Temperature Dependence of the Rheological Characteristics of Polidocanol Foam in Conditions of Continuous Shear Deformation

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Abstract: The foam sclerotherapy is a popular and highly effective method of varicose disease treatment allowing to obtain a positive result in more than 80% of cases. The foams characteristics depend on the kind of sclerosant, its concentration, a type of gas, gas/liquid ratio, and the technique of foam preparation. The present investigation, was carried out to assess the influence of temperature on the rheological characteristics of the foam prepared from an aqueous solution of a sclerosant (polidocanol) in conditions of continuous shear deformation. The dependence of the viscosity of the foam on the shear rate was investigated in the specified temperature range 10–25°C and in the specified shear range γ = 3.75–82.5 s^{-1} by the Brookfield LVDV-III Ultra CP viscometer connected to a Brookfield TC-102 Circulating Bath with Digital Controller. The viscosity of the foam prepared from a polidocanol solution of investigated concentrations (1%, 3%) increases on temperature decrease and concentration increase in the investigated ranges of temperatures and shear velocities, varying within 0.028–0.165 Pa·s.

Key-Words: sclerosant, foam, polidocanol, concentration, viscosity, rheological characteristics, temperature.

1 Introduction

Varicose disease is widely prevalent worldwide, with causes and symptoms ranging from straightforward to complex. Beyond the direct visibility of varicose veins, patients can suffer pain, skin pigmentation, inflammation, induration and skin ulceration as a result [1].

The traditional approach to treating large varicose veins and complicated venous pathology has been surgical. However improvement in sclerotherapy methods as well as other minimally invasive techniques has allowed for non-surgical treatment of large diameter vessels.

Polidocanol (POL, lauromacrogol 400, alcohol ethoxylate, $C_{30}H_{62}O_{10}$) is surface active agent used in the sclerotherapy treatment of varicose veins and vascular malformations. The another common used detergent is sodium tetradecyl sulfate (STD). POL is superior to STD as it has lower incidence of complications and shows greater stability than STD [2, 3]. Both agents administered intravenously as liquid or foam and function by endothelial lysis, exposure of the basement membrane collagen resulting in endovenous fibrosis.

Polidocanol (POL) is an alcohol that was introduced in 1936 as a surface anaesthetic. The basic molecule (hydroxypoliethoxy-dodecane) is formed by a lipophilic and by a hydrophilic part, and the amphipathic properties of POL explain the interaction with veins and skin. In 1960 Henschel used POL in varicose vein treatment; since 1967 this usage has spread worldwide, and several clinical trials have been performed to test this molecule in small and large varices. Sclerosant foams have predominantly replaced liquid agents in clinical practice [4]. Foam sclerosants have the added benefit of displacing the intravascular blood and hence maximizing contact of the active agent with the vessel wall and minimizing dilution and deactivation by blood components [5]. The foam sclerotherapy allows to obtain a positive result in more than 80 % of cases [6].

The foams characteristics depend on the kind of sclerosant, its concentration, a type of gas, gas/liguid ratio, and the technique of foam preparation [7].

The most popular method of foam preparation is Tessari's method [8], in which two syringes and three-way tap (connector) are used. The latter allows one to transfer contents of the syringes (a gas in one, and a liquid sclerosant in the other) from one to the another (up to 20 times).

The impact of different gases on the efficacy and safety of sclerotherapy is well described in the literature. Despite of smaller side-effects and larger volumes of CO_2-O_2 foam which could be applied safely [9], the half-life of room air foam is more than 3 times as long as that of CO_2 and 1.5 times as long as that of a mixture of CO_2 and O_2[10]. Authors of European guidelines for sclerotherapy recommend air as the gas component for generation of sclerosing foam and a ratio of liquid sclerosant to gas for the production of a sclerosing foam of 1 + 4 (1 part liquid + 4 parts air) [11].

In the treatment of primary truncal varicose veins, 3% polidocanol foam seems to be more effective than 1% polidocanol foam [12].

Velenzuela et al. [13] proved that foam sclerosants are more stable at cooler temperatures. In his study such parameters as surface tension, liquid drainage were analyzed.

Thus, the results of sclerotherapy and physical characteristics of the foam using different sclerosing agents, concentrations, and methods of preparing foams are well documented in the literature. At the same time the influence of the temperature factor on the viscosity of the foam sclerosant is still not fully understood. The present investigation, was carried out to assess the influence of temperature on the rheological characteristics of the foam prepared from an aqueous solution of a sclerosant (polidocanol) (1%, 3%) in conditions of continuous shear deformation in the specified temperature range (10, 15, 20, 25 °C).

