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Rheological behaviour of dextran sulfate solutions

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Abstract

The purpose of this research was to study the rheological behaviour of dextran sulfate solutions under different conditions. A PC controlled rotational viscometer with a cone and plate geometry equipped with a temperature controlled unit was used to measure apparent viscosity of dextran solutions at different temperatures (25, 40 and 60 oC) and concentrations (2, 5, 10 and 20%). Viscosity tests of dextran sulfate solutions were performed at a range of shear rates (8-230 1/s) and the rheological data were fitted using the Power Law equation to get consistency and flow behaviour indices. The results indicated that all dextran sulfate solutions showed Newtonian flow behaviour. The viscosity of dextran sulfate solutions was significantly affected by temperature, e.g. the viscosity of a 5% solution at 25, 40 and 60 oC was 16.7, 12.7 and 10.7 mPa.s, respectively.

KEYWORDS: Dextran Sulfate Solutions; Rheology; Newtonian.

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1 Introduction

Due to biocompatibility and biodegradability of dextran this polysaccharide and its derivatives have been widely used and investigated for various biomedical applications, especially their uses for the delivery of drugs, proteins, enzymes, and imaging agents.

Dextran is a bacterial polysaccharide produced from sucrose by extracellular dextransucrases. Most commercial dextrans are derived from the bacteria *Leuconostoc mesenteroides*, strain B-512F and contain a backbone of consecutive α -(1 \rightarrow 6) linkages, with the remaining being branched α -(1 \rightarrow 3) linkages. There have been dextrans produced from other strains of the *L. mesenteroides* as well as other bacteria, resulting in products which contain either different percentages of the branched α -(1 \rightarrow 3) linkages or branching at either position 2, 3 or 4. The dextrans from the strain B-512F are known to contain approximately 5% randomly distributed α -(1 \rightarrow 3) branched linkages of varying lengths (up to 50–100 residues). These very long branches are the important factor in determining the rheological properties of dextran solutions. It is also due to the high proportion of α -(1 \rightarrow 6) linkages that imparts high water solubility to the dextran molecules (Shi & Zhang, 2006).

Researchers have studied the rheological properties of aqueous solutions of dextran for a number of years. Several interesting behaviors, which depend on the structure and nature of the dextran samples used, have been reported from these studies. Commercial dextran from Pharmacia Co. of different molecular weights ranging from 40,000 to 2 million Da all showed Newtonian viscosity behaviour up to fairly high concentrations of 30%. The dependence of both intrinsic viscosity and shear viscosity on molecular weight indicates that the dextran molecules are non-linear and possibly highly branched, i.e. the branches contain very long polysaccharide chains, such that the polymers are in a highly compact conformation (Tirtaatmadja, Dunstan & Boger, 2001, Shi & Zhang, 2006)

In the last decades, much attention has focused on the biological properties of polysaccharides and their chemical derivatives, especially sulfated derivatives. The roles of sulfated polysaccharides in biological systems were involved in several cellular processes, such as molecular recognition, cell development and differentiation, and cell–cell interaction. Many sulfated polysaccharides exerted potent antioxidant, anticoagulant, antithrombotic and antiviral activities. They are also known to inhibit some tumor development and to show anticancer activity (Ledoux, Merciris, Barritault & Caruelle, 2003, Shi, Nie, Chen., Liu & Tao, 2007).

Dextran sulfate (DS) is a drug that was developed as an anti-coagulant to delay clotting of blood in people who had heart diseases or strokes. It has been used orally and intravenously as a treatment for hyperlipidemia. It also prevents the formation of syncytia (clumps of T-cells which form when uninfected cells gather around one or more HIV-infected cells) in the test-tube. Dextran sulfate is used during hybridization experiments

to accelerate the rate of nucleic acid hybridization (Ledoux, Merciris, Barritault & Caruelle, 2003).

Low molecular weight DS (8000 Da) has been reported to lead to a decrease in calculi glycosaminoglycans in animals and there was an inhibition in bladder-implanted stones growth (Tostesa, Martinussoa, Werneckb, Mouraob & Cardoso, 2004).

Heat-denatured RNase aggregation was efficiently prevented by DS at pH 7.8. DS binding was assumed to transform the protein into polyanionic species, and the complexes may have provided a sufficient level of electrostatic repulsion at pH 7.8 and 75 °C to prevent aggregation of the protein from proceeding (Tsai, Zanten & Betenbaugh, 1998). In a study Chung et al. (2007) reported that the interaction between DS and BSA varied with the pH values of the solution, which led to different extent of aggregation prevention by dextran sulfate.

