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Simulation of blood oxygenation in capillary membrane oxygenators using modified sulfite solution

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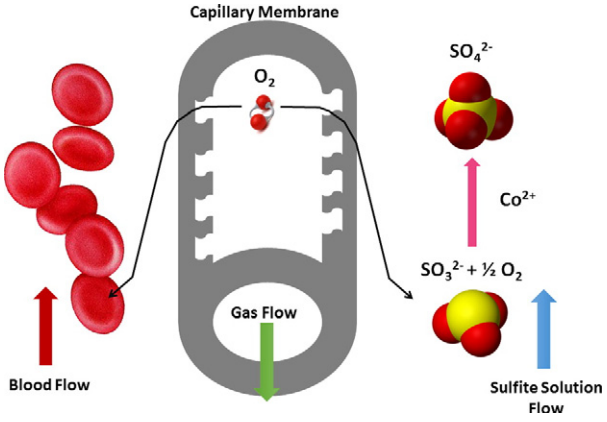
GRAPHICAL ABSTRACT



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ABSTRACT

Blood oxygenation is the main performance characteristic of capillary membrane oxygenators (CMOs). Handling of natural blood in in vitro investigations of CMOs is quite complex and time-consuming. Since the conventional blood analog fluids (e.g. water/glycerol) lack a substance with an affinity to capture oxygen comparable to hemoglobin's affinity, in this study a novel approach using modified sulfite solution is proposed to address this challenge. The solution comprises sodium sulfite as a component, simulating the role of hemoglobin in blood oxygenation. This approach is validated by *OTR* (oxygen transfer rate) measured using native porcine blood, in two types of commercially available CMOs. Consequently, the number of complicated natural blood investigations in the evolution procedure of newly developed oxygenators would considerably decrease. Moreover, the reassessing of failed devices, in clinics, would be performed more precisely using a modified sulfite solution than simple water/glycerol testing.

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1. Introduction

An oxygenator is a vital instrument, which substitutes the role of natural lung, in some critical extracorporeal applications, e.g. cardiopulmonary bypass surgeries [1,2]. Oxygen transfer rate is a major parameter evaluating the efficacy of an oxygenator [3,4]. In conventional investigations of *OTR* in oxygenators, natural human or animal blood is used [5]. However, the application of natural blood accompanies a lot of handling difficulties [6]. On the one hand, safety is a serious problem since human or animal blood may cause zoonotic or transmissible diseases. On the other hand, blood should be fresh, anti-coagulated (adding heparin, EDTA, citrate, etc.), and specifically prepared for each experimentation. For example, to investigate the *OTR* of a membrane oxygenator in vitro, blood parameters ought to be set to that of mixed venous blood requiring a complex preprocessing of blood through a deoxygenating circuit [7,8].

Considering blood nature, there are many factors affecting the blood's O_2 uptake (e.g. *Hct*, *BE*, p_{O_2}, p_{CO_2}). In this regard, global standard organizations such as FDA defined an almost wide range of fluctuations for the blood inlet parameters for the investigations of oxygenators' performance characteristics. This standard is known as DIN EN ISO 7199 for blood gas exchangers provided by the Association for the Advancement of Medical Instrumentation (AAMI). Table 1 shows general specifications for inlet blood based on the AAMI standard [9–13].

It is obvious that the reproducibility of in vitro studies with natural blood is challenging [14–17]. In addition, such investigations necessitate the use of different specific devices, such as blood gas analyzer and blood pressure sensors, to measure the blood parameters [18,19]. All these obstacles corroborate the need for a simple, straightforward and widely available alternative approach to measure blood oxygenation through membrane oxygenators.

Commonly, distilled and deionized water has been used as an alternative to blood in the gas exchange experiments of CMOs [20]. However, the Newtonian behavior of water, in contrast with the non-Newtonian behavior of blood, in addition to the low capacity of water to uptake and release oxygen, in comparison with the role of hemoglobin in blood, intensify the inaccuracy of such a method. It has been basically suggested to use glycerol in order to alter the viscosity of a solution [5,21–24]. The mixture of water and glycerol was proposed, in 1993, by Kreulen et al. to be used in the experimental studies of hollow fiber membrane modules as gas–liquid contactors [24]. In 1994, Gourlay and Taylor used this solution for simulating blood oxygenation through CMOs in vitro [25]. Later on, Wickramasinghe et al. modified the non-Newtonian behavior of this mixture adding a small amount of xanthan gum, and investigated the gas exchange in CMOs using this solution as a blood analog fluid [5,23,26].

Various solutions have also been used as blood substitutes simulating its gas exchange performance. Mottaghy et al., in 1976, showed the possibility of using fluorocarbon in liquid oxygenators for the first time [27]. Some new studies proposed the application of hemoglobin-based artificial oxygen carriers as a substitute with natural blood [28]. In 2003, R.M. Winslow investigated different paradigms for the preparation and characterization of hemoglobin-based red cell substitutes [29]. In such approaches, oxygen can bind chemically to hemoglobin substitutes parallel to physically dissolving in water, which shows a comparable oxygenation affinity to natural blood. Therefore, these methods have a great advantage to the simple mixture of water and glycerol where there is no substitute for chemical binding with oxygen. However, these blood substitutes are rather expensive and not widely available; and therefore, the practical simulation of blood oxygenation through capillary membrane oxygenator remains challenging.

