BLOOD MIMICKING FLUID FOR APPLICATION IN ANGIOGRAPHY IMAGING: THE EFFECT OF SURFACTANT ADDITION TOWARDS DENSITY AND VISCOSITY

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ABSTRACT: Modern 3D anatomical modelling and surgical simulation provide surgeons with technical training to practice realistic pre-surgery rehearsals, adapt to patient-specific anatomical structures and prepare for operation procedures with minimal health risks to patients. Blood-mimicking fluid is a biomimetic innovation developed for 3D medical simulator applications to mimic the non-Newtonian fluid properties of human blood. The ongoing challenge in blood mimicking fluid development is to replicate the shear-thinning behaviour and apparent viscosity of blood over a shear rate range of 0-1000 s^{-1} that occurs in human blood vessels. There is a limited investigation about the effect of surfactant concentration towards the density and viscosity of a blood-mimicking fluid. Surfactant is added in blood mimic to ensure the mixing of materials is homogenous. This research investigates the effect of surfactant addition in blood-mimicking fluids comprised of water-glycerol-based fluid, xanthan gum, corn starch and contrast agent. The density and viscosity were analyzed using a rheometer and densitometer, respectively. The increase of surfactant concentration in the blood-mimicking fluid is discovered to have no significant influence on the blood-mimicking fluid density but increased the overall shear-thinning viscosity of the blood-mimicking fluid.

***KEYWORDS**: Blood Mimicking Fluid; Blood Analogue Fluid; Surfactant;*

Viscosity; Density.

1.0 INTRODUCTION

Medical surgical simulation is continuously researched to develop cutting edge, state-of-the-art equipment that are expanding the medical and biomedical engineering sector. Surgical simulator is one such pivotal tool that is being designed to advance the realism of pre-surgery operations as training and rehearsal for surgeons of novice or experienced backgrounds to acquire the proper surgical skills, self-awareness, and self-confidence, without jeopardizing the health safety and success rate of live patients in the actual surgery. Traditional surgical simulation includes the application of animal subjects, cadavers, and standard human mannequin to provide simplified human anatomies without presenting specific physiological and pathological rare conditions, which can result with lack of understanding and response measure on unique anatomical complications during clinical practice.

With present innovation, modern three-dimensional (3D) blood anastomosis modelling and surgical simulation utilizes 3D printing technology capable of manufacturing extremely complicated geometries, to accurately reproduce a realistic replica of patient-specific anatomical structures. The 3D anatomical replicas are accessible for surgeons to gain technical proficiency in adapting the pathological conditions, applying appropriate operating gestures, and planning successful procedures with minimal operative risks [1].

It becomes clear that with these 3D printed anatomical replica simulations gaining preferences of surgeons and popularity in the medical industry, the biomimetic materials applied in the specified application also need developments for accurate and realistic characteristics that assist surgeons on tactile and visual feedbacks of blood and tissue deformation [2]. One such material innovation is the blood mimicking fluid or blood analogue fluid as another term, which is developed to replicate the physical, chemical, rheological and acoustical properties of real human blood for application in surgical simulations.

Over the past decades, a number of blood mimicking fluid formulations have been proposed in regards of the development of Doppler ultrasound and magnetic resonance (MR) angiography imaging performance, which non-invasively assess crucial blood

parameters while ensuring the patient's health safety and comfort [3]. Correspondingly, the sanitary and technical difficulties in handling biological blood by medical personnel during vitro experiment and medical simulation are reduced with the introduction of blood mimicking fluid solution.

Generally, a blood mimicking fluid formulation comprises of the primary water-glycerol base fluid that mimics a blood plasma, followed by adding other constituent materials that are suspended in the base fluid and manipulates the overall properties and characteristics of the blood mimicking fluid. The ongoing challenge in developing blood mimicking fluid formulations is the degree of similarity that the blood mimicking fluid can replicate a human blood, especially the non-Newtonian rheological characteristics of blood.

According to International Electrochemical Commission (IEC) 1685 specifications, the specified viscosity to achieve for a blood mimicking fluid must be approximately 4.0±0.4 mPa.s to resemble the asymptotic of blood that ranges from 3.5-5.55 mPa.s, while the overall blood mimicking fluid density is specified as 1.050±0.040 kg/m^3 which is closely identical the density of water, so that blood mimic component particles of identical density can remain buoyantly suspended in the base fluid [4].

In terms of fluid flow rheology, shear-thinning fluids reflects to the effect of shear stress deformation, as the apparent viscosity of the fluid decreases when subjected to increasing shear rates on a logarithmic scale. The power law equation computed in Equation 1 describes the relation of the apparent viscosity relative to shear rate [5].

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

where, μ is the apparent viscosity, $\dot{\gamma}$ is the shear rate, k signifies the fluid consistency index and n represents the non-Newtonian fluid behaviour index.

Presently, there are limited studies conducted on the effect of different surfactant concentration towards the viscosity and density of blood mimicking fluid during blood mimicking fluid formulation for angiography application. Most of the application focused on ultrasound measurement [6]. From a previous study conducted by Goncalves et al. on surfactant's role in blood mimicking fluid, the study is developing a multiphase blood mimicking fluid with the application

of Brij L4 surfactant suspended in pure water, with concentrations of 0.5 to 10 wt% of surfactant evaluated [7].

