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Development of Blood Mimicking Fluid Suspension using Polymer Particles

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Abstract. Surgical simulation has become a key tool in the training of surgeons and improving patient safety. Presently, surgeons rehearse surgeries on 3D-printed anatomical models that are patient-specific, and water is used to represent blood. Unlike water, blood is a shear thinning fluid. Hence, it makes the simulation less realistic, as it lacks tactile feedback. This experimental study aims to develop a blood mimicking fluid (BMF) with micro-sized polymer particles to enhance realistic tissue handling and blood flow for surgical simulations. The polymer particles are meant to represent red blood cells in human whole blood. A range of 5 wt% to 55 wt% of polymer particles were added into BMF composing of 85 vol% water, 15 vol% glycerol and 0.03 wt% xanthan gum. The viscosities of the BMF samples were then measured against a range of shear rates, from 0.1 s^{-1} to 1000 s^{-1}. The viscosity measurements were carried out at 25 ℃, at 1 atm, which is at standard ambient temperature and pressure, similar to surgical simulation environment conditions. The viscosities of the BMF samples were validated using Power Law model and also compared with human whole blood. It was found that the asymptotic viscosity at high shear rates increases with the percentage of polymer particles. In spite of that, the BMF samples still portray shear-thinning properties.

INTRODUCTION

Over the past few decades, surgical simulation has become a key tool in the training of surgeons and the maintenance of patient safety [1]. It is not only used to train new surgeons but also for rehearsing complicated surgeries. Previously, surgical simulations were being performed on cadavers. The use of cadavers has its disadvantages, as it is costly and there is no blood flow. With the rise on 3D printing for medical applications, these surgical simulations can be performed on 3D-printed anatomical models that are patient specific [2]. However, most of the time water with water-soluble dyes is being used to simulate blood in the model [3]. Water and blood have different physical and rheological properties. This makes the surgical simulation less realistic for the surgeon, as it lacks tactile feedback. The purpose of tactile feedback is to simulate the surgeon's feel of the target lesion during the procedure. This leads to the development of blood mimicking fluids (BMF), to replicate the physical properties and rheology of blood. The development of BMF minimizes the risks of surgeons being exposed to biological hazards that may threaten the health and safety of the environment [4].

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Unlike water, blood is a non-Newtonian fluid, and it shows shear-thinning properties [5]. This means that its viscosity decreases as shear rate increases. At high shear rates, it has an asymptotic viscosity of about 3.5 mPa.s [5]. It is necessary to observe the trend of blood viscosity against shear rate because blood flows with different shear rates in different blood vessels. Table 1 shows a summary of mean wall shear rates in different blood vessels [5]. The mean wall shear rates vary depending on the size of blood vessels. Overall range of wall shear rates ranges from 43 s^{-1} to 1600 s^{-1}.

TABLE 1. Summary of mean wall shear rates in different blood vessels [5]

Blood vessel	**Mean Wall Shear Rate (s^{-1})**
Ascending Aorta	45 – 300
Femoral Artery	300
Common Carotid	250
Carotid Sinus	240
External Carotid	330
Capillaries	400 – 1600
Large Veins	120 – 320
Vena Cava	44 – 64
Thoracic inferior	43 – 64

The rheological model that is commonly used for blood is the Power Law model, as shown in equation 1 [6]. Given that μ is the apparent viscosity, and $\dot{\gamma}$ is the shear rate. There are two indexes in the Power Law model that helps characterize the fluid. The flow consistency index is represented as k, and flow behavior index is represented as n. The typical n and k values for human blood are in the range of 0.718 to 0.74815, and 0.01568 Pa.s and 0.018567 Pa.s respectively [7].

$$\mu = k\dot{\gamma}^{n-1} \tag{1}$$

Hence, to enhance realistic tissue handling and blood flow for surgical simulations; micro-sized polymer particles were added into a BMF composition adapted from an experimental research by Ramnarine et al. [8]. The polymer particles are meant to represent the blood cells in blood. Average blood cells concentration in blood is 45% by volume [9]. Although there are some studies on rheology of BMF with polymer particles, the amount added into BMF is less than 5% [8]. In this experimental study, the effect of addition of different percentages (5 wt% - 55 wt%) of polymer particles on BMF viscosity will be investigated. The percentage of polymer particles studied is only up to 55 wt%. The apparent viscosity of the BMF will be studied at shear rates ranging from 0.1 s^{-1} to 1000 s^{-1}, at 25 ℃, and 1 atm, which is at standard ambient temperature and pressure, similar to surgical simulation environment conditions. The results are analyzed using the Power Law model.