Sulfite solution is a novel alternative that demonstrates a high affinity for oxygen uptake [6]. It has been already used to investigate *OTR* in gas–liquid contactors as described by Hermann et al. [30]. Moreover, in a bioreactor where there is a living organism consuming oxygen, sulfite solution can be employed to simulate such metabolic procedures [21,22,30]. This method is based on the oxidation of sulfite ions while converting to sulfate ions in the presence of a metal catalyst (e.g. Fe^{+}, Cu^{+}, Co^{2+}, and Mn^{+}) [30].

The aim of the present study is to modify the sulfite solution, in regard with the oxygenation and rheological properties of natural blood, in order to simulate the *OTR* through CMOs precisely. The method is then validated by comparison of the results of in vitro investigations with native porcine blood in two types of commercially available CMOs.

Table 1
AAMI standard values for the inlet blood in in-vitro investigations of blood gas exchangers.

Parameter	Standard value	Std. dev.	Unit
S_{O_2}	65.0	±5.0	(%)
p_{O_2}	40.0	±5.0	(mm Hg)
p_{CO_2}	45.0	±5.0	(mm Hg)
C_{Hb}	12.0	±1.0	(g_{Hb}/dl_{blood})
BE	0.0	±5.0	($mmol_{base}/l_{blood}$)
T	37.0	±2.0	(°C)

2. Material and methods

2.1. Preparation of sulfite solution

The sulfite solution comprises sodium sulfite, Na_2SO_3 acts as an oxygen uptake component, phosphate buffer solution works as an inhibitor for sudden pH drop, and cobalt catalyst as an accelerator for oxygen uptake.

In order to prepare the buffer for the sulfite solution [21,22,30], 3.56 (g) of Na_2HPO_4 (Merck KGaA, Darmstadt, Germany) was added to 100 ml distilled and deionized H_2O and 3.12 (g) of NaH_2PO_4 (Merck KGaA, Darmstadt, Germany) in another 100 ml of distilled and deionized H_2O. To set the pH level 8, as an initial pH level, NaH_2PO_4 and Na_2HPO_4 should be mixed together with a ratio of 4.7 (ml) to 95.3 (ml) respectively. Because, the resulting phosphate buffer is 0.2 (M), 6 (ml) of this solution dilute to 100 (ml) using the distilled and deionized H_2O to reach the final molarity of 0.012. Afterwards, 90 (ml) of 0.012 (M) phosphate buffer was nitrogenized by direct inserting of nitrogen gas, to eliminate possible dissolved oxygen molecules in the solution.

For the purpose of achieving 100 (ml) of 0.5 (M) sulfite solution, as a reference solution, 6.302 (g) of Na_2SO_3 was added to the prepared nitrogenized buffer solution. Inserting sodium sulfite to the buffer solution causes some changes in the pH level; and therefore, the final solution's pH was adjusted at 8 by adding 30 wt. H_2SO_4 (Merck KGaA, Darmstadt, Germany) and distilled and deionized H_2O to reach 100 (ml) solution in the end [22].

As a catalyst substance, $CoSO_4$ (Merck KGaA, Darmstadt, Germany) was used in this study [30]. While the catalyst concentration has a direct effect on the reaction rate, a range of catalyst concentration was investigated by sets of experiments coming henceforth. The distilled and deionized water was provided using GFL double distillation water stills 2104 (GFL mbH, Burgwedel, Germany).

This viscosity of native porcine blood in the normal range of body temperature (37 (°C)) is about 3–4 (cP) [31]. In order to simulate the rheological properties of natural blood with the prepared sulfite solution, its viscosity should be altered toward that of natural blood. Usually, glycerol is used for changing the viscosity of an aqueous solution. However, we found that glycerol interferes with the oxidation reaction of sulfite solution due to its OH functional groups; and subsequently, pH does not change. Therefore, polyethylene oxide (PEO) (Sigma Aldrich, St. Louis, MO, USA) was employed in this study, as a substance without any interfering functional group, for changing the viscosity of sulfite solution.

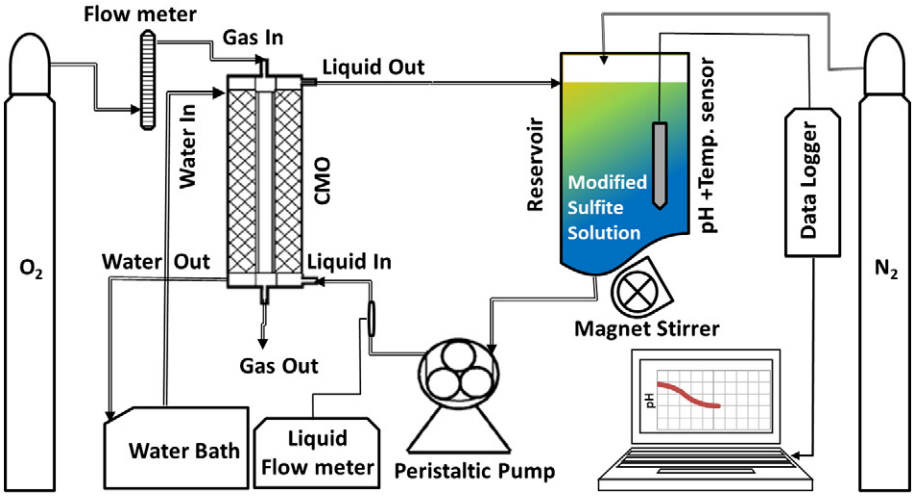

Fig. 1. The schematic diagram of the experiment circuit of modified sulfite solution.