Another past research study conducted by Oglat et al. is referred for the blood mimicking fluid mixture proposed, comprising of distilled water, propylene glycol and glycerol [8]. For the purpose of dispersing the scattering particles used in blood mimicking fluid, a non-ionic surfactant was added in different amount in order to investigate the important properties influenced by the different surfactant compositions. For the viscosity of the proposed blood mimicking fluid however, Oglat et al. reported findings that supports the work of Goncalves et al. that an increasing viscosity from 0 mPa.s to 35 mPa.s was observed with the linearly increasing non-ionic surfactant concentrations of 1-7 wt% added [8].

The primary objectives of this research are to analyze the effect of surfactant on viscosity and density of blood mimicking fluid compositions through quantitative tests analysis, and to compare the viscosity and density experimental results with biological blood. Contrast agent is considered in the formulation for application in angiography imaging technique.

2.0 METHODOLOGY

2.1 Materials

The blood mimicking fluid sample formulation comprises of distilled water, 99.5% purity of glycerol (Sigma Aldrich, US), xanthan gum from Xanthomonas campestris (Sigma Aldrich, US), corn starch (Sigma Aldrich, US), Omnipaque Iohexol contrast agent (GE Healthcare Shanghai, China) and Synperonic A7 alcohol ethoxylate surfactant (Croda Pte Ltd, Singapore).

2.2 Preparation of Blood Mimicking Fluid

The base fluid mixture that functions as a suspension medium for other blood mimicking fluid components and a control reference sample, was prepared with a weight composition of 60 wt% distilled water and 40 wt% glycerol. The higher constituent ratio of glycerol added was set to achieve a higher overall viscosity level of the specified mixture since glycerol is more viscous, in order to have the base fluid attain an equivalence of the average haematocrit level for human at 40.1%. Blood mimicking fluid samples categorized into five sample sets of

varying weight compositions of distilled water, xanthan gum (XG), corn starch (CS), and Synperonic A7 surfactant (SA), while the weight composition of glycerol and volume of contrast agent added were kept constant. Depending on the blood mimicking fluid sample's composition, the individual components were calculated for their amount to be added according to the weight percentage composition set for the sample and their corresponding weight. Following that, the required amount for a particular material was measured using an analytical balance. For blood mimicking fluid components that are handled in terms of volume, they were measured and prepared using a measuring cylinder. Once the individual component materials were prepared at the right quantity, they are mixed all together using a hot plate magnetic stirrer.

i. Preparation of Base Fluid

The water-glycerol base fluid is prepared by mixing distilled water and glycerol, under constant stirring by the hot plate magnetic stirrer. Firstly, the weights of glycerol and water corresponding to sample's weight percentage composition were calculated to produce a 250 ml worth of sample.

After calculating out the correct weights, the amount for both components were measured and prepared using measuring cylinders, followed by gradually pouring glycerol into the water containing in a beaker while subjected to a constant stirring rate of 400 rpm, at 25 °C. Once the two components have mixed homogenously and formed a clear, transparent solution after 10 minutes, the base fluid is transferred into labelled plastic storage bottles and store in a chemical chiller at 5 °C, to cease microbial activities and prevent biodegradation for long-term storage. The composition of the base fluid sample comprised of 60 wt% of water and 40 wt% of glycerol (Set A).

ii. Addition of Surfactant and Polysaccharides

Table 1 tabulates the compositions of blood mimicking fluid samples from Set B, C and D, with each sample set assigned with a different experimental objective to investigate but in general, the objectives are mainly related to investigating the effect of surfactant concentration added. Set B comprises of blood mimicking fluid samples that contains the water-glycerol base fluid, increasingly added with surfactant. After preparing the base fluid, the specific amount of surfactant was gradually added into it from a small beaker and magnetically stirred

for 20 minutes at 25 °C until the mixture turned opalescent, ready to be transferred into storage bottles and stored in the chemical chiller at 5°C.

Table 1: Blood mimicking fluid samples composition

Experimental Objective	Samples	Components	Composition Ratio (wt/wt%)				
			Water	Glycerol	XG	CS	Surfactant (SA)
Effect of surfactant amount added on blood mimicking fluid base fluid	B1	Water: Glycerol: SA	59.50	40.00	-	-	0.50
	B2		59.10	40.00	-	-	0.90
	B3		58.50	40.00	-	-	1.50
	B4		58.00	40.00	-	-	2.00
Effect of surfactant amount added on blood mimicking fluid composition containing XG	C1	Water: Glycerol: XG:SA	59.99	40.00	0.01	-	-
	C2		59.49	40.00	0.01	-	0.50
	C3		59.09	40.00	0.01	-	0.90
	C4		58.49	40.00	0.01	-	1.50
	C5		57.99	40.00	0.01	-	2.00
Effect of surfactant amount added on blood mimicking fluid composition containing XG and CS	D1	Water: Glycerol: XG:CS:SA	59.98	40.00	0.01	0.01	-
	D2		59.48	40.00	0.01	0.01	0.50
	D3		59.08	40.00	0.01	0.01	0.90
	D4		58.48	40.00	0.01	0.01	1.50
	D5		57.98	40.00	0.01	0.01	2.00

For Set C and D, polysaccharides (XG and CS) are added with a fixed amount of 0.01 wt% respectively into blood mimicking fluid sample compositions, with varying surfactant concentration added. The specified weightage amount of XG and CS added is according to the peer recommendation of a previous research that discovered blood mimicking fluid with 0.01 wt% of XG and CS each suspended in the base fluid exhibits viscosity with the highest similarity to human blood, among other blood mimicking fluid formulations [9].

