



Rheology of artificial blood

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Abstract

The rheology of artificial blood studies the properties of flow and the deformation of blood substitutes designed to imitate the behavior of natural blood. These synthetic fluids must reproduce essential characteristics such as non-Newtonian viscosity, thixotropy, and elasticity, in order to ensure efficient oxygen transport and optimal interaction with biomedical devices. The understanding of the rheological mechanisms allows to improve the formulation of artificial blood for clinical applications, notably in transfusion, in extracorporeal circulation, or in biomedical research. What domains combine experimental approaches and numerical modeling to optimize functional performances and biocompatibility of products.

Keywords: Rheology, artificial, blood

Introduction

Rheology, the study of the deformation and flow of matter, plays a central role in understanding and designing artificial blood substitutes. Blood is a highly complex biological fluid with unique flow properties that differ significantly from simple Newtonian fluids like water. Its behavior is governed not only by the plasma (a mostly Newtonian liquid) but also by suspended cellular components, primarily red blood cells (RBCs), which contribute to its non-Newtonian characteristics. Artificial blood aims to replicate or approximate these properties while fulfilling the primary physiological role of oxygen transport. Therefore, an understanding of blood rheology is essential for the development of safe and effective artificial blood products. Natural blood exhibits shear-thinning behavior, meaning its viscosity decreases as the shear rate increases. This property is crucial for efficient circulation, allowing blood to flow easily through large vessels at high shear rates while maintaining sufficient viscosity at low shear rates in capillaries to ensure proper oxygen delivery. Additionally, blood demonstrates viscoelasticity, aggregation, and deformability, largely due to the presence and mechanical properties of RBCs. These cells can deform significantly to pass through microvessels smaller than their resting diameter, a feature critical for microcirculation. Any artificial substitute must account for these properties to avoid complications such as impaired perfusion or increased cardiac workload.

Artificial blood can be broadly classified into two categories: hemoglobin-based oxygen carriers (HBOCs) and perfluorocarbon (PFC) emulsions. HBOCs are derived from hemoglobin molecules that are modified chemically or encapsulated to function outside the RBC membrane. Their rheological behavior differs from whole blood because they lack cellular components, making them closer to Newtonian fluids. However, their viscosity and oxygen-carrying capacity can be adjusted through molecular modifications and concentration. On the other hand, PFC emulsions consist of tiny droplets of synthetic compounds capable of dissolving large amounts of oxygen. These emulsions behave as colloidal suspensions, and their rheological properties depend on droplet size, concentration, and stability.

One of the main challenges in artificial blood design is replicating the optimal viscosity. Blood viscosity is a key determinant of vascular resistance and, consequently, blood pressure and tissue perfusion. If an artificial blood substitute is too viscous, it may increase resistance and strain the cardiovascular system. Conversely, if it is too thin, it may fail to adequately perfuse tissues or carry sufficient oxygen. Thus, achieving a balance is critical. Moreover, artificial blood must maintain stable rheological properties under varying physiological conditions, such as changes in temperature, pH, and shear rate.

Another important consideration is the interaction of artificial blood with the vascular endothelium. Natural blood cells influence the flow profile within vessels, creating a cell-free layer near the vessel walls that reduces friction and enhances flow efficiency. This phenomenon, known as the Fahraeus-Lindqvist effect, contributes to the reduced apparent viscosity of blood in small vessels. Artificial substitutes that lack deformable cells may not replicate this effect, potentially leading to altered microcirculatory dynamics. Researchers are exploring ways to mimic these interactions, such as designing particles with flexible membranes or specific surface properties.

The stability and aggregation behavior of artificial blood components also impact rheology. In natural blood, RBC aggregation at low shear rates increases viscosity, which can be beneficial for maintaining hemostasis but problematic in pathological conditions. Artificial systems must avoid unwanted aggregation or phase separation, as these can lead to blockages or inconsistent oxygen delivery. Emulsion stability in PFC-based substitutes, for instance, is a critical factor in maintaining predictable flow behavior.