2.2. Regulation of sodium sulfite concentration

While sodium sulfite binds with oxygen, it can simulate the role of hemoglobin in blood oxygenation. Therefore, the final concentration of Na_2SO_3 can be regulated based on any assumed hemoglobin concentration.

As an example, considering $C_{Hb} = 12.12\ (g_{Hb} \cdot dl^{-1}_{blood})$, the total oxygen chemically bond to hemoglobin would be 162.41 ($ml\ O_2/l_{blood}$), which would be equal to 0.007 (mol O_2). Taking into account the sodium sulfite reaction with O_2, if the solution is desired to uptake 0.007 (mol O_2) in each liter, 0.014 (mol) or 1.76 (g) Na_2SO_3 is required per liter of solution (considering the molar mass of Na_2SO_3 as 126.04 (g/mol)). In order to reach such a concentration of Na_2SO_3 in the final solution, 2.8 (ml) of 0.5 (M) prepared solution should be diluted to 100 (ml). Therefore, the modified sulfite solution with a regulated sodium sulfite concentration can simulate the total oxygen uptake of natural blood in respect with its assumed hemoglobin concentration.

2.3. Experiment setup

The circuits for investigating the *OTR* of CMOs using modified sulfite solution and native porcine blood are demonstrated in Figs. 1 and 2 respectively. In these setups, the following equipment were principally employed: peristaltic pump PD5206 (Heidolph Instruments GmbH&Co. KG, Schwabach, Germany); pH meter 8601 (AZ Instrument Co., Taichung, Taiwan) with its relevant USB connection and data logger program; PT-100 Ω temperature sensor connected to Stöckert temperature measuring system (Stöckert Instrumente GmbH, Freiburg, Germany); Water bath WiseCircu WCB22 (Daihan Scientific Co. Ltd., Gangwon-do, S. Korea); Gas flow meter (Dwyer Instruments Inc., Michigan, IN, USA); liquid flow meter, T110 ultrasonic liquid flow meter (Transonic Systems Inc., Ithaca, USA); magnet stirrer C-Mag HS7 (IKA-Werke GmbH&Co. KG, Staufen, Germany); silicon tubes and connectors (Raumedic AG, Dietzenbach, Germany); and viscometer DV-II with LV spindle (Brookfield Engineering Laboratories Inc., Middleborough, MA, USA). Experiments were performed on two types of commercial cylindrical CMOs, i.e. HILITE® 2800 and HILITE® 7000 (Medos AG, Stolberg, Germany), commonly used for pediatric patients and adults respectively. Both of these oxygenators have an integrated heat exchanger used to regulate the temperature of the liquid phase (i.e. modified sulfite solution and native porcine blood).

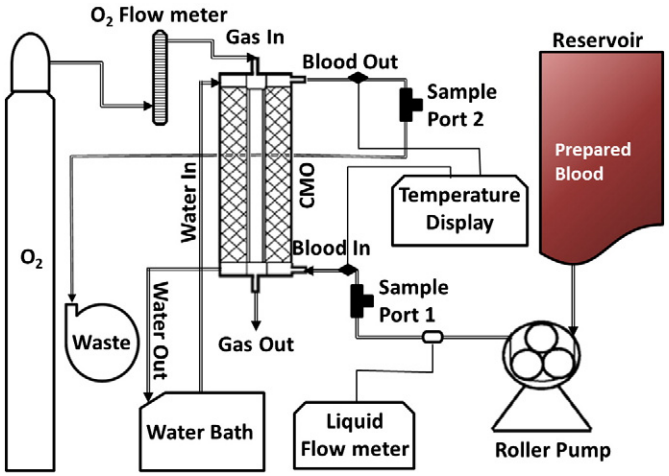

Fig. 2. The schematic diagram of the experiment circuit of natural blood.

The setup of investigations using modified sulfite solution experiments was designed as a closed circuit (shown in Fig. 1). The prepared modified sulfite solution was inserted into the Medos 1.5 l reservoir (Medos AG, Stolberg, Germany) and its empty space was filled with nitrogen gas to prevent the oxidation reaction of sulfite solution at this gas–liquid interface. In addition, the magnet stirrer C-Mag HS7 was placed under the reservoir in order to properly mix the solution. The pH of the solution was monitored online, using the pH sensor, located in the reservoir; and, the data was collected with a computer via the relevant data logger. The pH meter 8601 has also an integrated temperature sensor, which was used to measure the temperature of sulfite solution as well. The solution temperature itself was regulated using the integrated heat exchanger of the CMOs utilizing the water pumped through WiseCircu WCB22 water bath. To oxidize the sulfite solution, pure O_2 flowed inside the capillary membranes of the gas exchanger of CMOs. The oxygen flow was adjusted by Dwyer gas flow meter and its ratio toward that of liquid was set at 1:1 for all experiments.