After the base fluid was prepared, the specific amount of XG and CS were weighted using an analytical balance to measure as the amount

of XG and CS added. With the correct quantities for both XG and CS carefully prepared, they are transferred into the base fluid starting with XG, followed by CS while the mixture is constantly stirred using the hot plate magnetic stirrer for homogeneity in the mixture solution.

Since the polysaccharides are harder to disperse in the base fluid and capable of clumping together easily, the solution was to constantly stir the sample mixture at a higher stirring rate of 600 rpm, at 55 °C for an average of 30 minutes each sample until the lumps were absent and fully dispersed. Following that, the appropriate amount of surfactant is gradually transferred into the sample mixture under the same constant stirring settings. Once the sample mixtures turned opalescent, the samples are immediately transferred into storage bottles and stored in the chiller at 5 °C, to inhibit any microbial growth that can cause biodegradation of the blood mimicking fluid samples.

iii. Addition of Contrast Agent

For the last samples of set E, Table 2 tabulates the formulated sample compositions which include the addition of contrast agent with XG, CS and varying amount of surfactant added into the blood mimicking fluid samples.

Table 2: Blood mimicking fluid samples composition with contrast agent (CA)

Experimental Objective	Samples	Components	Composition Ratio (wt/wt%)				
			Water	Glycerol	XG	CS	SA
Effect of surfactant amount added on blood mimicking fluid composition containing XG, CS and CA	E1	Water: Glycerol: XG:CS: SA CA (constant of 4 v/v %)	59.98	40.00	0.01	0.01	-
	E2		59.48	40.00	0.01	0.01	0.50
	E3		59.08	40.00	0.01	0.01	0.90
	E4		58.48	40.00	0.01	0.01	1.50
	E5		57.98	40.00	0.01	0.01	2.00

Similar to the sample preparation procedure for samples that contain polysaccharides, an extension step is to add a fixed volume of CA into the mixture containing the polysaccharides dissolved in base fluid, followed by adding surfactant as the last component. According to the angiocardiographic procedures recommended for Omnipaque 350 CA, the recommended dosage added for adult patients is 3 ml to 14 ml for arteriography procedure, with 10 mL dosage as the usual CA volume

injected into bloodstreams for adult angiography [10]. Therefore, a fixed volume of 10 mL CA which corresponds to 4 v/v %was added into each sample of Set E via a 10 ml syringe, followed by magnetically stirring the new mixture at 600 rpm for another 20 minutes. Following that, surfactant is then gradually added into the sample mixture and continue with the same constant stirring conditions until the sample mixture turn homogenous and opalescent in appearance. Once the sample was mixed thoroughly, it was stored in the chiller at 5°C.

iv. Density Measurement

The Anton Par DMA 35 Basic handheld digital density meter was utilized to measure the density of all the different blood mimicking fluid samples prepared for this experiment. The density meter is used to directly collect the blood mimicking fluid samples with the help of its in-built pump and subsequently measure their density value on spot, with an uncertainty of ±0.001 g/cm3 and ±0.2 °C for density and temperature respectively. After pumping in the specimen of the samples, the integrated hydrometer processes the specimen's density and specific gravity at certain temperature, displaying the validated final result within a minute interval.

The results are digitally displayed with the final density or concentration at a final temperature reading taken for quantitative analysis, and only 2 mL of sample specimen is required to give the result without wasting unnecessary quantity of sample. Prior to collecting samples with the density meter, the filling tube of the specified equipment needs to be rinsed with distilled water to avoid undesirable contaminations in the inner tube when taking the density readings for samples.

The same rinsing procedure was also carried out after each blood mimicking fluid sample reading, to rinse the filling tube with water first, followed by rinsing with the next sample solution before taking actual experimental readings. Whenever the filling tube is rinsed with distilled water, a calibration test reading is conducted on the density of distilled water and the density reading will be compared to the standard water density calibration table available in the Anton Par DMA 35 handbook, by checking for the density value of water at the actual measured temperature and compare the deviation with the actual density reading.

When carrying out the density measurement on the blood mimicking fluid samples, the room temperature is controlled at a constant 25 °C in

order to replicate the temperature conditions of a laboratory and simulation environment. To ensure accurate measurement readings, the density measurement procedure will be conducted a minimum of three times to obtain each reading's information and average results for all samples.

v. Viscosity Measurement

The HAAKE MARS Modular Advanced Rheometer was utilized to measure the apparent viscosity of each blood mimicking fluid samples when subjected to shear rates and increasing rotational speed, and rheological characterization of Newtonian and non-Newtonian fluids. The rheometer studies the relationship between the shear stress and strain of the blood mimicking fluid samples in order to determine the deformation behaviour of the varying composition samples.

Prior to starting the rheological sample testing, the appropriate geometries for the rotor head, adapter and specimen cup holder were cleaned and adjusted on the rheometer testing platform, which in this experiment, Rotor CC26 Ti, TMPXX Adapter and TM-PE-C Cup CC CB26 DIN were employed. Next, the RheoWin Job Manager software was booted in the rheometer configured computer, to set up the testing parameters and settings.

All blood mimicking fluid samples were tested at a controlled temperature of 25 °C in order to replicate a surgical simulation environment, with the viscosity test running with a shear rate range of 0.1-1000 s-1, with a divided number of 100 interval readings from the specified range. After setting up the geometry attachments and test simulation settings, the rheometer was calibrated once per usage of the rheometer by readjusting the zero-level point of the measuring rotor via command on the RheoWin software. Once the zero-level point was achieved, the measuring rotor was lifted up so that the specimen cup holder can detached from the measuring platform and filled with 10 mL of the blood mimicking fluid sample to be tested. With the sample specimen in place, the measuring rotor was commanded to go to the inputted gap, which in this case was set as 1 mm as the selected geometric rotor plate comes into contact with the sample fluid.