Advances in materials science and bioengineering are enabling the development of more sophisticated artificial blood systems. For example, encapsulating hemoglobin within biodegradable polymers or liposomes can create particles that better mimic the size, shape, and deformability of RBCs. These innovations aim to reproduce not only the oxygen-carrying function but also the rheological behavior of natural blood. Computational modeling and microfluidic experiments are also being used to study and optimize the flow properties of these substitutes under conditions that simulate human circulation.

Rheology is a fundamental aspect of artificial blood research, influencing its performance, safety, and clinical viability. Replicating the complex flow behavior of natural blood remains a significant challenge, requiring a multidisciplinary approach that integrates fluid mechanics, biology, and materials science. As research progresses, a deeper understanding of rheological principles will continue to guide the design of artificial blood substitutes that can effectively support or replace natural blood in medical applications^[1, 5].

Materials and method

Materials:

Components for artificial blood:

- Aqueous solution with synthetic polymers (e.g. polyethylene glycol, polyvinylpyrrolidone) to adjust viscosity
- Microspherical or nano-particles (e.g. polystyrene, silica gel) to simulate blood cells
- Electrolytes (NaCl, KCl) to maintain conductivity and osmotic balance
- Stabilizing agents and preservatives to prevent degradation

Instruments and equipment

Rotary or capillary rheometer to measure viscosity and viscoelastic behavior

Thermostat to maintain constant temperature (37°C, body temperature)

Optical or electron microscope to evaluate particle distribution

Pipettes, test tubes, sterile containers

Methods

Preparation of artificial blood:

The components were mixed in established proportions to obtain a solution with physicochemical properties similar to natural blood. Particle dispersion was achieved by magnetic stirring and ultrasonication for homogenization.

Rheological measurement:

Artificial blood samples were placed in the rheometer. Measurements were performed at different shear rates (0.1 – 100 s⁻¹) and at body temperature (37°C). Dynamic viscosity and non-Newtonian behavior (pseudoplasticity tendency) were determined.

Stability verification:

Samples were monitored over time to verify rheological changes and particle sedimentation.

Result and discussions

Figure 1 represents the dependence of dynamic viscosity on shear rate for artificial blood.

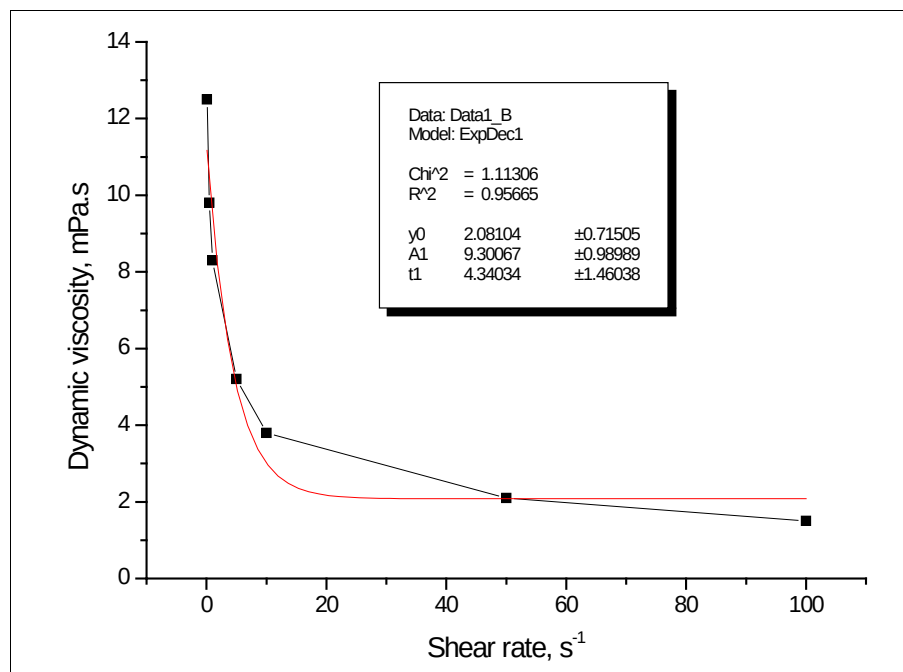


Fig 1: Shear rate dependence of dynamic viscosity for artificial blood.