As the oxidation reaction initiates, the pH value of the sulfite solution, which was primarily set around 8, gradually decreases and becomes constant around 4. The decrease of pH is due to the conversion of sulfite to sulfate ions, resulting in releasing hydrogen ions. While the reduction time can be exactly measured, using pH sensor data, the relative *OTR* would be calculated considering the total amount of oxygen uptake, based on the total concentration of sodium sulfite in the modified solution.

The open circuit used for native porcine blood experiments (Fig. 2) was designed similar to the clinical application of oxygenators in cardiopulmonary bypass surgeries. In these experiments, the reservoir was

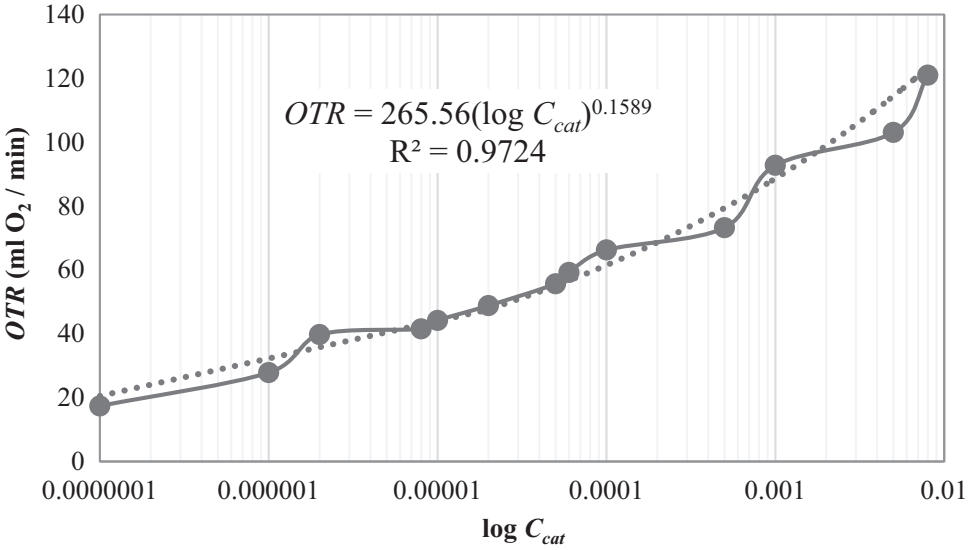

Fig. 3. *OTR* versus logarithmic scale of catalyst concentration.

filled up with the deoxygenated native porcine blood prepared due to AAMI standard (refer to Table 1). The blood temperature was adjusted to 37 (°C) using the integrated heat exchanger of the CMO. The blood's temperature was monitored at both liquid inlet and outlet of testing the CMO using temperature sensors. To boost the accuracy, the liquid flow, which was regulated by the roller pump, was measured additionally by the ultrasonic liquid flow meter. Pure oxygen was flowed into the gas phase (inside the capillary membranes) while its flow rate to that of liquid was always kept at 1:1.

Samples of liquid were taken from sample ports 1 and 2 located at the inlet and outlet of the testing CMO respectively. Then, the blood gas analyzer ABL 700 (Radiometer, Copenhagen, Denmark) investigated the samples. Differences of partial pressures of O_2 between the inlet and outlet samples would determine the *OTR* of testing CMO, at the specific blood flow rate.

3. Results

Identification of effective factors on sulfite solution's *OTR* capability and its rheological properties is essential for proper simulation of blood oxygenation. In this respect, a wide range investigation of factors affecting the sulfite solution oxidation, e.g. catalyst concentration and temperature, was performed. To simulate blood's viscosity, the effect of polyethylene oxide (PEO) concentration to sulfite solution's viscosity was studied. Afterwards, the *OTR* of testing CMO was calculated at different flow rates of sulfite solution and various catalyst and PEO concentrations at the same time. The modified sulfite solution was then determined considering the appropriate sodium sulfite, $CoSO_4$ and PEO concentrations. Finally, the results of in vitro experimentations were presented to validate the proposed approach of *OTR* calculation based on modified sulfite solution oxidation.

3.1. Catalyst concentration

To determine the range of catalyst concentrations required for the simulation of blood oxygenation, a set of experiments in various $CoSO_4$ concentrations was performed, based on the circuit shown in Fig. 1. In all these experiments the gas (O_2) and liquid (sulfite solution) flow rates were kept constant at 1000 (ml/min) and temperature at 23 (°C) through the HILITE®2800 CMO. The oxygen flow rate to that of the sulfite solution was regulated at 1:1. The final concentration of sodium sulfite in the 1.5 (l) solution was set to be able to capture 243.62 (ml)