METHODOLOGY

Preparation of blood mimicking fluid

The materials used for the preparation of this BMF were distilled water, glycerol (Sigma Aldrich, US), xanthan gum (Sigma Aldrich, US), surfactant (Synperonic A7, Sigma Aldrich, US) and polymer particles (Orgasol 2001 EXD NAT 1, Arkema, France). Synperonic A7 is used as the surfactant, whereas the type of polymer particle used in this experimental research is a spheroidal powder of polyamide 12, with an average diameter of 10 μm and a density of 1.03 g/cm^3 [10].

Preparation of base fluid

First and foremost, the base fluid was prepared with 85 vol% of water, 15 vol% of glycerol and 0.03 wt% of xanthan gum, using a magnetic stirrer. This composition was adapted and then altered from Ramnarine et al. [8]. To ensure the base fluid is homogenous, the measured amount of xanthan gum was gradually mixed into the water.

After allowing the xanthan gum and water mixture to stir until it was clear with no lumps, the glycerol was added in gradually and stirred for about 15 minutes.

Addition of Polymer Particle and Surfactant

In this experimental research, six BMF samples were prepared. Each sample has different amounts of polymer particles, varied at 5 wt%, 15 wt%, 25 wt%, 35 wt%, 45 wt% and 55 wt%. The polymer particles were added into the base fluid, and stirred for about an hour, until all the polymer particles were thoroughly mixed. Since the polymer particles are much less dense than the base fluid, 0.9 vol% of Synperonic A7 was added into the mixture as the surfactant, and was stirred for 15 minutes. The purpose of the surfactant was to allow the polymer particles to be neutrally buoyant in the base fluid. The BMF was done after allowing it to degas for a day.

Viscosity Measurement

The rheometer (HAAKE MARS III, Germany) was used to measure the viscosity of the BMF samples at different shear rates, ranging from 0.1 s^{-1} to 1000 s^{-1}. A sample size of 10 ml was needed for each test. The sample was put into the cup (HAAKE MARS III CCB26, Germany), and the viscosities at different shear rates were measured as the rotor (HAAKE MARS III CC26, Germany) spun at different speeds. Before putting the sample into the cup, the sample was swirled gently to ensure it was perfectly mixed. The viscosity measurements were taken at 25 ℃, at 1 atm, which is at standard ambient temperature and pressure, similar to surgical simulation environment conditions. The viscosity measurement for each sample was repeated three times to obtain an average reading.

Density Measurement

Density is a measure of a substance's mass-to-volume ratio. Hence, to measure the density of the samples, the density formula was used, whereby the mass of the sample was divided by the volume of the sample. The mass of the samples was measured using an electronic balance, and the volume was measured in a measuring cylinder. Measurements were repeated for three times to obtain an average result.

Refractive Index Measurement

The refractometer (Abbe, Germany) was used to obtain the refractive index of the BMF samples. A dropper was used to place a drop of the sample onto the refractometer. The readings were taken after adjusting the knob to the correct position. Readings were repeated for three times for each sample to obtain an average reading.