2 Materials and Methods

Foam was prepared by a Tessari's method (gas/liguid ratio is 4:1). The ampoule with 1% and 3% Polidocanol (Aethoxysklerol; Kreussler Pharma, Wiesbaden, Germany), syringes (Becton Dickenson, Fraga, Huesca, Spain) and three-way taps (B Braun Medical, Sheffield, UK) ware placed in the freezer (1 degree º C) 5 minutes before the application to reduce its temperature. The plungers were moved through 20 full strokes to disperse the air in liquid (Fig. 1).

Fig. 1. Tessari's method of foam preparation from polidocanol solution

A stroke was defined as a movement emptying and refilling the syringe initially filled with liquid. One stroke approximately took 1 second. Prepared foam was injected from syringe to the test-tube. After this self-filling transfer pipet for getting 0.5 ml of foam from the test-tube and injection to the measuring cell was used.

The dependence of the viscosity of the foam on the shear rate was investigated in the specified temperature range 10–25°C and in the specified shear r ange γ=3.75–82.5 s^{-1} by the Brookfield LVDV-III Ultra CP viscometer connected to a Brookfield TC-102 Circulating Bath with Digital Controller.

Equipment for investigating rheological characteristics of cooled polidocanol solution foam is shown in Fig. 2.

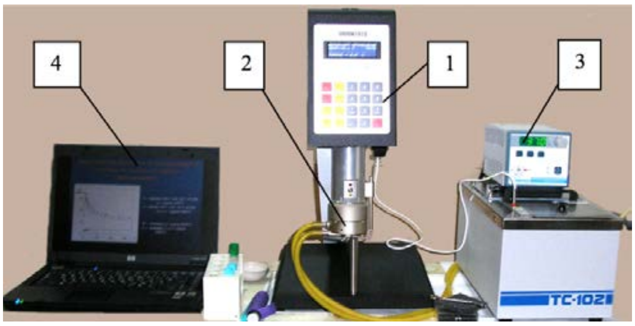

Fig. 2. Equipment. 1 – Brookfield LVDV-III Ultra CP viscometer; 2 – Measuring cell; 3 – Brookfield TC-102 Circulating Bath with Digital Controller; 4 – Computer

The measurement error for a CPE-40 spindle rotating at a certain speed [14] is presented in Table 1.

Table 1. The error of viscosity measurement at different shear rates

$\Delta\eta$, Pa·s	$\dot{\gamma}$, s^{-1}	$\Delta\eta$, Pa·s	$\dot{\gamma}$, c^{-1}	$\Delta\eta$, Pa·s	$\dot{\gamma}$, s^{-1}
0.00028	82.5	0.00044	52.5	0.0012	22.5
0.00031	75	0.00051	45	0.0015	15
0.00034	67.5	0.00061	37.5	0.0031	7.5
0.00038	60	0.00077	30	0.0061	3.75

The measurement unit of a rheometer with a cone /plate geometry allows one to determine the absolute viscosity of a very small sample (volume 0.5 ml) of fluid investigated at a certain shear rate [14]. The accuracy of temperature measurement is ±0.1°C. A sample of cooled polidocanol foam in viscometer cell before measurement is shown in Fig.3.

Fig. 3. A sample of cooled polidocanol foam in viscometer cell before measurement

3 Results

Prior to the experiment the test measurements of a reference standard fluid, i.e., distilled water (viscosity η =1.002 mPa·s at 20°C), were carried out at the temperature 20°C in the range of shear rates 150–300 s^{-1} and viscosity η = 1.02–1.03 mPa·s.

A satisfactory correlation obtained with the data described in [15] allowed one, after test measurements, to start experiments on determining the viscosity of cooled polidocanol solution foam samples. The results of measurements are shown in Figs. 4 and 5.

The dependences of viscosity on shear rate for 1% polidocanol solution foam samples at temperatures t=10–25oC in the range of shear rates =3.75–82.5 s-1 are shown in Fig. 4a. It is found that the viscosity of the foam under the conditions mentioned decreases and changes in the range 0.130–0.028 Pa·s.

