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The Value of Comparative Hemorheological Studies

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Editorial

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EDITORIAL NOTE

Comparative studies are useful tools to investigate structure-function relationships in medicine and biology if the animal models are well selected. The rheology of many animal blood suspensions has been investigated, and data are available concerning RBC membrane properties [1,2]. Animal models play a role in basic cardiovascular research, but also in the development of medical devices or in the forensic field of bloodstain pattern analysis when human blood is unavailable for ethical or practical reasons. Knowing the behavior of animal blood under different flow conditions is therefore crucial for the study outcome; at best, the animal blood properties are similar to those of the human standard. Comparability is achieved if there is a match in intrinsic (deformability, surface properties) and extrinsic (size, shape) RBC properties and in the coupling between blood cells and blood plasma. At perfect comparability the flow resistance would be the same, but having only the same hematocrit is not enough. Nature has evolved so many different RBC phenotypes for the same physiological task, so that blood rheology rather reflects a fingerprint for each species; a perfect match for all circumstances can never be found. The use of animal blood is therefore always a compromise, however the species selection can be optimized when defining under which flow condition the animal blood should match human blood.

Flow can be simple but also very dynamic and kinetically mixed. Driving forces can cover a wide range. For example, in artificial blood pumps, membrane oxygenators or dialysis systems, wall shear rates range from 100 s^{-1} up to

40,000 s^{-1} [3,4], and are far beyond any influence of cell-cell interactions. If the bulk behavior of blood in terms of shear viscosity is the limiting variable, species-specific differences become smaller and smaller with increasing shear rate, which makes it possible to select the animal model based on its availability and not solely on the blood flow property. The mechanical resistance of the cell membrane against high hydraulic forces, and the ability of the blood cells to cope with unphysiological flow conditions in artificial containments will dominate the species selection. But there are also conditions where blood does not flow as intensely (e.g. in dead zones in pumps, lateral flow extensions in vessels, blood droplets on tilted surfaces in a crime scene) or where shear rates are minimal (e.g. in the axial stream in laminar flow). Under such conditions, the coupling issues (short ranged cell-plasma coupling to generate RBC rouleaux, or longe ranged cell-plasma-coupling to generate linearily ordered RBC-structures normal to the flow direction) take full effect and complicate the selection of the animal model (Figure 1). Especially the thixotropy of blood based on RBC aggregation carries the risk of phase segregation under shear flow. In the worst case, the developing shear bands lead to instabile flow [5]. Due to the pronounced aggregability of equine RBCs, inhomogeneities in the bulk sample must be expected with time (due to shear banding and RBC sedimentation; which one occurs depends on the kind of flow), which makes horse blood unsuitable for experimental studies in which healthy human blood should be simulated [6]. A so far unexplored feature is the species-specific behavior of blood in contact with artificial walls. On artificial surfaces such as steel wall slip occurs when the wetting of the liquid is suboptimal [7]; viscosity and shear moduli become underestimated. A similar surface dependence has been reported recently with blood plasma [8]. The behavior of whole blood on artificial surfaces is more complex, as cells can selectively adhere to them [9,10], fundamentally altering the interface to blood when there is flow. Blood also wets different surfaces differently [11], e.g. in contact to a superhydrophobic surface a blood drop can almost form an oblate sphere (Figure 2). On sandblasted steel plates the contact angle of blood is increased in comparison to polished steel plates. Contact issues may be the reason for the observed discrepancy between the set pressure difference and the flow rate achieved through oxygenators [12,13]. The situation becomes further complicated if highly unsteady and mixed flows occur [14], like when blood impacts a wall in a gunshot crime scene. Consequently, shear viscosity and surface tension of blood drops cannot always explain the pattern of bloodstains.

Figure 1. Horse (+EDTA) blood in a microscopic shearing chamber (CSS450, Linkam Scientific Instruments, Salfords, UK) at 0.1 and 5 s^{-1} shear flow. While the RBC rouleaux are randomly arranged at rest, at slightly higher shear rates, long-range coopereativity triggered by blood plasma aligns them perpendicular to the shear direction.