Analysis Using Power Law Model

The Power Law model is one of the most commonly used non-Newtonian rheological models for blood. Although there may be other models that consider more parameters than the Power Law model, the Power Law model has an advantage over the others. This is due to its simplicity and the availability of exact solutions in some geometries and flow conditions, contributing natural benchmarks for the numerical codes. Based on the Power Law model, the logarithmic form can be written as in equation 2, where μ is the viscosity, $\dot{\gamma}$ is the shear rate, n is the flow behavior index, and k is the flow consistency index.

$$\log \mu = (n-1)\log \dot{\gamma} + \log k \tag{2}$$

With the logarithmic form of the Power Law, linear fitting in Microsoft Excel can be done to analyze the results achieved by the BMF samples, where the x-axis and y-axis will be $\log \dot{\gamma}$ and $\log \mu$ respectively. Linear regression, R^2 was used to determine the best-fit line. The results were then plotted and compared with viscosity data of healthy whole human blood, as reported by Jung et al. [11]. They collected the blood viscosities of 297 healthy individuals, using a scanning capillary tube viscometer.

RESULTS AND DISCUSSION

Viscosity of Blood Mimicking Fluid with Different Amounts of Polymer Particles

Six BMF samples with different amounts of polymer particles were tested. The viscosities of each sample at different shear rates were measured, and the results are shown in Figure 1. Similar to human whole blood, all the BMF samples show shear-thinning properties, whereby their viscosities decrease as the shear rate increases. This is due to the base fluid containing xanthan gum, making it a shear-thinning fluid. Without xanthan gum, glycerol-water mixture is a Newtonian fluid. Since all the BMF samples show the same trend, the thing that differentiates them is the effect of percentage of polymer particles added into them. It is observed that the addition of polymer particles increased the asymptotic viscosity of the BMF, without affecting the shear-thinning property of the BMF. The more the polymer particles added, the higher the asymptotic viscosity is. Without polymer particles, the asymptotic viscosity is at 3.6 mPa.s, which is exactly like human whole blood [11].

After addition of polymer particles of 5 wt%, 15 wt%, 25 wt%, 35 wt%, 45 wt% and 55 wt%, the asymptotic viscosities are 4.5 mPa.s, 5.9 mPa.s, 7.1 mPa.s, 9.3 mPa.s, 11.1 mPa.s and 17.8 mPa.s respectively. This is due to more particles in the BMF, saturating the fluid, making it more viscous. With this piece of information, further studies can be done to modify the base fluid composition to a lower asymptotic viscosity to allow any of the BMF samples with polymer particles match the viscosity-shear rate curve of human whole blood.

To analyze the flow behavior and flow consistency of the BMF samples, the logarithmic plot based on the Power Law is presented in Figure 2. The flow behavior index, n, flow consistency index, k, and the linear regression, R^2 for each BMF sample, are tabulated in Table 2. The percentage differences of n and k for each BMF sample are tabulated in Table 3.

The flow behavior index, n, tells the type of fluid. When $n<1$, it is a shear thinning fluid; $n=1$, it is a Newtonian fluid; $n>1$, it is a shear thickening fluid [12]. Based on the results in Table 3, it is proven that all the fluids are shear-thinning fluids. The percentage difference for n ranges from 4% to 22%. Closest to human whole blood being BMF sample with 0 wt% polymer particles, followed by BMF with 45 wt% polymer particles. Overall, the value of n increases from sample 0 wt% to 25 wt% polymer particles, and then decreases gradually from 35 wt% polymer particles onwards.

On the other hand, the flow consistency index, k, is to give an idea of the fluid viscosity. However, k can only be compared with fluids having similar flow behavior indexes [12]. In this case, looking at 5 wt%, 15 wt% and 25 wt% polymer particles samples, as they have similar flow behavior indexes, k generally increases as the amount of polymer particles increases. This proves that the viscosity of the BMF sample increases with the amount of polymer particles. The percentage difference for k ranges from 8% to 1052%, closest to human whole blood being BMF sample with 35 wt% followed by 25 wt% polymer particles. In whole, the k value decreases from sample 0 wt% to 5 wt% polymer particles, and then increases exponentially from 15 wt% to 55 wt% polymer particles.