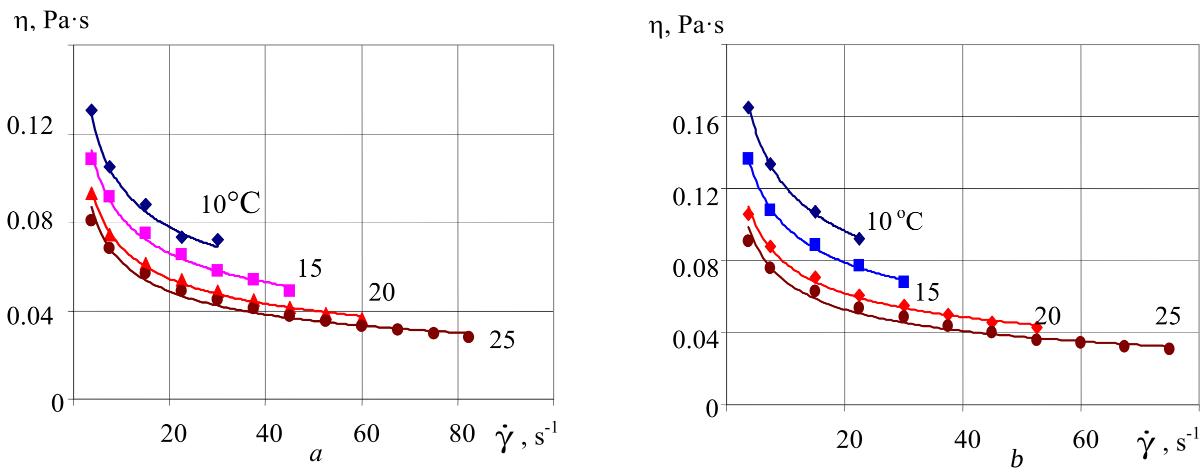

Fig. 4. The dependences of the viscosity on the shear rate for the foam prepared from a polidocanol solution of different concentrations (*a* – 1%; *b* – 3 %) on the shear rate in the specified temperature range 10–25 °C

The dependences of viscosity on shear rate for 1% polidocanol solution foam samples at temperatures t=10–25°C in the range of shear rates $\dot{\gamma}$=3.75–82.5 s^{-1} are shown in Fig. 4*a*. It is found that the viscosity of the foam under the conditions mentioned decreases and changes in the range 0.130–0.028 Pa·s.

The dependences of viscosity on shear rate for 3% polidocanol solution foam samples at temperatures t=10–25 °C in the range of shear rates $\dot{\gamma}$ = 3.75–75 s^{-1} are shown in Fig. 4*b*. Under these conditions, the viscosity of the foam is found to decrease and changes in the range 0.165–0.031 Pa·s, i.e., it increases with concentration.

The dependences of viscosity on t he shear rate obtained are described by the power-law rheological model [16]: $\eta = \tau / \dot{\gamma} = K(\dot{\gamma})^{n-1}$, where τ is the shear stress, Pa; η is the viscosity, Pa·s; K is the consistency index, Pa·s^n; n is the flow index, and $\dot{\gamma}$ is the shear rate, s^{-1}.

The temperature dependence of the model parameters in the investigated temperature range can be approximated with the accuracy of R^2=0.9–0.99 by a linear function:

foam from a 1% polidocanol solution: K = -0.0034t + 0.222, Pa·s^n;

n = -0.0032t + 0.731;

foam from a 3% polidocanol solution: K = -0.0068t + 0.319, Pa·s^n;

n = -0.0032t + 0.716.

Table 2. The values of the parameters of the rheological model for polidocanol solution foam samples of various concentrations at different temperatures

t,°C	10		15		20		25	
c, %	1	3	1	3	1	3	1	3
K, Pa·s^n	0.19	0.26	0.17	0.21	0.15	0.17	0.14	0.16
n	0.70	0.68	0.68	0.67	0.67	0.66	0.65	0.63

The ranges of the model parameters was determined to be in a specified temperature range:

foam from a 1% polidocanol solution: K = 0.14–0.19 Pa·s^n, n = 0.65–0.7;

foam from a 3% polidocanol solution: K = 0.16–0.26 Pa·s^n, n = 0.63–0.68.

The dependence of viscosity on shear rate for cooled polidocanol solution foam saples of various concentrations and temperatures, the degree of heating of syringes at the temperature t = 10°C in the range of shear rates $\dot{\gamma}$=3.75–22.5 s^{-1} is shown in Fig. 5.

