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The effect of the mixing temperature on the viscosity of blood mimicking fluid for application in medical simulator under angiography imaging

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Abstract. Bench-top medical simulator is used for rehearsing medical treatment procedure to treat abnormal blood flow in blood vessels. The blood vessels are 3D-printed, and flow is simulated using blood mimicking fluid. It is crucial that the fluid can replicate the tactile feedback of actual blood during simulation which contributed by blood viscosity. There are limited studies regarding the effect of mixing temperature during blood mimicking fluid preparation towards the viscosity of blood mimicking fluid. This experiment aims to investigate the effect of mixing temperature variation of 25℃, 37℃ and 88℃ towards blood mimicking fluid that made up of xanthan gum, corn starch, water, and glycerol. The viscosities of samples are measured against a range of shear rates, from 0.1 s^{-1} to 1000 s^{-1} using a rheometer. Generally, shear thinning viscosity was observed and the viscosity data was fitted to power law viscosity model. The viscosity decreased as the mixing temperature increased. Power law fluid consistency index, *K* and non-Newtonian fluid behaviour index, *n* showed deviation of more than 8% from the actual blood.

Introduction

Medical surgical simulation is known to be the future for healthcare education. Surgical simulator includes human cadavers, bench top models and virtual reality systems to recreate real life surgical situations for both novice and expert practitioners to sharpen their skills [1]. Among others, bench top surgical simulator provides an economical medical simulation with 3D printing technology and supported by advancement in biomimetic material [23]. Blood mimicking fluids also known as blood analogue fluids used to mimic the physical properties of actual blood for the surgical simulation application to improve the tactile feedback.

The challenge of blood mimicking fluid formulation is to match the actual blood rheological and mechanical properties. Blood is defined as a non-Newtonian and shear thinning fluid. Shear thinning occurs as the apparent viscosity of fluid decreases with increasing shear rate. The blood viscosity model can be described as a power law behavior as shown in Equation 1 [2]

$$\mu = K\dot{\gamma}^{n-1} \quad (1)$$

where, μ is the apparent viscosity, γ represents the shear rate, *K* signifies the fluid consistency index whereas n is the non-Newtonian fluid behaviour index. The value of coefficient *K* and *n* for actual blood are 18.215 mPa.s and 0.727 respectively [2]. The non- Newtonian characteristics are affected by the size and shape of flow conduits. Cardiovascular circulation system comprises various subsystems such as arteries and veins, blood capillaries and porous tissues where shear thinning properties of blood is significant [3].

Polysaccharides such as xanthan gum and starch has been used in formulating blood mimicking fluid to provide non-Newtonian characteristics. There are limited studies regarding the effect of mixing temperature during the blood mimicking fluid preparation towards the viscosity properties through the addition of different polysaccharides in the water-glycerol base fluid [4,6]. In this work, the blood mimicking fluid formulation is focused to investigate the effect of mixing temperature during the addition of polysaccharides
which are xanthan gum and corn starch into water-glycerol base fluid. Addition of iodine-containing contrast media or contrast agent to the formulation is necessary since it enable the visualization of blood vessel under angiography imaging in the medical simulator.

Methodology

The blood mimicking fluid sample formulation contains 99.5% purity of glycerol (Sigma Aldrich, US), distilled water, xanthan gum from Xanthomonas campestris (Sigma Aldrich, US), corn starch (Sigma Aldrich, US) and contrast agent of Iohexol 350 (Omnipaque) from GE Healthcare Shanghai, China. The blood mimicking fluid samples comprises three different temperatures with three different ratios respectively with glycerol-water base, xanthan gum (XG), corn starch (CS) and contrast agent (CA). Blood mimicking fluid composition is tabulated in Table 1.

Table 1: Blood mimicking fluid compositions

Material	**Composition (%w/w)**
Distilled water	59.93
Glycerol	40.00
Xanthan Gum (XG)	0.01
Corn Starch (CS)	0.01
Contrast Agent (CA)	0.05

The samples were prepared by measuring the glycerol, water and CA using a measuring cylinder whereas the XG and CS were measured using an analytical balance. The experimental set up is shown in Figure 1.

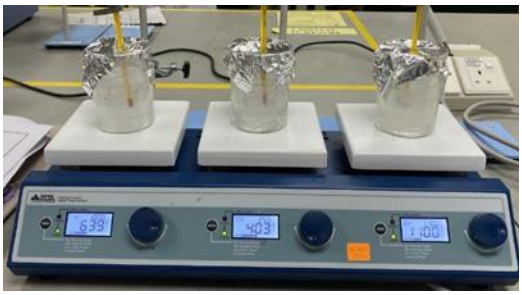

Fig. 1. Experiment set-up for blood mimicking fluid formulation

The fluid was prepared by mixing all of the materials using the hot plate with magnetic stirrer until is homogenously mixed according to the published method [15]. The XG, CS and glycerol

were stirred on the hot plate with a temperature of 50 ℃ until there were no lumps present. Once the formation of lumps diminished, distilled water was gradually added to the side of the beaker.