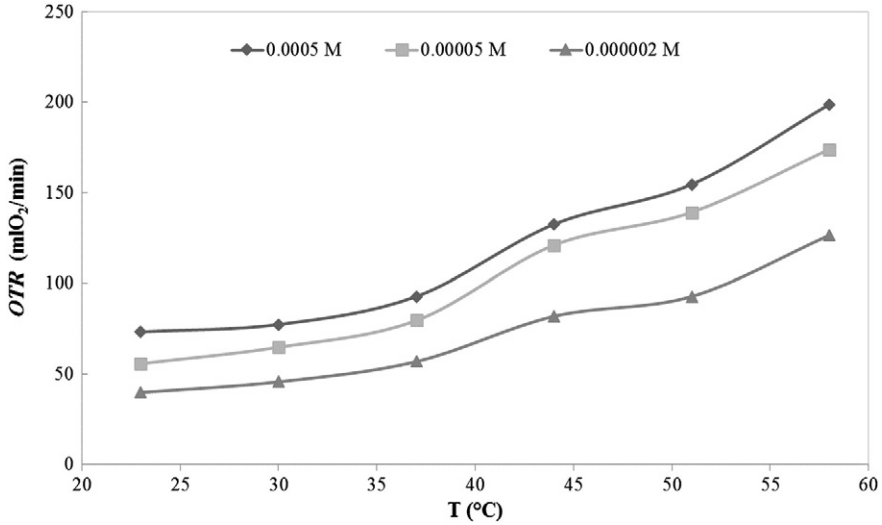

Fig. 4. Effects of temperature variations on *OTR* in different catalyst concentrations.

Table 2
Results of viscosity changes by adding PEO at a shear rate of 10 (s^{-1}).

PEO wt.%	Viscosity (cP = 1000 × Pa·s)
0.5	1.3
1	2.1
2.5	2.9
5	4.4

oxygen in total, which would be equal to the total oxygen chemically bound to hemoglobin in blood with $C_{Hb} = 12.12$ ($g_{Hb}\cdot dl_{blood}^{-1}$). The trend of *OTR*, calculated by the measurement of pH drop time, to the logarithmic concentration of catalyst is depicted in Fig. 3.

3.2. Temperature

Temperature has a great impact on the oxidation rate of sulfite solution [22,30]. To study this effect in an oxygenator, the temperature of the sulfite solution was regulated by WiseCircu water bath through the heat exchanger of the CMO (Fig. 1). The temperatures were then increased from 23 to 58 (°C) by an order of 7, to meet 37 (°C) which is the typical clinical operating condition of a CMO in clinical applications. As depicted in Fig. 4, increasing the temperature would cause an escalation in the oxidation rate, keeping the concentration of catalyst constant. Other operating conditions were considered similar to the catalyst concentration investigations.

3.3. Viscosity

To examine the viscosity, sulfite solutions with different weight percentages of PEO were examined by Brookfield DV-II viscometer with LV spindle. These tests were performed at 37 (°C) in different shear rate categories. The results showed that in both high and low shear rates the viscosity remains almost constant. The following table demonstrates the result of weight percentage added to PEO on the viscosity of sulfite solution.

The resulting diagram can be depicted using the presented data of Table 2 to find out the required amount of PEO for any assumed viscosity using the provided trend line.

Considering Fig. 5, it can be computed that by adding 2.76, 3.53 and 4.3 wt.% PEO the viscosities of 3, 3.5 and 4 (cP) are achieved respectively.

3.4. Liquid flow rates

The effects of sulfite solution flow rate on *OTR* were investigated using the flow rates of 400, 1200, 2000 and 2800 (ml/min) which were employed in combination with different catalyst concentrations as well as zero and 3.53 wt.% of PEO (in accordance with the viscosity modification to reach the viscosity of 3.5 (cP)). These experiments were performed, based on the circuit shown in Fig. 1, with a specific concentration of sodium sulfite to capture 243.62 (ml) oxygen in total. As it is shown in Fig. 6, the increase of flow rate as well as catalyst concentration would lead to the augmentation of *OTR*. Moreover, it is well demonstrated that the adding of PEO causes considerable negative effect on *OTR*.

3.5. OTR simulation in CMOs

Two types of commercial available CMOs, i.e. HILITE® 2800 and 7000, were used in this study as a pediatric and adult oxygenator respectively. The concentration of modified sodium sulfite with 3.53 wt.% of PEO is adjusted, based on 12.12 (g_{Hb}/dl_{blood}) due to AAMI standard (Table 1), to capture 162.41 (ml O_2/L_{ss}). This modified sulfite solution was utilized to investigate the *OTR* of HILITE® 2800 CMO, with the flow rates of 400, 1200, 2000 and 2800 (ml/min) and HILITE® 7000 CMO, with the flow rates of 1000, 3000, 5000 and 7000 (ml/min) which are in accordance with the flow rates commonly used in in vitro natural blood investigations. The *OTR* results for both HILITE® 2800 and 7000 CMOs are presented in the following figure.

In order to validate the proposed approaches for simulating the *OTR* of a CMO, both HILITE® 2800 and 7000 CMOs were examined through the oxygenation circuit (Fig. 2), running with native porcine blood due to the AAMI standard (Table 1). The outcomes of *OTR*, in in vitro blood investigations are shown in Fig. 8.

4. Discussions

Investigation of oxygen transfer rate with the changing of catalyst concentration reveals the increase of *OTR* with the increase of $CoSO_4$ concentration (Fig. 3). In lower concentration of catalyst (10^{-7} to 8×10^{-6} (M)), these changes are almost linear; however, in higher concentration of catalyst (higher than 5×10^{-3} (M)), *OTR* increases dramatically which indicates the changing of reaction order in higher catalyst concentration. Moreover, the logarithm of catalyst concentration can be well correlated with *OTR* by the power law relationship presented in Fig. 3.