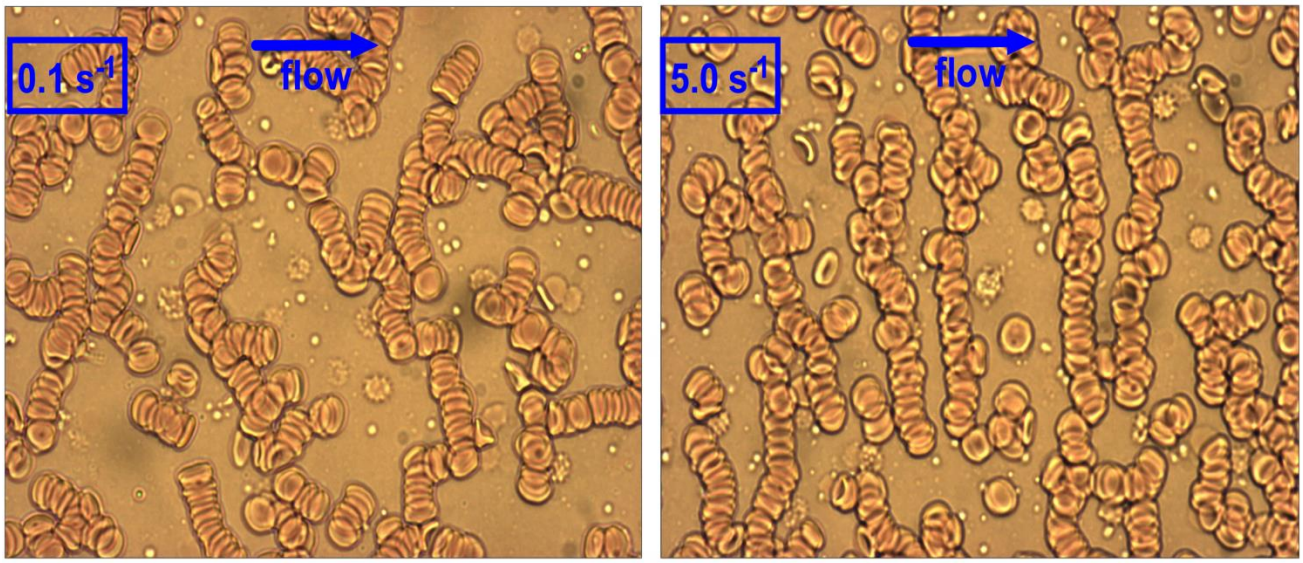
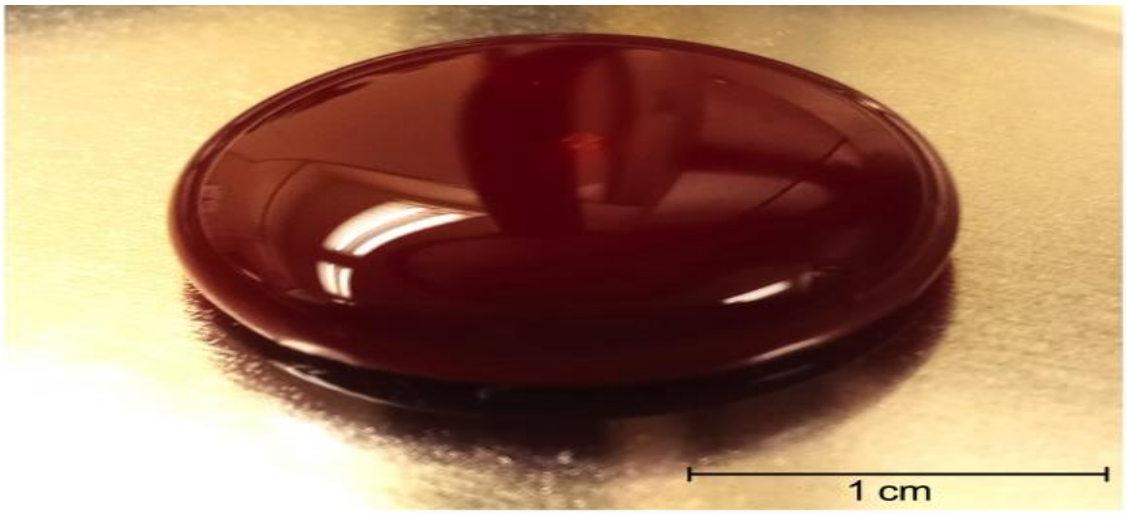