The measurement was started, and the rotor began to rotate at an increasing rotational speed to compute the viscosity measurement at the stated shear rate range. Concurrently, the RheoWin Data Manager software's integrated server will begin the data plotting of viscosity

against shear rate based on real time responding measurements relayed by the rheometer. For each sample run, the duration of the simulation test taken for the specified shear rate range with 100 intervals was 10 minutes. To ensure accuracy is not compromised, each blood mimicking fluid sample were tested on a triplicate basis. The computed results were tabulated to plot viscosity against shear rate graph for studying the effect of surfactant towards viscosity and viscosity comparison with human blood.

3.0 RESULTS AND DISCUSSION

i. Density Measurement of Blood Mimicking Fluid Samples

Table 3 showcases the average densities for all blood mimicking fluid samples that were computed from triplicate density readings of each individual blood mimicking fluid sample. The ideal density for blood mimicking fluid formulation is given as 1.050±0.040 kg/m^3 by IEC 1685 and shall be taken as comparison to the densities of blood mimicking fluid samples formulated in this experiment.

Table 3: Average density

Sample Set	Samples	Components	Average Densities (g/cm^3)
A	A1	Water: Glycerol	1.0991±0.0001
B	B1	Water: Glycerol: SA	1.1123±0.0004
	B2		1.104±0.0009
	B3		1.1124±0.0008
	B4		1.1115±0.0008
C	C1	Water: Glycerol: XG:SA	1.0951±0.0001
	C2		1.0983±0.0003
	C3		1.0986±0.0004
	C4		1.0989±0.0003
	C5		1.0901±0.0012
D	D1	Water: Glycerol: XG: CS: SA	1.0976±0.0004
	D2		1.0971±0.0002
	D3		1.0974±0.0001
	D4		1.0939±0.0016
	D5		1.0970±0.0007
E	E1	Water: Glycerol: XG:CS:CA:SA	1.1093±0.0002
	E2		1.1088±0.0001
	E3		1.1091±0.0002
	E4		1.1090±0.0003
	E5		1.1123±0.0005

Sample C5 exhibits the closest density to the IEC 1685 specification of 1.0901 g/cm3. Sample E2 exhibits an average density of 1.1088 g/cm3 which is the closest out of the other four set E samples with the density value state by IEC 1685. In terms of the effect of Synperonic A (SA) surfactant concentration, it can be generally interpreted from Table 3 that the blood mimicking fluid samples containing increasing amount of surfactant does not deviate much from their corresponding sample set's fixed blood mimicking fluid sample without surfactant added.

The overall result interpretation on the effect of surfactant towards density is blood mimicking fluid is considered negligible changes from the increasing addition of surfactant. As mentioned in previous section of this paper, Oglat et al. also reported the proposed blood mimicking fluid not influenced by the non-ionic surfactant added, with the highest blood mimicking fluid density reading measured at 1.015 g/cm3 [8]. This may be due to the water-glycerol based fluid making up a significant percentage of the blood mimicking fluid samples composition (97-99.49 wt%), so any addition of chemicals will not have significant influence on the overall density of the blood mimicking fluid.

ii. Viscosity Measurement of Water-Glycerol Base Fluid

Figure 1 graphically depicts the relationship between apparent viscosity and shear rate plot with respect to the power law equation in Equation 1.

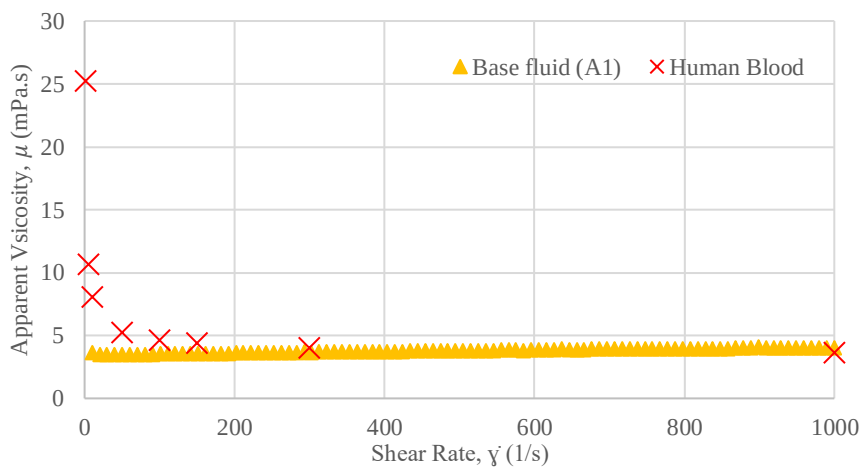

Figure 1: Apparent viscosity against shear rate for water-glycerol base fluid and human blood [5]

It can be observed that the base fluid has an almost linear relationship between viscosity and shear rate, with slight increase in viscosity with increasing shea rate. The slight increase in viscosity throughout the shear region of 0-1000 s-1 may be due to the initial low zero shear viscosity of the base fluid and the extremely slow starting rotational speed of the measuring rotor subjected on the fluid, as it increased to its supposedly stable viscosity range with the increasing shear rate. Nevertheless, it is still indicated that the base fluid viscosity is independent of the influence by increasing shear rate. In other words, the base fluid exhibits Newtonian fluid properties, with the average constant viscosity experimentally determined as 3.7794±0.1683 mPa.s. On the contrary, the human blood can be clearly observed as a non-Newtonian fluid exhibiting pseudoplastic shear-thinning characteristics, as the apparent viscosity decreases with increasing shear rate in a logarithmic manner. Therefore, it is graphically shown that the conventional water-glycerol base fluid was not mimicked the ideal shear-thinning ability of human blood [5].