The effect of temperature on the *OTR* of modified sulfite solution is demonstrated in Fig. 4. By increasing the temperature from 23 to 58 (°C), the *OTR* elevates up to 3.2 times. This increment corroborates the excessive impact of temperature on the oxidation of sulfite solution. In addition, the trend does not change noticeably in growing catalyst concentration. It can be concluded that, in sulfite solution oxidation, the catalyst concentration has a direct effect on the reaction rate while

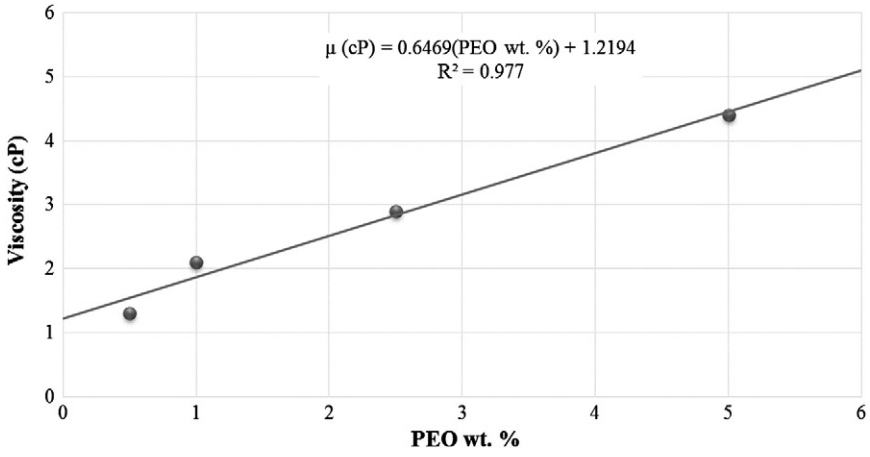

Fig. 5. Viscosity of sulfite solution due to added PEO and the relative linear trend line.

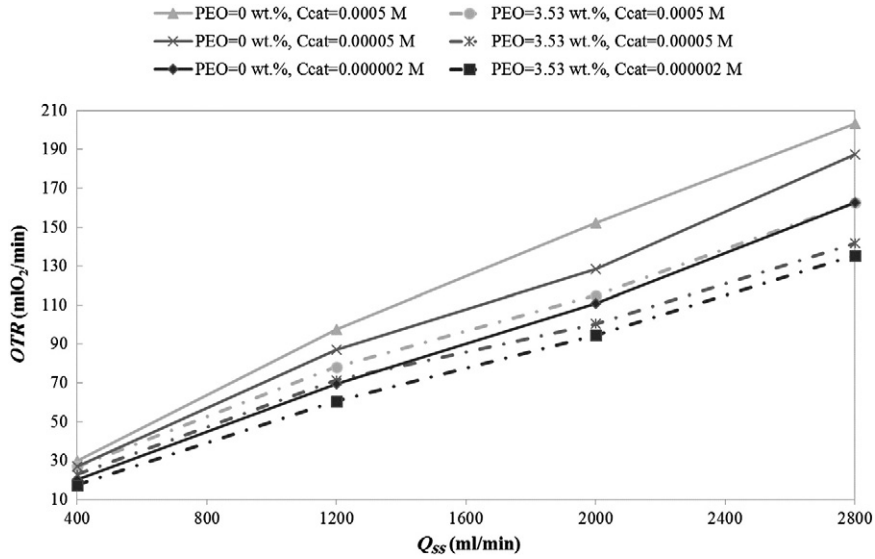

Fig. 6. Effects of sulfite solution's flow rates on *OTR* in different catalyst concentrations and PEO (wt.%).

it does not have a considerable effect on the mechanism of oxygen transfer rate. Contours of *OTR* increment regarding both temperature and catalyst concentration are shown in Fig. 9.

It is obvious in Fig. 9 that higher *OTRs* are achievable by increasing both the temperature and catalyst concentration of the sulfite solution. It can also be predicted that each 10 (°C) temperature rising would cause an approximate increase of 25 (ml/min) in the relevant *OTR*. However, this trend shifts to left by growing the concentration of catalyst. An interesting outcome of these investigations is shown in Fig. 10, where the trend of *OTR* toward the time of pH drop is depicted.

According to Fig. 10, the decline of the reaction rate by the reduction of catalyst concentration at different temperatures is evident. It is noticeable that the curves' trends follow each other; and also, *OTRs* in higher catalyst concentration at lower temperatures are overlapped by those in lower catalyst concentration at higher temperatures. It can be claimed that the effects of the variation of catalyst concentration and temperature on sulfite oxidation reaction are almost the same. In addition, Fig. 10 indicates that for all applied catalyst concentrations, *OTRs* at 23, 30 and 37 (°C) are near to each other the same as *OTRs* at 44, 51 and 58 (°C). However, a significant gap between these two groups is recognized. Therefore, it could be assumed that the critical temperature for the oxidation reaction of sulfite solution is between 37 and 44 (°C).

There is an almost linear relationship between modified sulfite solution's flow rate and *OTR* (Fig. 6). This phenomenon is due to the increase of mass transfer driving force by the growth of liquid flow velocity, which has a direct relation to the flow rate. This behavior seems to be similar in in vitro investigations using modified sulfite solution as well as natural porcine blood (Figs. 7 and 8 respectively).