Figure 2. A drop of human blood (+EDTA, 40% hematocrit, 2 mL) on polydimethylsiloxane (PDMS) coating (Silicone Med-6015 (NuSil Technology, Carpienteria, CA, USA) on a disposable tinplate rheometer plate (Anton Paar, Graz, Austria)).



All these features and conditions are far from understood, as yet. But what has been elaborated sufficiently, is the *in-vitro* rheology of blood from those animal species that are regularly used in research. Simple and transient shear flows and conventional techniques were applied [6,15,16]. These studies enable the formulation of models of how a blood sample can be adjusted to a desired viscosity value by changing its hematocrit. Because shear thinning of blood is species-specific, these mathematical models must also account for the species-specific shear rate dependence of viscosity, and it will be difficult to define a blood type that is appropriate for all conditions. Good comparability exists between pig and human blood at high shear rates because pig RBC deformability is comparable to human: a change in hematocrit and/or temperature changes the viscosity of pig blood like it would

change the viscosity of human blood [6]. The aggregability of pig RBCs is also similar to that of human RBCs [1], so good agreement would be expected even at low shear rates. But pig blood yields at twice the shear stress of human blood at the same hematocrit [17], and blood viscosity shows a high hematocrit-dependence at 10 s^{-1} shear rate. Both features do not identify pig blood as the best match for applications at low wall shear rates. Especially intriguing is also the significant dependence of pig blood viscosity from the temperature [6].

To avoid the viscidity of pig blood at low temperature, one might think about using ruminant blood. Concerning the family of bovidae we took a closer look at sheep blood. Sheep RBCs are smaller and therefore more spherical than human RBCs. Their maximal elongation measured by ectacytometry is only two third that of human erythrocytes (EImax ≈ 0.4 compared to ≈ 0.6 in human) [18], which is the result of this sphericity. Not only do they deform less than human RBCs, they also hardly aggregate and sediment, making the suspension behavior more inert to changes in velocity. Generally speaking, sheep blood suspensions lack much of the complexity resulting from RBC aggregation. Therefore, the risk of phase separation is lower, but on the other hand the incidence for turbulences is higher. The viscosity of blood suspensions from sheep and human are surprisingly consistent at 10 s^{-1} shear rate concerning the dependence on hematocrit and temperature [6]. At shear rates lower than this value, the minute aggregability of sheep RBCs will come into play and comparability will no longer exist.

To sum up, a hematocrit fit between human and animal blood is not sufficient to derive the identical blood viscosity value over a broad range of shear rates. In order to establish a specific viscosity value in freshly drawn sheep, pig, and horse blood, one must first determine the representative shear rate range and test temperature at which the animal blood is to be used, and then the hematocrit can be changed using the formulas given to obtain a desired viscosity value [6]. The mathematical models of this study allow including many test temperatures (12°C-37°C) and hematocrit values (30%-60%) into this match.

The reader may allow a short note on rat blood, a species that is used in biomedical research and in toxicology testing in several OECD standards. Rat blood contains about one million platelets per microliter of blood (five times more than human blood), which not only alters hemostasis and the plasticity of blood clots, but also the viscosity and yield stress of the liquid blood [17-21]. Rats are a good model to study the role of platelets in blood flow in the presence of very low levels of RBC aggregation, but simulating human conditions is limited due to this unique fingerprint of rat blood hemorheology.