The speed of the magnetic stirrer was gradually increased to 600 rpm and the temperature of the plate was set. Three variation of mixing temperature was investigated at 25℃, 37℃ and 88℃. 25℃ is referring to room temperature and 37℃ is according to human average body temperature. The temperatures of 88℃ is selected since the aqueous xanthan gum solution viscosity decreased when the temperature above 80℃ [5]. This implied the weakening of intermolecular interactions that may assist good mixing.

The rapid freeze quench technique is applied to ensure to property at high mixing temperature is retained [7]. Once the samples were rapidly mixed after 30 minutes, it is transferred into a labelled storage bottle and stored in the freezer for quenching at -15 ℃. The samples were quenched for 24 hours before taken out to ambient room surrounding conditions. CA was added to the samples, it was stirred at 600 rpm for 30 minutes. Once samples were mixed thoroughly, it was stored in the chiller at 5℃ to avoid bacterial growth.

The HAAKE™ MARS™ Modular Advanced Rheometer was utilised to measure the viscosity of each blood mimicking fluid sample. The rheometer functions are based on the torque applied at a certain rotational speed or shear rate. The rheometer studies the relationship between the stress and strain of samples in order to analyse the deformation properties. The blood mimicking fluid viscosity was measured at different shear rates ranging from 0-1000 s^{-1}. During the viscosity measurement, the sample of 10 ml is required. The samples must be homogenized and in room temperature before conducting the test. Every sample testing was conducted at constant, controlled temperature of 25℃ to match the ambient conditions during surgical simulation environment. The rheometer was fitted with the coaxial cylinder which are Becher and Cup CCB26 DIN with Rotor size CC26 Ti. Once the geometries were set up, the rheometer was set to measure its zero-level controlled by the RheoWin software prior the blood mimicking fluid sample measurements. The software and its data manager comprise an integrated server for the data plotting of viscosity against shear rate. The time taken for each blood mimicking fluid sample measurement is 10 minutes. The results were tabulated and graphs of viscosity against shear rate were plotted for the data comparison with actual human blood.

The non-Newtonian fluid behaviour is explained through power-law model in Equation 1 and can be described as a logarithmic form as shown in Equation 2.

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

Equation 2 is described as a linear fitting graph. The x-axis and y-axis are $\log\ \gamma$ and $\log\ \mu$ respectively. The gradient of graph is (n-1), hence the fluid behaviour index can be taken from the gradient. The fluid consistency index K can be obtained from the y-intercept of linear graph. The results of blood mimicking fluid samples were compared with actual human blood data reported by Jung et al [2]. The average actual blood data was derived from 297 healthy individuals consisting of 123 men and 174 women. The viscosity values from this investigation were taken as a reference basis to compare the measured viscosity of blood mimicking fluid with actual human blood.

Result and Discussion

Figure 2 depicted the relationship between viscosity and shear rate with variation of mixing temperature of 25℃, 37℃ and 88℃ respectively. A total of one hundred readings were taken to develop the relationship between viscosity and shear rate.

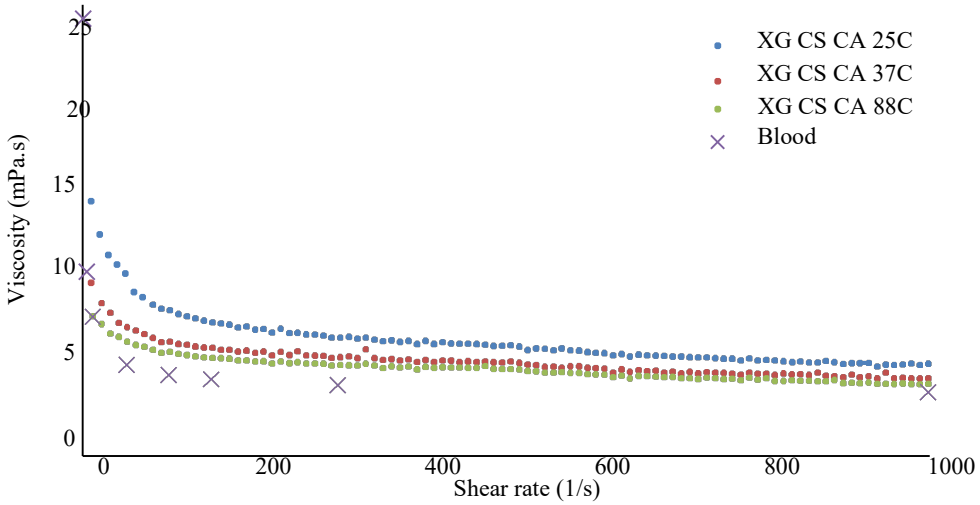

Fig. 2. Viscosity against shear rate for xanthan gum-corn starch-water glycerol base and contrast agent with variation of mixing temperature.