Moreover, Fig. 6 obviously demonstrates the noticeable effect of catalyst concentration on *OTR*; and also, it interestingly reveals that the catalyst performance is apart from the effect of liquid flow rate on *OTR*. Considering this outcome along with the effects of catalyst concentration and temperature on *OTR* (shown in Fig. 4), it can be concluded that the impact of catalyst concentration on the sulfite solution's *OTR* is independent of operating factors.

As can be seen in Fig. 6, when the specified concentration of polyethylene oxide (PEO) was added to the sulfite solution, in various catalyst concentrations, *OTR* has been decreased subsequently. This effect could be due to the clustering phenomenon, which has been observed in many macromolecular solute systems. Since PEO makes a kind of cage or chelating-like structures dissolving in water [32], the sodium sulfite molecules are likely to be entrapped, and consequently, the total oxygen uptake capacity of the solution is decreased. Therefore, the concentration of PEO should be carefully taken into account in the

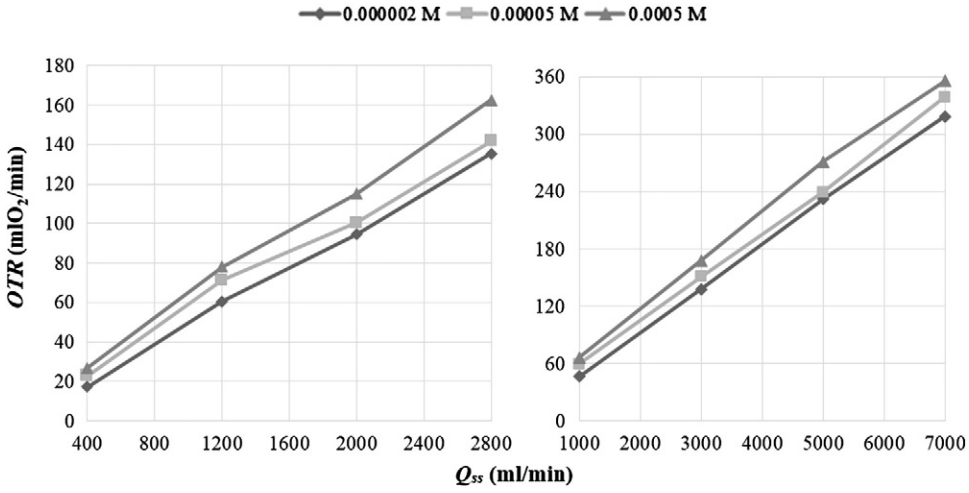

Fig. 7. *OTR* of HILITE®2800 CMO (left) and HILITE®7000 CMO (right) measured based on the oxidation of modified sulfite solution with different catalyst concentrations.

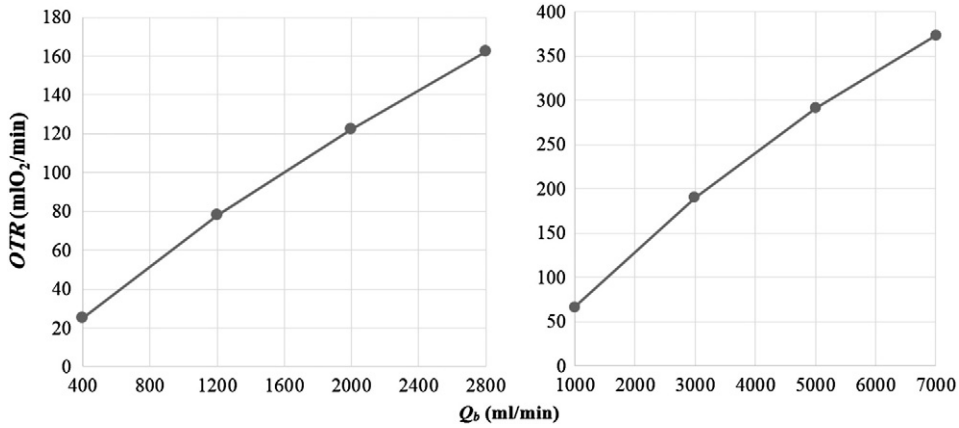

Fig. 8. *OTR* of HILITE®2800 CMO (left) and HILITE®7000 CMO (right) at different native porcine blood flow rates.

modification process of sulfite solution. It can be claimed that the performance of catalyst is also not affected by PEO concentration.

The courses of *OTR* using modified sulfite solution in CMOs (Fig. 7) and in vitro experiments using native porcine blood (Fig. 8) reveal the same trends and behaviors. The *OTR* of modified sulfite solution can be matched with the *OTR* of native porcine blood by the regulation of catalyst concentration. Comparing Figs. 7 and 8, the appropriate catalyst concentration in modified sulfite solution is 0.0005 (M) in order to suitably simulate the oxygenation of native porcine blood prepared due to the AAMI standard (refer to Table 1).

5. Conclusions

The sulfite solution is an appropriate substitution to natural blood in order to simulate the blood oxygenation behavior. To improve the performance of this solution, numbers of modifications and investigations are performed in this study. Comparing the results manifests that by adding 3.53 (wt.%) PEO and 0.0005 (M) $CoSO_4$ to the 0.014 (M) sodium sulfite solution, the oxygenation of prepared native porcine blood due to the AAMI standard can be properly simulated.