REFERENCES

1. Windberger U. Blood suspensions in animals. In: Dynamics of blood cell suspensions in microflows. CRC Press, Florida, United States, 2019. pp:371-419.
2. Baier D, et al. Red blood cell stiffness and adhesion are species-specific properties strongly affected by temperature and medium changes in single cell force spectroscopy. Molecules. 2021;26:2771. [Crossref] [Google Scholar] [PubMed]
3. Ronco C, et al. Blood and dialysate flow distributions in hollow-fiber hemodialyzers analyzed by computerized helical scanning technique. J Am Soc Nephrol. 2002;13:S53-S61. [Crossref] [Google Scholar] [PubMed]
4. Fraser KH, et al. A quantitative comparison of mechanical blood damage parameters in rotary ventricular assist devices: Shear stress, exposure time and hemolysis index. J Biomech Eng. 2012;134:081002. [Crossref] [Google Scholar] [PubMed]

5. Ovarlez G, et al. Phenomenology and physical origin of shear localization and shear banding in complex fluids. Rheologica Acta. 2009;48:831-844. [Crossref] [Google Scholar]
6. Ecker P, et al. Animal blood in translational research: How to adjust animal blood viscosity to the human standard. Physiol Rep. 2021;9:e14880. [Crossref] [Google Scholar] [PubMed]
7. Noirez L. Probing submillimeter dynamics to access static shear elasticity from Polymer Melts to Molecular Fluids. In: Polymers and polymeric composites: A reference series. Springer, New York, USA. 2020.
8. Windberger U, et al. Capillary-size flow of human blood plasma: Revealing hidden elasticity and scale dependence. J Biomed Mater Res A. 2022;110:298-303. [Crossref] [Google Scholar] [PubMed]
9. Angarska JK, et al. Red blood cell interaction with a glass surface. In: Ohki S (Eds) Cell and model membrane interactions. Springer, Boston, Massachusetts, USA. 1991. pp: 199-213.
10. George JN, et al. Adhesion of human erythrocytes to glass: The nature of the interaction and the effect of serum and plasma. J Cell Physiol. 1971;77:51-59. [Crossref] [Google Scholar] [PubMed]
11. Agathopoulos S, et al. Wettability and interfacial interactions in bioceramic-body-liquid systems. J Biomed Mater Res. 1995;29:421-429. [Crossref] [Google Scholar] [PubMed]
12. Broman LM, et al. Pressure and flow properties of cannulae for extracorporeal membrane oxygenation II: Drainage (venous) cannulae. Perfusion. 2019;34:65-73. [Crossref] [Google Scholar] [PubMed]
13. Broman LM, et al. Pressure and flow properties of cannulae for extracorporeal membrane oxygenation I: Return (arterial) cannulae. Perfusion. 2019;34:58-64. [Crossref] [Google Scholar] [PubMed]
14. Hodgkinson R, et al. Extensional flow affecting shear rheology: Experimental evidence and comparison to models. J Rheol. 2022;66:793. [Crossref] [Google Scholar]
15. Horner JS, et al. A comparative study of blood rheology across species. Soft Matter. 2021;17:4766-4774. [Crossref] [Google Scholar] [PubMed]
16. Windberger U, et al. A comparative approach to measure elasticity of whole blood by small amplitude oscillation. Rheol: open access. 2017;1:1-5.
17. Windberger U, et al. The role of plasma for the yield stress of blood. Clin Hemorheol Microcirc 2023;83:1-15.
18. Plasenzotti R, et al. Red blood cell deformability and aggregation behaviour in different animal species. Clin Hemorheol Microcirc. 2004;31:105-111. [Google Scholar] [PubMed]
19. Siller-Matula JM, et al. Interspecies differences in coagulation profile. Thromb Haemost. 2008;100:397-404. [Crossref] [Google Scholar] [PubMed]
20. Dibiasi C, et al. Viscoelasticity and structure of blood clots generated *in-vitro* by rheometry: A comparison between human, horse, rat, and camel. Clin Hemorheol Microcirc. 2018;69:515-531. [Crossref] [Google Scholar] [PubMed]
21. Windberger U, et al. Laboratory rat thrombi lose one-third of their stiffness when exposed to large oscillating shear stress amplitudes: contrasting behavior to human clots. Int J Transl Med. 2022;2:332-344. [Crossref] [Google Scholar]