At low shear rates, the viscosity is higher, due to the arrangement of particles and their behavior similar to cell aggregates. As the shear rate increases, the viscosity decreases, indicating a pseudoplastic behavior, typical of natural blood^[6, 12].

The shear rate dependence of dynamic viscosity is a critical factor in evaluating the performance of artificial blood substitutes. Unlike natural blood, which exhibits pronounced shear-thinning behavior due to the presence and deformability of red blood cells, many artificial systems tend to behave more like Newtonian fluids, with relatively constant viscosity across varying shear rates. This difference

can significantly impact microcirculatory flow and overall hemodynamic efficiency.

An ideal artificial blood substitute should mimic the shear-thinning nature of real blood to ensure optimal perfusion under both low and high shear conditions. At low shear rates, higher viscosity helps maintain adequate oxygen delivery, while at high shear rates, reduced viscosity minimizes vascular resistance and cardiac workload. Achieving this balance remains a key challenge, particularly for hemoglobin-based and perfluorocarbon-based systems that lack cellular structure.

Recent advancements focus on incorporating deformable particles or engineered carriers to better replicate these rheological properties. Ultimately, understanding and

controlling shear-dependent viscosity is essential for developing artificial blood that is both physiologically compatible and clinically effective.

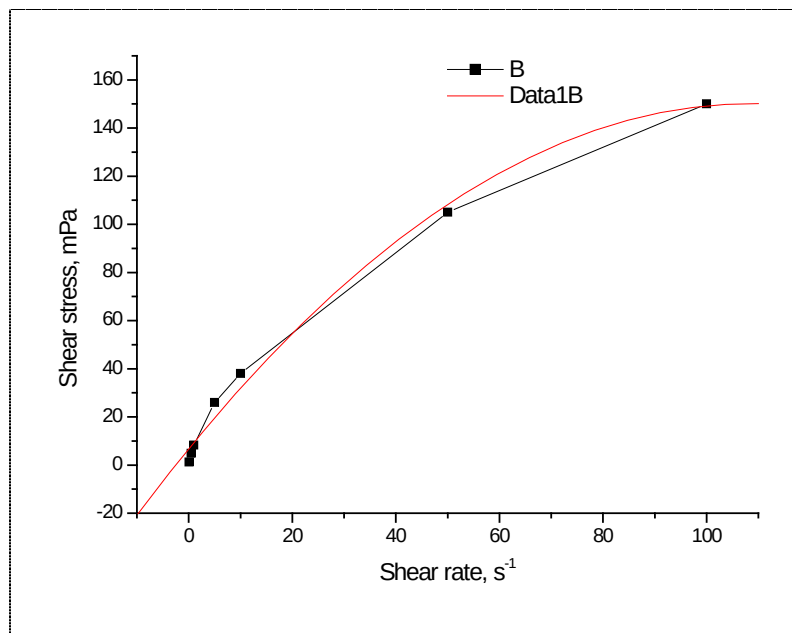


Fig 2: Shear stress dependence on shear rate for artificial blood

The relationship between shear stress and shear rate is fundamental to understanding the flow behavior of artificial blood and its compatibility with human circulation. In natural blood, this relationship is nonlinear due to its non-Newtonian, shear-thinning nature, where shear stress increases with shear rate but at a decreasing slope. This behavior is largely attributed to red blood cell deformability, alignment, and aggregation dynamics. In contrast, many artificial blood substitutes, particularly hemoglobin-based oxygen carriers and perfluorocarbon emulsions, often exhibit a more linear relationship, characteristic of Newtonian fluids.