iii. Viscosity Measurement of Water-Glycerol Base Fluid Samples at varying Surfactant Concentrations

Figure 2 graphically depicts the viscosity against shear rate plot for blood mimicking fluid water-glycerol base fluid samples containing 0 wt% surfactant (A1), 0.5 wt% surfactant (B1), 0.9 wt% surfactant (B2), 1.5 wt% surfactant (B3) and 2.0 wt% surfactant (B4) respectively, and for human blood. The most notable observation is the overall apparent viscosity of the blood mimicking fluid base fluid increased with the higher amount of surfactant added into the sample composition, as sample B1 containing 0.5 wt% surfactant was found to achieve an average apparent viscosity of 5.5894±0.1577 mPa.s with increasing shear rate as compared to the average apparent viscosity of default base fluid at 3.7794±0.1683 mPa.s.

The apparent viscosities were increasingly higher for sample B2, B3 and B4, with sample B4 showcasing the highest viscosity readings relative to shear rate. Therefore, it is interpreted that the addition of surfactant increases the viscosity of the blood mimicking fluid base fluid, as this can be explained by the surfactant's critical micelle concentration (CMC) parameter. The rapid increase in viscosity from each subsequent sample with higher surfactant concentration is mainly due to the increasing micelles formed by the surfactant in the mixture, which exceeded the surfactant's CMC and the formation of visible bubbles suspended in the fluid [11]. As a result, the increasing volume

fraction of bubbles suspended in the base fluid increases the overall viscosity of the base fluid.

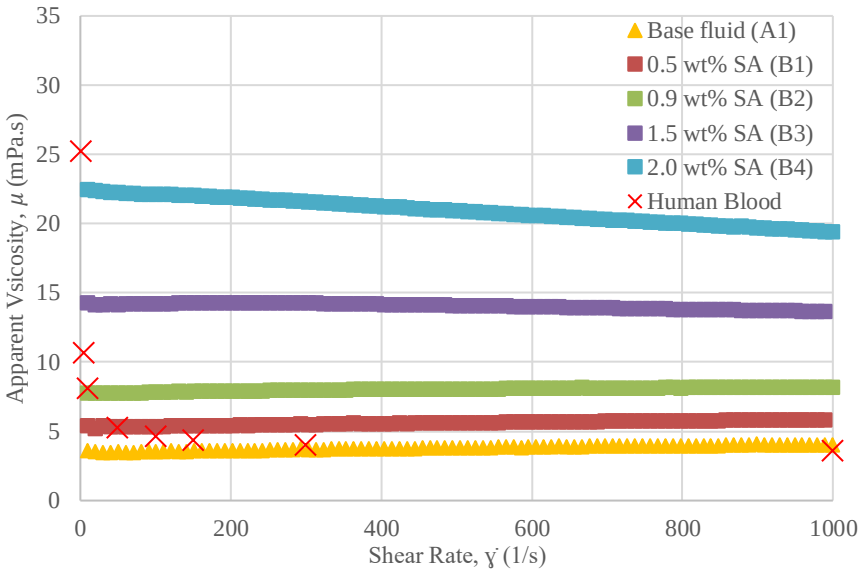

Figure 2: Apparent viscosity against shear rate for water-glycerol base fluid samples with varying surfactant concentrations, and for human blood [5]

In terms of rheological observation, sample B1, B2 and B3 portrayed Newtonian fluid characteristics closely that are similar to the water-glycerol base fluid, with slight fluctuations in viscosities due to the significantly low stating rotational speed subjected during rheometer testing. However, sample B4 containing the highest surfactant concentration of 2.0 wt% surfactant exhibits a sharp shear-thinning behaviour as the apparent viscosity decreases with increasing shear rate, labelling it a non-Newtonian fluid.

The abnormal shear-thinning characteristic associate with a supposedly Newtonian base fluid is due to the micelles suspended in the base fluid that can influence the rheological properties to be different, from Newtonian to non-Newtonian [11]. This statement is supported with the CMC principles, as the increasing micelles formed exceeded CMC limit, the oversaturation of micelles in the base fluid

resulted with the presence of free micelles that does not interact with the blood mimicking fluid component molecules present. Therefore, the presence of free micelles increases the free water suspension in the base fluid and significantly decrease the overall viscosity of the base fluid [12]. In terms of similarity with real human blood, it is visibly clear that the sample with the closest viscosity with human blood (Sample A1) wasn't able to exhibit the shear thinning behaviour of blood. Indeed, Sample B4 exhibited shear-thinning behaviour but the degree of shear-thinning is not to the same extent of a human blood, not to mention its overall viscosity range is too high to match with the viscosity of human blood.

iv. Viscosity Measurement of Blood Mimicking Fluid Samples with Xanthan Gum at varying Surfactant Concentrations

Figure 3 shows the viscosity against shear rate plot for blood mimicking fluid samples comprising of the base fluid with XG and varying concentration of surfactant mixed, and for actual human blood [5].