The $CoSO_4$ catalyst is correlated with oxygen transfer rate as *OTR* (ml O_2/min) $= 265.56(\log C_{cat}\,(\mathrm{M}))^{0.1589}$ ($R^2 = 0.9724$). Our investigations reveal that operating factors (especially temperature) do not affect the performance of catalyst in oxidation of sulfite solution. In addition, PEO changes the viscosity of sulfite solution as μ (cP) $=$ 0.6469(PEO wt.%) $+$ 1.2194 ($R^2 = 0.977$); nevertheless, its negative effect on *OTR* should be carefully considered. However, temperature and liquid flow rate have a direct positive influence on sulfite solution's *OTR*. It is concluded that the critical temperature for the oxidation reaction of sulfite solution is between 37 and 44 (°C); and therefore, the temperature of this method should be precisely kept constant at 37 (°C).

The applicability of this approach is demonstrated in two types of commercial adult and pediatric CMOs. Comparing simulation results with in vitro porcine blood investigations corroborates the effectiveness of modified sulfite solution to simulate blood oxygenation, which is a major concern, in oxygenators. On the one hand, the proposed approach can significantly reduce the number of sophisticated natural blood experiments in the evaluation process of the performance characteristics of CMOs.

On the other hand, based on clinical regulations, in case mortality occurs during cardiopulmonary bypass surgery, the oxygenator should be

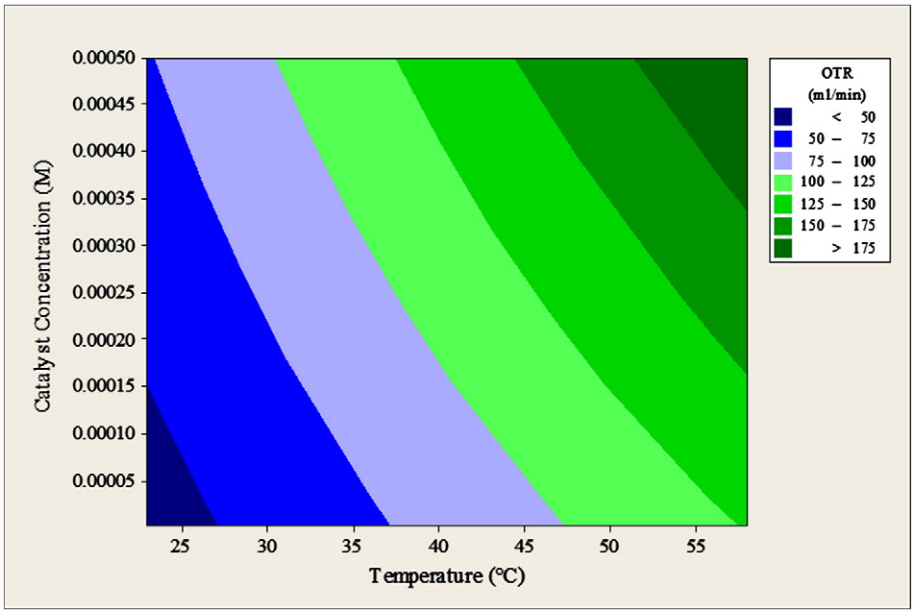

Fig. 9. Contours of *OTR* according to catalyst concentrations and temperatures.

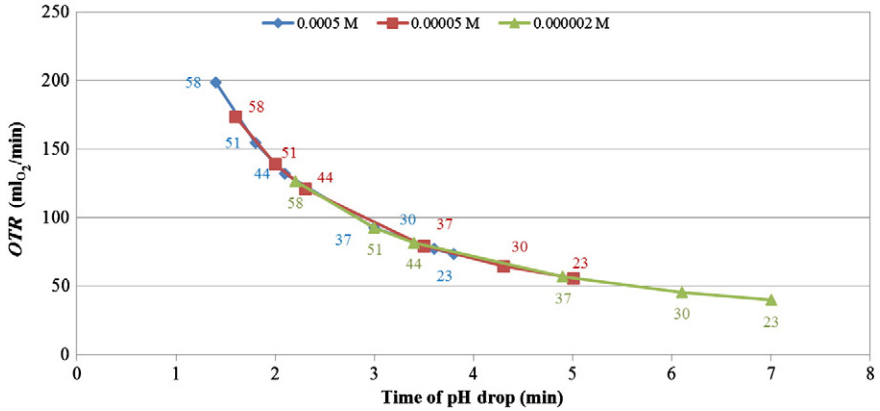

Fig. 10. *OTR* vs. time in different catalyst concentrations at different temperatures (shown on markers).

reassessed for its blood oxygenation capability. This critical evaluation would indicate if it was the fault of oxygenator manufacturer or cardio-technician. The proposed approach, in this study, could highly promote the accuracy of reassessing procedure while, conventionally, the blood oxygenation capability of a failed oxygenator has been only investigated using water/glycerol.

Nomenclature

Symbols	Description	Unit
C_{Cat}	Catalyst concentration	M
C_{Hb}	Hemoglobin concentration	M
Hct	Hematocrit	%
OTR	Oxygen transfer rate	ml O_2/min
Q_b	Blood flow rate	ml/min
Q_{SS}	Sulfite solution flow rate	ml/min
T	Temperature	°C
μ	Kinematic viscosity	cP
Abbreviations		
CMO	Capillary membrane oxygenator	
PEO	Polyethylene oxide	

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