This difference has important physiological implications. A linear shear stress–shear rate relationship may lead to

suboptimal flow regulation, especially in microcirculation where varying shear conditions are critical for efficient oxygen delivery. Without shear-thinning properties, artificial blood may either impose excessive stress on vessel walls at high shear rates or fail to maintain sufficient stress at low shear rates, affecting perfusion.

Recent research aims to address these limitations by introducing structured or deformable components that better replicate the nonlinear rheological behavior of natural blood. Achieving an appropriate shear stress response across a wide range of shear rates remains essential for improving the safety, functionality, and clinical applicability of artificial blood substitutes.

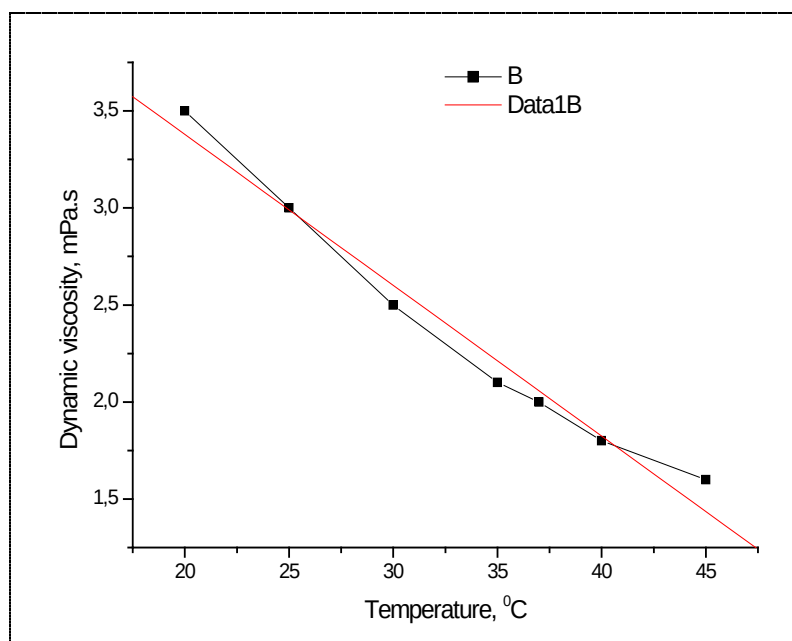


Fig 3: Temperature dependence of dynamic viscosity for artificial blood.

Viscosity decreases with increasing temperature, as the fluid becomes less viscous at higher temperatures, a common phenomenon in biological and artificial fluids^[13, 19].

The temperature dependence of dynamic viscosity is a crucial parameter in assessing the performance and reliability of artificial blood systems. As illustrated in Figure 3, dynamic viscosity typically decreases with increasing temperature, reflecting enhanced molecular mobility and reduced molecular interactions within the fluid. This trend is consistent with both natural blood plasma and most artificial blood formulations, including hemoglobin-based oxygen carriers and perfluorocarbon emulsions.

From a physiological perspective, maintaining appropriate viscosity across the normal human body temperature range is essential for stable hemodynamic function. Even small deviations in temperature can significantly influence flow resistance, particularly in microcirculation. At lower temperatures, increased viscosity may impair perfusion and oxygen delivery, while excessively low viscosity at higher temperatures could reduce shear forces necessary for efficient vascular function.

Artificial blood substitutes must therefore be carefully engineered to exhibit minimal and predictable viscosity changes within clinically relevant temperature ranges. Stability under hypothermic or hyperthermic conditions is especially important in medical scenarios such as surgery or trauma care. Overall, understanding temperature-viscosity relationships supports the optimization of artificial blood for safe and effective clinical use.

Conclusions

The study of the rheology of artificial blood is essential for the development of biomimetic fluids that reproduce as faithfully as possible the mechanical properties of natural blood. By analyzing its viscoelastic behavior and the response to variations in velocity and shear forces, it was possible to optimize the composition of artificial blood to ensure efficient blood flow and increased biological compatibility. In conclusion, rheological understanding helps to create products with medical applicability in transfusion, dialysis or tissue engineering, contributing to the safety and efficiency of modern treatments.

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