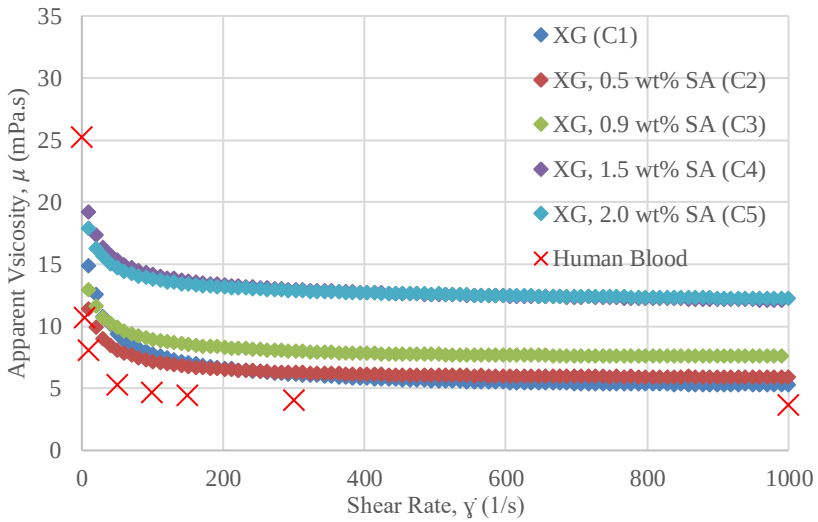

Figure 3: Apparent viscosity against shear rate for blood mimicking fluid samples containing xanthan gum with varying surfactant concentrations, and for human blood [5]

It is observable that all five of the specified samples are exhibiting similar degree of shear-thinning behaviour of a non-Newtonian, pseudoplastic fluid with the apparent viscosities decreasing with shear rate until they reach a lower viscosity plateau at higher shear region, in

which a Newtonian fluidic behaviour is observed.

The shear-thinning properties observed are contributed by the presence of xanthan gum in the sample mixtures. Similar case with the results obtained from Figure 2, the overall viscosities of the blood mimicking fluid samples shown in Figure 3 increases with each subsequent sample with higher surfactant concentration. This can be explained based on the application of surfactant that is responsible for dispersing the blood mimicking fluid component particle (XG) in the base fluid for homogeneity, thus increasing the overall viscosity of the blood mimicking fluid.

The viscosity difference between sample C4 and C5 containing 1.5 wt% and 2.0 wt% respectively is noted to be insignificant, in which sample C4 with lower surfactant concentration of the two showcases higher viscosity in the lower shear region of 0-400 s-1 and sharper decrease in viscosity in the higher shear region onwards. This can be explained as the limitation of the surfactants CMC, as the generation of micelles interacting with other blood mimicking fluid component particles from the high surfactant concentration added in sample C4 occurs at a higher formation rate, this leads to an increase in the overall viscosity and also the rate of free micelles formed. Hence, the increasing saturation of free micelles in the sample mixture causes a significant decrease in viscosity of the blood mimicking fluid sample [12].

Based on the results of Figure 2 and 3, it is concluded that the non-ionic surfactant used for this experiment increases the viscosity for both Newtonian and non-Newtonian fluids. From Figure 3, sample C2 with 0.5 wt% surfactant showcases a shear-thinning trend and apparent viscosity of the highest similarity out of all Set C samples with human blood in the lower shear region of 0-200 s-1. At higher shear rates, the sample without surfactant addition (C1) portrays the most similar shear-thinning gradient and viscosity range with human blood.

v. Viscosity Measurement of Blood Mimicking Fluid Samples with Xanthan Gum and Corn Starch at varying Surfactant Concentrations

Figure 4 depicts the relationship between viscosity and shear rate of blood mimicking fluid samples containing 0.01 wt% XG, CS each with the addition of varying surfactant concentrations, and for human blood.

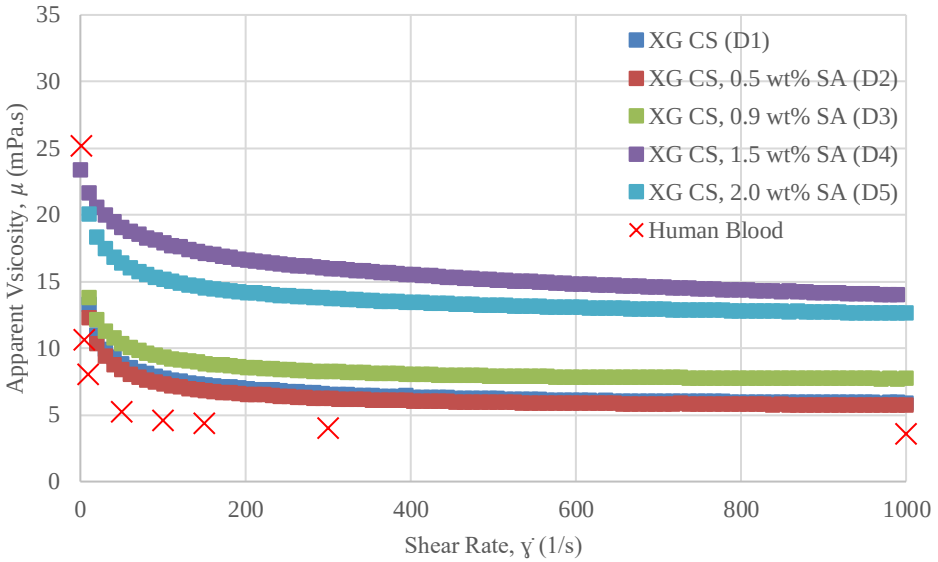

Figure 4: Apparent viscosity against shear rate for blood mimicking fluid samples containing xanthan gum and corn starch with varying surfactant concentrations, and for human blood [5]

Comparing Figure 3 and Figure 4, it is visibly clear that the overall viscosity results of the Set D samples plotted in Figure 4 are higher than Set C samples in Figure 3. That is due to the addition of CS into the blood mimicking fluid samples which is capable of synergizing the intermolecular interactions with XG as polysaccharides, creating more significant viscosity effect [13].

