessary to perform measurements of its viscosity at very low shear rates, where the viscosity is anomalous. Sequential measurements of red blood cell velocity in nailfold capillaries of man[13] demonstrated that very low velocities do occur intermittently in the healthy subject. Since plasma viscosity is a prime determinant of the flow in small blood vessels and in capillaries, its measurement at different shear rates will be important for the understanding of blood flow regulation in microcirculation.

* We are grateful to OM Laboratories, Geneva, for providing the Contraves Low Shear 30 viscometer.

1 J.-P. Barras, Helv. med. Acta *34*, 468 (1968).
2 H. Schmidt-Schönbein, Proc. int. Un. physiol. Sci. *12*, 97 (1977).
3 R. Fahraeus and T. Lindqvist, Am. J. Physiol. *96*, 562 (1931).
4 F.R. Spinelli and C.D. Meier, Biorheology *11*, 301 (1974).
5 B. Folkow and E. Neil, in: Circulation, p.25, Oxford University Press, New York 1971.
6 E.W. Merrill, G.C. Cokelet, A. Britten, R.E. Wells, Circulation Res. *13*, 48 (1963).
7 E.B. Vadas and E.A. Hosein, Can. J. Physiol. Pharmac. *56*, 245 (1978).
8 C.D. Meier and F.R. Spinelli, Proc. VIIth Int. Congr. Rheology, p.318. Chalmers University of Technology, Gothenburg, Sweden, 1976.
9 H. Chmiel, Biorheology *11*, 87 (1974).
10 S.E. Charm and G.S. Kurland, J. appl. Physiol. *25*, 786 (1968).
11 J.-P. Barras, in: Ecoulement stationnaire d'une suspension d'érythrocytes humains au travers d'un tube de section circulaire uniforme, p. 19. Imprimerie Saint Paul, Fribourg 1967.
12 P.R. Rand, E. Lacombe, H.E. Hunt and W. Austin, J. appl. Physiol. *19*, 118 (1964).
13 A. Bollinger, P. Butti, J.-P. Barras, H. Trachsler and W. Siegenthaler, Microvasc. Res. *7*, 61 (1974).

Evidence for a neuronal release of isotopically labelled γ-amino-n-butyric acid (GABA) from the rat dorsal medulla in vivo[1]

J.A. Assumpção, N. Bernardi, C.G. Dacke and N. Davidson

Department of Physiology, Marischal College, University of Aberdeen, Broad Street, Aberdeen AB9 1AS (Scotland), 7 June 1978

Summary. High potassium and electrical stimulation consistently increase efflux of labelled GABA from the in vivo superfused rat dorsal medulla in a calcium-dependent fashion. The depolarizing alkaloid, veratridine, also evokes a large increase in efflux of labelled GABA. These data strongly suggest release from a neurotransmitter pool in this region.

There is considerable pharmacological evidence that the inhibitory amino acid GABA, or a similar substance, is an important neurotransmitter in regions of the dorsal medulla such as the dorsal column nuclei[2-4]. A logical step in the positive identification of GABA as a neurotransmitter in this region would be the demonstration of its neuronal release from intact (i.e. in vivo) tissue. There are, however, conflicting reports as to whether high potassium stimulation does[5] or does not[6] increase the efflux of labelled GABA from an in vivo dorsal medulla preparation. We have reinvestigated this problem using veratridine, electrical and high potassium stimuli, all 3 of which have in common a depolarizing action on neuronal tissues. A part of these data has been published previously in abstract form[7].

Materials and methods. Adult rats were anaesthetized with a 1% chloralose–10% urethane solution (8 ml kg^{-1} i.p.) and the dorsal surface of the medulla oblongata exposed. Approximately 2 h before the start of the experiment the animal was given an i.p. injection of amino-oxyacetic acid (20 mg kg^{-1}) to reduce GABA catabolism. A small acrylic superfusion chamber (internal volume 30 µl) was sealed in place concentric with that part of the cuneate nucleus providing the maximum ipsilateral forepaw evoked potential. Any GABA pools were labelled via their reuptake systems by 60 min exposure of the pial surface to cerebrospinal fluid (C.S.F.) containing either [1-^{14}C] labelled GABA (specific activity 2 µCi ml^{-1}, molar concentration 4.1×10^{-5} M) or [2,3-^{3}H] GABA (specific activity 10 µCi ml^{-1}, molar concentration 1.8×10^{-7} mM).

In control experiments the non-neurotransmitter amino acid L-[G-^{3}H] leucine (specific activity 10 µCi ml^{-1}, molar concentration 4×10^{-5} mM) was used. After a 60-min labelling period of closed cycle superfusion with the isotope (total volume 400 µl) the isotope was removed and superfusion continued at 50 µl min^{-1} with surrogate C.S.F. All solutions were buffered with Tris to pH 7.4 and osmolalities matched before use at 315 mOsm kg^{-1} H_2O. 5-min fractions of superfusate were collected serially in glass vials containing 6 ml Multisol II (Intertechnique Ltd) and 0.1 ml distilled H_2O and radioactivity estimated by liquid scintillation spectrometry. Counting efficiency was constant for ^{14}C isotopes but quench correction was routinely carried out for ^{3}H isotopes.

Chromatographic analyses were carried out on thin layer cellulose plastic plates using standard ascending chromatography.

Results and discussion. The figure, A, shows the spontaneous efflux of [1-^{14}C] GABA from the in vivo superfused dorsal medulla. When plotted semi-logarithmically this efflux consists of 2 or more phases for which lines of best fit have been computed by the least squares method. Although