It was observed that the viscosity profile decreases as the mixing temperature increases. Higher temperature may have altered the intermolecular bonding between xanthan gum, corn starch, contrast agent, water and glycerol. The bonds may have weakened at higher temperature that leads to reduce in viscosity. There will be conformational changes in XG chains at mixing temperatures above 36℃ [19]. XG has a chemical structure of trisaccharide side chain which is closely aligned with the polymer backbone leading a single, double, or triple helix stiff chain [20]. At higher temperatures, the XG secondary structure will convert from an ordered helical structure to flexible and disordered, where the side chains were extended away from backbone. When XG is mixed in distilled water at 25℃, weak structure is formed since the molecules are more associated to hydrogen bonding [19]. According to Rochefort et al. the XG will convert to coil-like structure due to the dissociation of molecules and major changes in rheological properties [20].

The viscosity of XG based samples are dependent on the dissolution temperature. When the mixing temperature is above 60℃, the viscosity of XG decreases with increasing temperature. This is due to the order-disorder transition of the XG molecule. The mixing temperature of 88℃ gradient is almost closer to actual blood because the helix-coil transition of XG will only occur for temperatures exceeding 70℃.

Typically, suspensions of CS and water exhibits shear thickening behaviour [21]. The shear thickening behaviour occurs when particles hydro clustering occurs which are due to hydrodynamic lubrication. It was stated that CS suspensions will show two different viscosity regimes when increasing shear rate, where, at low shear rates ($0.01\text{-}1s^{-1}$) exhibits shear thinning behaviour whereas at higher shear rates ($>1s^{-1}$) shear thickening can be observed [22]. Based on the CS samples prepared, the concentration of CS added was minimal. Shear thinning behaviour may be observed due to the lower starch concentrations ranging 10-30 wt% because the starch suspensions exhibits weak thickening behaviour and increasing in critical thickening shear stress was observed [22]. Due to low concentrations of starch present, shear thickening properties are less visible.

The combination of XG and CS polysaccharides will create a synergism on their respective viscosity and the overall viscosity of the substance. Two polysaccharides will create a stronger effect on viscosity compared to individual contribution of each polysaccharide [18]. This is because XG consists of a distinctive rigid, rod like structure which is highly responsive to shear than a random coil structure of CS. This is due to the close structural alignment of the trisaccharide side chains with (1-4) linked cellulose backbone. Also, the XG is capable to enwrap

the starch molecules which slightly increases the viscosity [18]. The XG and CS combined sample with the mixing temperature of 88℃ displays a gradient much closer to actual blood data. The significant high mixing temperature was able to break the rigid structure of XG molecules which were bind to the hydrogen bonding to interact with dissolved amylose molecules present in CS.

The data from Figure 2 were fitted into a linear logarithmic plot according to Equation 2 and shown in Figure 3. The graphs were plotted based on the power law model. The data of actual blood is plotted together for comparison [2].

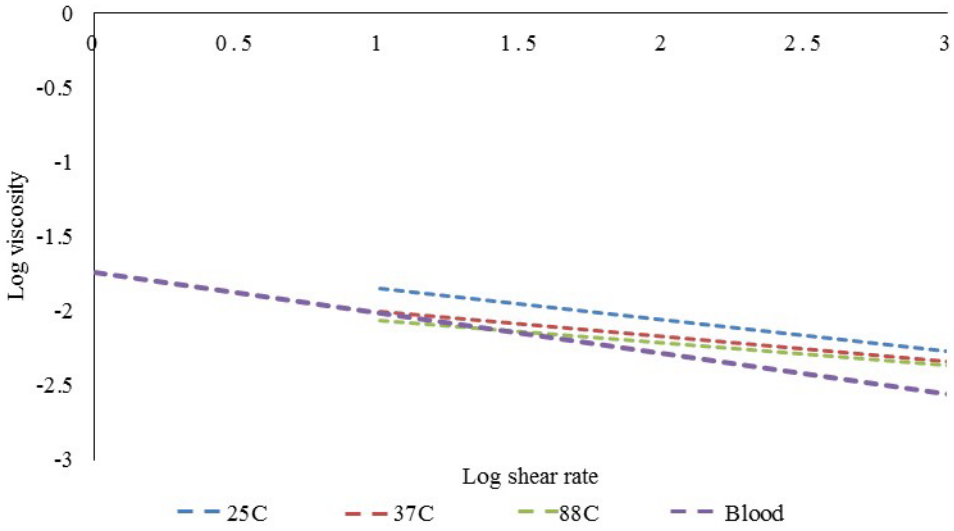

Fig. 3. Logarithmic plot of Figure 2 according to Equation 2.