Based on Figure 4, it is observed that the overall viscosity of the blood mimicking fluid sample with the lowest surfactant added of 0.5 wt% surfactant (D2) is lower than the sample without surfactant added (D1). The overall viscosity of the subsequent sample with 0.9 wt% surfactant (D3) increased higher than sample D1 and D2, followed by a significant increase in viscosity for the subsequent sample D4 with higher surfactant concentration. However, the sample with the highest surfactant concentration added of 2.0 wt% (D5) is observed to portray a relatively lower overall viscosity than sample D4.

The results from Figure 4 does not validate that increasing surfactant concentration will necessarily result with an increase in viscosity under increasing shear rates. For the case of sample D4 and D5, in can be similarly deduced like the previous case with sample C4 and C5, which

the degree of free micelles saturation in the sample D5 is higher than in sample D4, leading to a significant decrease in overall viscosity of sample D5. As for the decrease in overall viscosity from non-surfactant sample D1 to sample D2, this result occurrence may be linked to the intermolecular interactions aspect of the blood mimicking fluid formulation, in which the surfactant's role in the two blood mimicking fluid sample compositions have different effect on the rheological properties.

All five blood mimicking fluid samples plotted in Figure 4 exhibits good shear-thinning characteristics. For sample D4 however, a strong shear-thinning behaviour is observed for the shear rate region of 200 to 1000 s-1, which deviates from human blood as it should be more Newtonian-like at high shear rates, showing a slightly linear viscosity to shear rate trend. Goncalves et al. also reported a similar finding in which a very high surfactant concentration used in blood mimicking fluid resulted with a shear-thinning trend that deviates greatly from the shear-thinning graph of human blood [7].

Out of all the five samples in Figure 4, sample D2 containing 0.01 wt% of XG, 0.01 wt% of CS and 0.5 wt% of surfactant mimics the overall viscosity from 0-1000 s-1 and the shear-thinning pattern of human blood with the highest similarity by far.

vi. Viscosity Measurement of blood mimicking fluid Samples with Xanthan Gum, Corn Starch and Contrast Agent at varying Surfactant Concentrations

Figure 5 depicts the relationship between viscosity and shear rate for blood mimicking fluid samples containing 0.01 wt% XG, CS each, with the addition of 10 ml of CA and varying surfactant concentrations, and for human blood. Similar to the case of sample D1 and D2 that was previously discussed, the overall viscosity of the blood mimicking fluid sample with 0.5 wt% surfactant (E2) is observed to be lower than the non-surfactant added sample (E1), according to Figure 5.

The overall viscosity for the remaining three samples increases with the higher amount of surfactant added for their respective composition, with the sample added with 2.0 wt% surfactant portraying the highest overall viscosity out of Set E samples. Furthermore, it is evidently clear that all five blood mimicking fluid samples exhibits obvious shear-thinning characteristics of a pseudoplastic fluid, with the exception of

sample E2. Although sample E2 has an overall viscosity that is most similar to that of the human blood, its composition exhibits a weak shear-thinning pattern around the shear rates of 0-200 s-1, followed by a slightly resembling linear Newtonian viscosity-shear rate trend at higher shear rates onward.

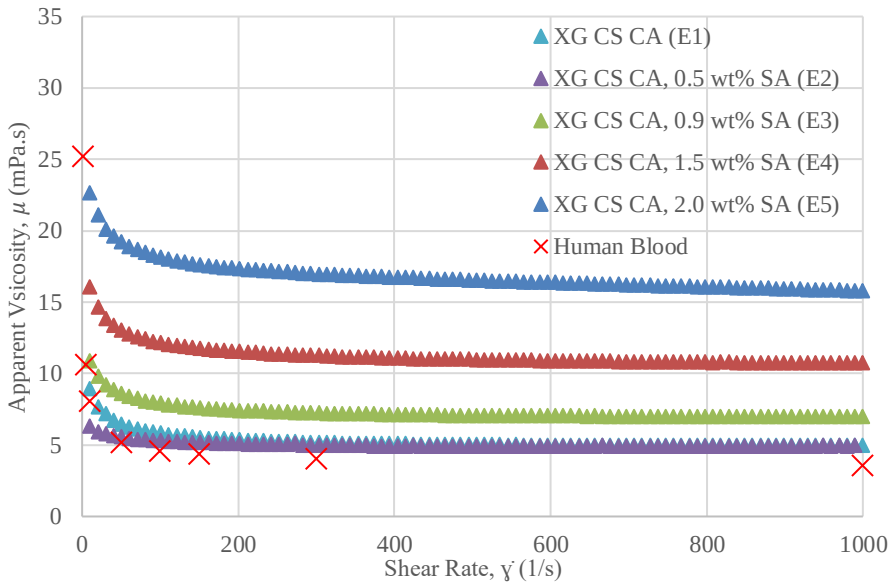

Figure 5: Apparent viscosity against shear rate for blood mimicking fluid samples containing xanthan gum, corn starch and contrast agent with varying surfactant concentrations, and for human blood [5]

According to a study on the effect of contrast media conducted by Pugh [14], it was reported that iodinated contrast media has the ability to produce rheological alterations when injected into a non-Newtonian blood, primarily due to the viscosity and osmolality difference between the contrast media and blood. Hence, it can be interpreted that the CA added in Set E samples has shear-thickening properties which might have reduced the overall shear-thinning ability of the blood mimicking fluid samples.