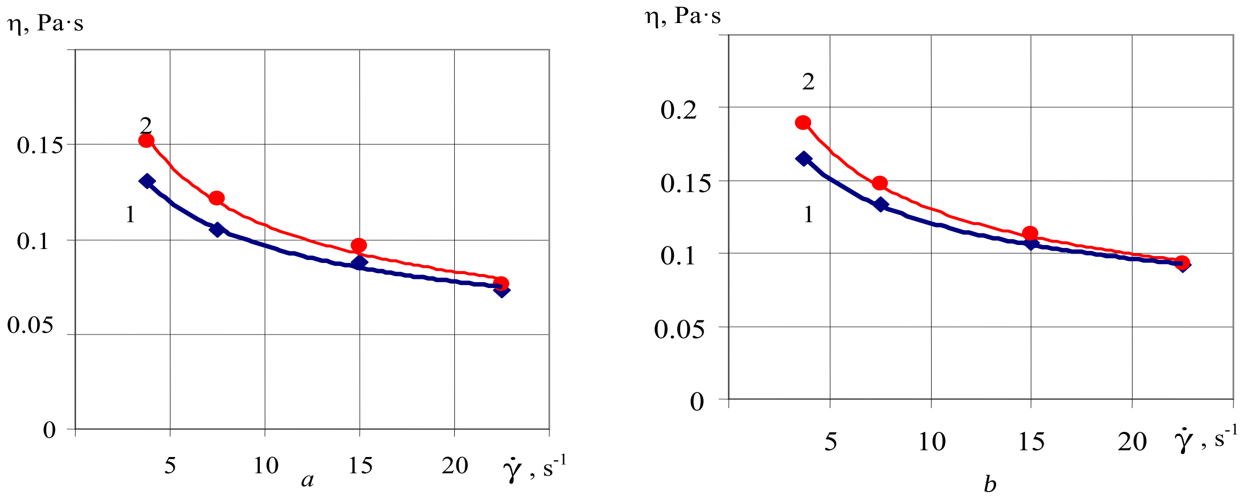

Fig. 5. The dependence of the viscosity on the shear rate for the foam prepared from a polidocanol solution of the different concentrations (*a* – 1%; *b* – 3%) at the temperature 10°C: 1 – a ncooled syringes; 2 – cooled syringes

As is clear from Fig. 5, the viscosity of the cooled foam of the polidocanol solution of various concentrations at the temperature t=10^{o}C in the range of shear rates $\dot{\gamma}$ = 3.75–22.5 s^{-1} is higher in the case where preliminary cooled syringes are used.

4 Conclusions

The viscosity of the foam prepared from a polidocanol solution of investigated concentrations (1%, 3%) increases on temperature decrease and concentration increase in the investigated ranges of temperatures and shear velocities, varying within 0.028–0.165 Pa·s.

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References:

[1] Kundu S, Lurie F, Millward SF, et al. 2007. J Vasc Surg. 46(3):582-9.
[2] Ravi M, Kate V, Ananthakrishnan N. 2001. Indian J Med Res 113:228-33.
[3] McAree B1, Ikponmwosa A, Brockbank K, et al. Eur J Vasc Endovasc Surg 43(6):721-5
[4] Eckmann DM. 2009. Expert Opin Investig Drugs 18(12): 1919–1927.
[5] Hamel-Desnos C., Allaert F.A. 2009. Phlebology 24(6):240-6.
[6] Rasmussen L.H., Lawaetz M, Bjoern L., et al. 2011. Br J Surg 98(8):1079-87
[7] Parsi K. 2015. Phlebology 30, 5, 306–315
[8] Cavezzi A, Tessari L. 2009. Phlebology 24: 247-251.
[9] Hesse G., Breu F.X., Kuschmann A., et al. 2012. Phlebologie 2; 41: 77–88.
[10] Peterson J.D. Goldman M.P. 2011. Dermatol Surg 37(1):12-7.
[11] Rabe E, Breu FX, Cavezzi A, et al. 2014. Phlebology 29(6):339-54.
[12] Ceulen R.P., Bullens-Goessens Y.I., Pi-VANDE Venne S.J., et al. 2007. Dermatol Surg 33(3):276-81.
[13] Valenzuela GC, Wong K, Connor DE, et al. 2013. Eur J Vasc Endovasc Surg 46(5):593-9.
[14] Brookfield DV-III Ultra Programmable Rheometer/Operating I nstructions. Manual No. M/98-211-B0104 – 122 p.
[15] Reference Book for Chemists 1962 vol 1 (Moscow: Goschimizdat) p 985.
[16] Smolskii B.M., Shulman Z .P., Gorislavets V.M. 1970 Rheodynamics and heat transfer of nonlinear viscoplastic materials (Minsk: Nauka i Technika).