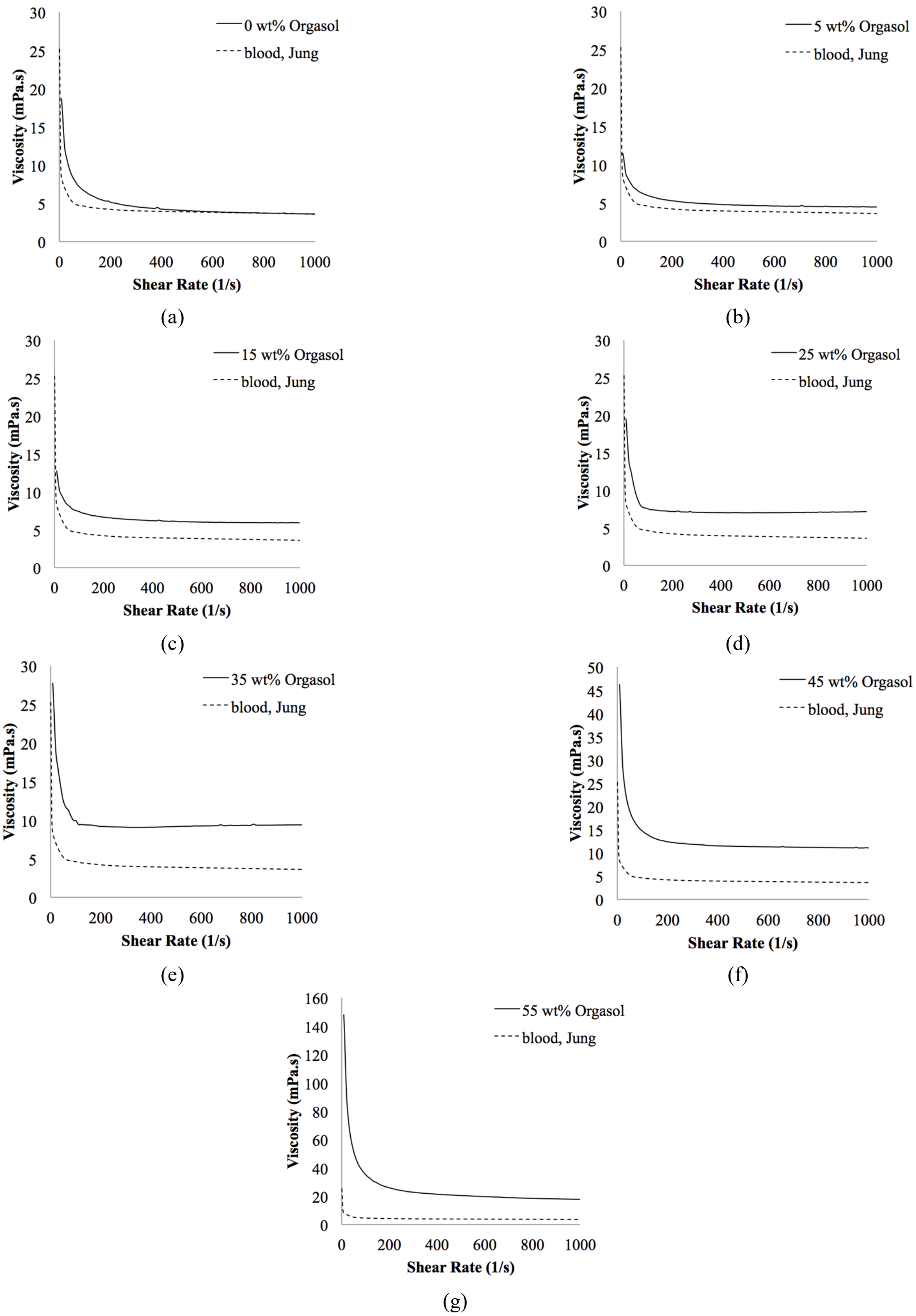

FIGURE 1. Viscosity against shear rate of BMF with polymer particles of (a) 0 wt%, (b) 5 wt%, (c) 15 wt%, (d) 25 wt%, (e) 35 wt%, (f) 45 wt% and (g) 55 wt%, compared with human whole blood.