The *K* and *n* coefficients of each plot were tabulated in Table 2. It is evident that the graph displays a non-Newtonian pseudoplastic behaviour.

Table 2. Linear fittings parameter from Equation 2

Samples	Log *K*	*K*	n-1	*n*	R^2
XG CS CA 25℃	-1.6317	0.023	-0.2123	0.7877	0.9907
XG CS CA 37℃	-1.8323	0.015	-0.1689	0.8311	0.9731
XG CS CA 88℃	-1.9167	0.012	-0.1506	0.8944	0.9601
Blood [4]	-1.7396	0.018	-0.2730	0.7270	0.9096

The data in Table 2 is calculated by using Equation 2. Based on Table 2, it was noticed that the fluid consistency index, *K* decreases with increasing mixing temperature whereas the non-Newtonian fluid behaviour index, *n* increases with increasing mixing temperature. The percentage deviation among the coefficients of blood mimicking fluid samples and actual blood were calculated and summarized as Table 3.

Table 3. Percentage deviation from actual blood data and each blood mimicking fluid sample

Blood mimicking fluid samples	*K*	% deviation (*K*)	*n*	% deviation
XG CS CA 25℃	0.023	27.78	0.7877	8.35
XG CS CA 37℃	0.015	-16.67	0.8311	14.32
XG CS CA 88℃	0.012	-33.33	0.8494	16.84

As shown in Table 3, sample with mixing temperature 25℃ had the lowest non- Newtonian index of 8.35% higher than actual blood. However, the consistency index *K* was significantly large, with a differences of 27.78%. The difference mixing temperature used in this study resulted in different *K* and *n* values. As the temperature increased from 25℃ to 88℃, the *K* value decreases, and the n value increases. Blood mimicking fluid Samples with mixing temperature 88 has the deviation of *K* with 33.33% lower than actual blood data whereas the deviation of *n* coefficient was 16.84% lower than the actual blood.

Table 4 compares the *K* and *n* values obtained in this investigation with other published results. In general, the shear thinning viscosity is sensitive towards the material and composition added where it will affect the *K* and *n* values. Present study shows that blood mimicking fluid of the same composition of XG and CS mixed at different temperature causes the changes to shear thinning characteristics demonstrated by *K* and *n* value. Increasing the mixing temperature resulted in higher *n* values but lowering the *K* values. Lee et. al [14] conducted the same experiment at a constant mixing temperature of 25°C but without the addition of CS. As the concentration of XG reduced, *K* values increased while *n* values decreased. Elblbesy and Hereba measured viscosity of blood mimicking fluid without CS and CA [17]. It was discovered that decreasing the concentration of glycerol decreases the *K* values while increasing the *n* values. Increasing the concentration of xanthan gum increases the *K* values while decreasing the *n* values.

Table 4 K and n values of the fluids in the current study and published data

Fluid composition				***Mixing temperature***	***K*** **(Pa.s^n)**	***n***	***Reference***
Gly (v/v%)	**XG (w/v%)**	**CS (w/v%)**	**CA (v/v%)**				
40	0.01	0.01	0.05	88°C	0.012	0.849	Present study
40	0.01	0.01	0.05	37°C	0.015	0.831	Present study
40	0.01	0.01	0.05	25°C	0.023	0.788	Present study
40	0.08	Not studied	0.05	25°C	0.034	0.598	[14]
40	0.07	Not studied	0.05	25°C	0.028	0.621	[14]
40	0.06	Not studied	0.05	25°C	0.025	0.622	[14]
40	0.02	Not studied	Not studied	25°C.	0.016	0.816	[17]
35	0.02	Not studied	Not studied	25°C.	0.013	0.820	[17]
35	0.05	Not studied	Not studied	25°C.	0.046	0.681	[17]

Conclusion

The increasing of mixing temperature was found to affect the viscosity of the fluid. As the mixing temperature increases the measured viscosity decreases. At an increasing temperature, degradation of intermolecular forces and thermal stability explained the decrease in viscosity. Based on the findings from Power Law viscosity analysis, the *K* and *n* values measured in the experiment having deviation from actual blood property for more than 8%. Further improvement

is recommended to focus on the viscosity measurement at shear less than $10s^{-1}$. Other non-linear blood viscosity models are recommended to be considered to account for more rheological factors.

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