4.0 CONCLUSION

The addition of non-ionic surfactant does not have any significant effect on the densities of the various blood mimicking fluid compositions comprising of water-glycerol base fluid, xanthan gum, corn starch and contrast agent.

The water-glycerol based fluid makes up a large percentage of the blood mimicking fluid samples composition so other constituents added into the blood mimicking fluid composition will not have significant influence on the overall density of the blood mimicking fluid. On the other hand, the addition of non-ionic surfactant affected the apparent viscosity of blood mimicking fluid formulations. In general, the higher the surfactant concentration added into the blood mimicking fluid, the higher the overall viscosity of the blood mimicking fluid. High surfactant concentration of greater than 2 wt% in blood mimicking fluid was found to grant the Newtonian base fluid shear thinning characteristics with viscosity decreasing as the shear rate increases and increases the shear-thinning properties of blood mimicking fluid. According to the viscosity profile, the blood mimicking fluid containing 59.48 wt% water, 40 wt% glycerol, 0.01 wt% xanthan gum, 0.01 wt% corn starch, 4vol/wt % contrast agent and 0.5 wt% of surfactant showcases the closest viscosity profile with the actual human blood. It is recommended to further investigate the rheologcal properties by comparing with blood rheological models .

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6.0 REFERENCES

[1] S. Maroni, V. Mauri, E. Negrello, L. Pugliese, A. Pietrabissa and F. Auricchio, "Quantitative assessment of 3D printed blood vessels produced with J750™ digital anatomy™ for suture simulation," 2022, doi: 10.1101/2022.01.09.475308.

[2] A. Pietrabissa, S. Marconi, E. Negrello, V. Mauri, A. Peri, L. Pugliese, E. M. Marone, and F. Auricchio, "An overview on 3D printing for abdominal surgery," *Surgical Endoscopy*, vol. 34, no. 1, pp. 1–13, 2019.

[3] T. A. Fuhrmann, A. Schlesinger, M. Schultz, and K-V. Jenderka, "Blood Mimicking Fluid for Reproducing Rheological and Acoustical Blood Properties," *Proceedings of the 46th Annual Ultrasonic Industry Association*

Symposium, 2017.

[4] M. Z. Matjafri, A. A. Oqlat, N. Suardi, M. A. Oqlat, M. A. Abdelrahman, and A. A. Oqlat, "A review of suspension-scattered particles used in blood-mimicking fluid for Doppler ultrasound imaging," *Journal of Medical Ultrasound*, vol. 26, no. 2, p. 68, 2018.

[5] J. M. Jung *et al.*, "Reference intervals for whole blood viscosity using the analytical performance-evaluated scanning capillary tube viscometer," *Clin. Biochem.*, vol. 47, no. 6, pp. 489–493, 2014, doi: 10.1016/j.clinbiochem.2014.01.021.

[6] X. Zhou and P. R. Hoskins, "Testing a new surfactant in a widely-used blood mimic for ultrasound flow imaging," *Ultrasound*, vol. 25, no. 4, pp. 239–244, 2017.

[7] I. Gonçalves, J. Varelas, G. Coutinho, A. Moita, D. Pinho, R. Lima, J. Miranda, E. Veja, J. Montanaro, and A. Moreira, "Dynamic flow behaviour of a blood analogue fluid in microchannels for microcirculation studies," *Proceedings of the 14th International Joint Conference on Biomedical Engineering Systems and Technologies*, 2021.

[8] A. A. Oglat, M. Z. Matjafri, N. Suardi, M. A. Oqlat, A. A. Oqlat and M. A. Abdelrahman, "A New Blood Mimicking Fluid using Propylene Glycol and their Properties for a Flow Phantom Test of Medical Doppler Ultrasound ," *International Journal of Chemistry, Pharmacy & Technology*, vol. 2, no. 5, pp. 220–231, 2017.

[9] N. Perrira, A. S. Shuib, S. W. Phang and A. S. Muda, "The Formulation of Blood Mimicking Fluid for Application in Medical Simulator under Angiography Visualisation," *B.S. Thesis*, School of Engineering, Taylor's University, Selangor, 2021.

[10] "Omnipaque (Iohexol Injection): Uses, Dosage, Side Effects, Interactions, Warning." https://www.rxlist.com/omnipaque-drug.htm (accessed October 18, 2022).

[11] E. Rosenbaum, M. Massoudi, and K. Dayal, "Surfactant stabilized bubbles flowing in a newtonian fluid," *Mathematics and Mechanics of Solids*, vol. 24, no. 12, pp. 3823–3842, 2019.

[12] N. C. Crawford, L. B. Popp, K. E. Johns, L. M. Caire, B. N. Peterson, and M. W. Liberatore, "Shear thickening of corn starch suspensions: Does concentration matter?," *J. Colloid Interface Sci.*, vol. 396, pp. 83–89, Apr. 2013, doi: 10.1016/J.JCIS.2013.01.024.

[13] Annu and S. Ahmed, "Advanced green materials: An overview," *Advanced Green Materials*, pp. 1–13, 2021.

[14] N. D. Pugh, "Haemodynamic and rheological effects of contrast media: The role of viscosity and osmolality," *European Radiology*, vol. 6, no. S2, 1996.