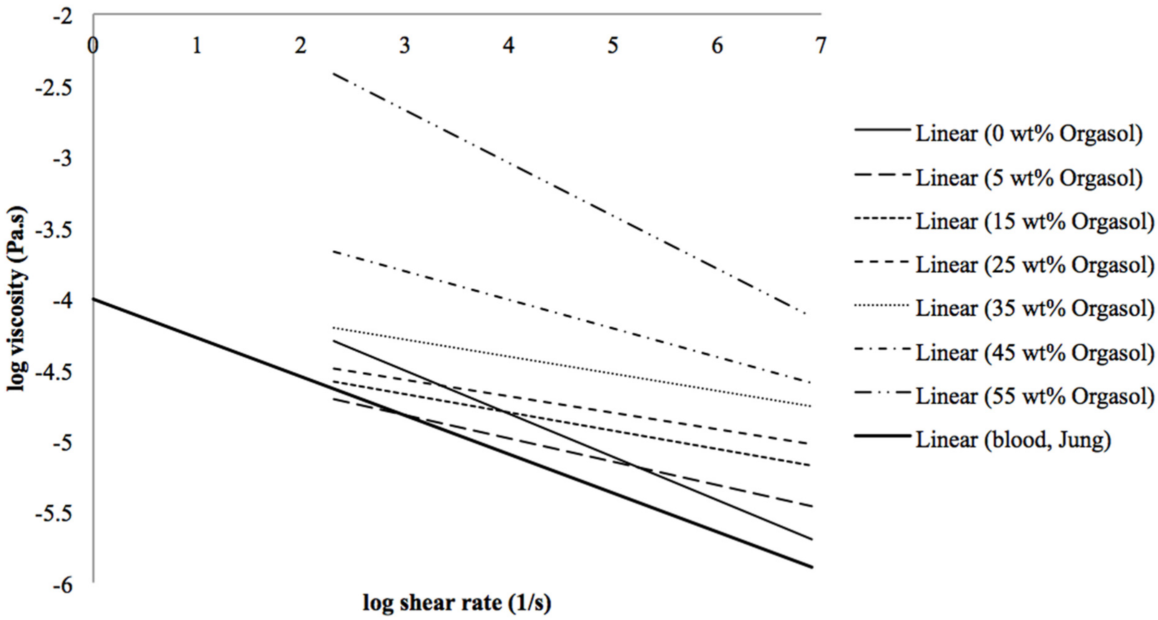

FIGURE 2. Logarithmic plot for BMF samples and human whole blood.

TABLE 2. Linear fitting parameters of Power Law model for BMF samples and human whole blood

Sample	n-1	n	log k	k	R^2
Blood	-0.2730	0.7270	-4.0055	0.0182	0.9096
0 wt%	-0.3036	0.6964	-3.5982	0.0274	0.96197
5 wt%	-0.1639	0.8361	-4.3303	0.0132	0.9303
15 wt%	-0.1286	0.8714	-4.2889	0.0137	0.9109
25 wt%	-0.1157	0.8843	-4.2268	0.0146	0.5642
35 wt%	-0.1202	0.8798	-3.9297	0.0196	0.5179
45 wt%	-0.2011	0.7989	-3.2070	0.0405	0.7870
55 wt%	-0.3717	0.6283	-1.5626	0.2096	0.9297

TABLE 3. Percentage difference of n and k based on human whole blood

Sample	n	% difference of n	k	% difference of k
0 wt%	0.6964	4.21	0.0274	50.55
5 wt%	0.8361	15.01	0.0132	27.47
15 wt%	0.8714	19.86	0.0137	24.73
25 wt%	0.8843	21.64	0.0146	19.78
35 wt%	0.8798	21.02	0.0196	7.69
45 wt%	0.7989	9.89	0.0405	122.53
55 wt%	0.6283	13.58	0.2096	1051.65

Density of Blood Mimicking Fluid with Different Amounts of Polymer Particles

Density also plays a role in providing tactile during surgical simulation. The densities of the BMF samples are plotted in Figure 3. It shows that the density decreases as the amount of polymer particles increases. The density of polymer particles could explain this. Polymer particles are less dense than the base fluid. When more of the BMF sample consists of polymer particles, the density of the BMF will take more of the polymer particle's density. Comparing it with human whole blood density of 1.06 g/cm^3 [5], the BMF with 15 wt% polymer particle is the closest. It has a density of 1.05 g/cm^3. However, to achieve the same density as human whole blood, the polymer particles percentage has to be 20.56 wt%.

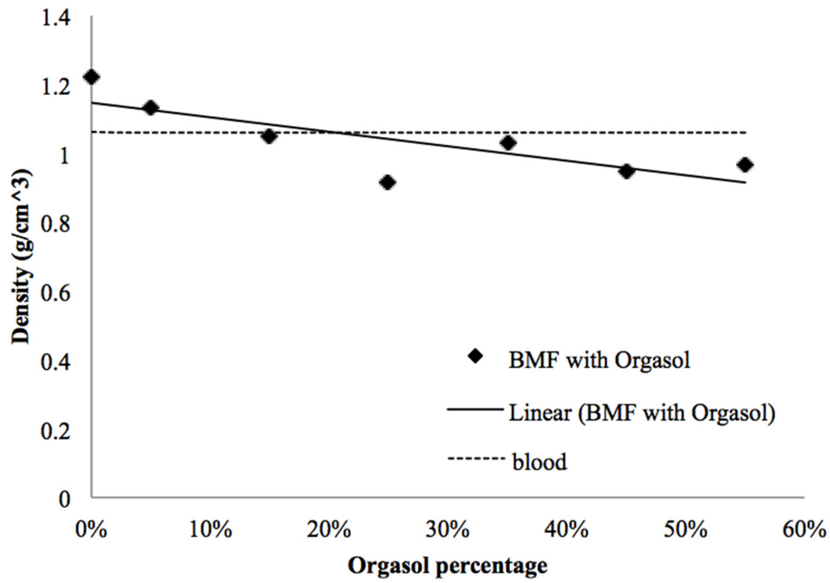

FIGURE 3. Density of BMF samples with different percentages of polymer particles.

Refractive Index of Blood Mimicking Fluid with Different Amounts of Polymer Particles

Refractive index is one of the important optical properties of blood, and possesses a special significance for medical application [13]. It is necessary for BMF that are applied in particle image velocimetry and ultrasound measurements. For instance, in particle image velocimetry, the displacement of the focal plane is required and it depends on the refractive index of the BMF [14]. Thus, the refractive indexes of the BMF samples are reported in Table 4. It is found that at 0 wt% polymer particles, the refractive index is the lowest. There are no particles present in the fluid to refract the light. Despite that, when 5 wt% of polymer particles is present in the base fluid, the refractive index shoots up, then slowly decreases as the amount of polymer particles increase.

TABLE 4. Refractive index of BMF samples with different percentages of polymer particles.

Sample	Refractive Index			
	Trial 1	**Trial 2**	**Trial 3**	**Average**
0 wt%	1.3543	1.3544	1.3543	1.3543
5 wt%	1.3558	1.3558	1.3558	1.3558
15 wt%	1.3558	1.3556	1.3557	1.3557
25 wt%	1.3555	1.3554	1.3554	1.3554
35 wt%	1.3551	1.3550	1.3550	1.3550
45 wt%	1.3548	1.3545	1.3546	1.3546
55 wt%	1.3546	1.3547	1.3547	1.3547

CONCLUSION

In general, the addition of polymer particles has affected the viscosity of the BMF with 85 vol% water, 15 vol% glycerol and 0.03 wt% xanthan gum. As the amount of polymer particles added increase, the viscosity of the BMF increases. Although the BMF samples remain as shear thinning fluids with the addition of polymer particles, at 45 vol%, which resembles the actual concentration of blood cells, the percentage difference of the shear thinning property with human whole blood is 9.89%. The asymptotic viscosity is 11.1 mPa.s, which is higher than whole blood. With that, the next phase of study could work on altering the composition of the base fluid, starting with a base fluid that is less viscous, aiming the asymptotic viscosity of actual blood of 3.6 mPa.s. By doing so, the desirable percentage of polymer particles could achieve the human whole blood viscosity. This would contribute to the development of a more realistic BMF, improving the tactile accuracy for surgical simulations.

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