The potentials of dextran sulfate as a polyanionic polysaccharide and a functional ingredient has recently been the subject of some research projects. For example, dextran sulfate has been shown to act as protectant for proteins such as beta-lactoglobulin and alpha-lactalbumin in whey protein systems against heat induced aggregation. Dextran sulfate at appropriate polymer ratios has been reported to act a protective agent against beta-lactoglobulin aggregation as shown by a decrease in turbidity and an increase in protein solubility (Vardhanabhuti & Foegeding, 2008). Complexation of bovine serum albumin with DS at low ionic strength has been reported to protect proteins against pressure-induced aggregation (Galazka et al., 1999). Allahdad et al. (2009) produced dextran sulfate-lysozyme conjugates using Maillard reactions and reported that the produced conjugate is effective in improving the solubility at alkaline pH values and different temperatures and in increasing heat stability and emulsifying properties. These findings indicate promising potentials for dextran sulfate applications in food related systems to be used as a functional ingredient.

It also has received much attention in designing nanoparticles in combination with other biopolymers such as chitosan (Chen, Mohanraj, Wang & Benson, 2007). Nanostructures composed of dextran sulfate/ruthenium nanoparticles adsorbed on phospholipid monolayers at a liquid-liquid interface have been prepared and characterized electrochemically in relation to their potential use in drug delivery systems (Santos, Garcia-Morales, Murtomaki, Manzanares & Kontturi, 2007).

The interest in dextran sulfate polymer has increased since it is used as an anti-atherosclerotic drug and potent agent against HIV infection. The molecular mechanisms of its actions are still not fully understood (Mahner, Lechner & Nordmeier, 2001). Phase I/II clinical studies have also confirmed the safety and acceptability of dextran sulfate as a vaginal microbicide. Dextran sulfate is now being evaluated as a microbicide to prevent the sexual transmission of HIV (de Meijere, Brezesinski, Zschornig, Arnold & Mohwald, 1998, *aidsinfo.nih.gov*).

Despite many other polysaccharides, dextran sulfate as an active component has found many applications in physiological media, pharmaceuticals and drugs and is continuing to be the subject of many research projects which can lead to more applications. Being such an important polysaccharide, its rheological behavior would have practical applications in determining processing conditions e.g. in formulation, handling and transportation and interpreting its activities in biological systems either as a drug or a functional food when physical conditions change. There have been some reports showing the effect of shear dependent behavior of DS and its activities in physiological media e.g. shear-dependent inhibition of granulocyte adhesion to cultured endothelium by dextran sulfate has been reported by Ley, Lundgren, Berger and Arfors (1989). Therefore the main aim of this research project is to evaluate the rheological properties of dextran sulfate solutions at a range of concentrations at different temperatures.

2 Materials and methods

2.1 Materials

Analytical grade dextran sulfate sodium salt from *Leuconostoc* spp (catalogue number: D7037) with the average molecular weight of 5000 Da (as measured using low angle laser light scattering (LALLS) by the supplier) was purchased from Sigma Co. (USA). All other chemicals used were of analytical grade unless otherwise mentioned.

2.2 Preparation of dextran sulfate solutions

For rheological behaviour study dextran sulfate solutions of 2, 5, 10 and 20 % (w/v) in distilled water were prepared at room temperature (25 °C) using a low speed laboratory mixer at 100 rpm. The prepared solutions were left for 1 hour at room temperature for complete hydration before being loaded for viscosity measurements.

2.3 Viscosity measurement of dextran sulfate solutions

A PC controlled rotational viscometer (Brookfield, model DVII-Pro, Brookfield Engineering, USA) with a cone and plate geometry (CP51) equipped with a temperature controlled unit was used to measure the viscosity of dextran sulfate solutions at different temperatures (25, 40 and 60 °C) and concentrations (2, 5, 10 and 20%). Viscosity tests of dextran sulfate solutions were performed at a range of shear rates (8 to 230, 1/s) and the rheological data were fitted using the well known Power Law equation (equation 1) to get consistency and flow behaviour indices. Analysis of the viscosity data was performed using the software “Rheocalc” supplied by the viscometer’s manufacturer.

3 Results and Discussion

Rheological behaviour of dextran sulfate solutions at different concentrations and temperatures was studied. Figures 1, 2 and 3 are the plots of shear stress versus shear rate of dextran sulfate solutions at 25, 40 and 60 °C, respectively.

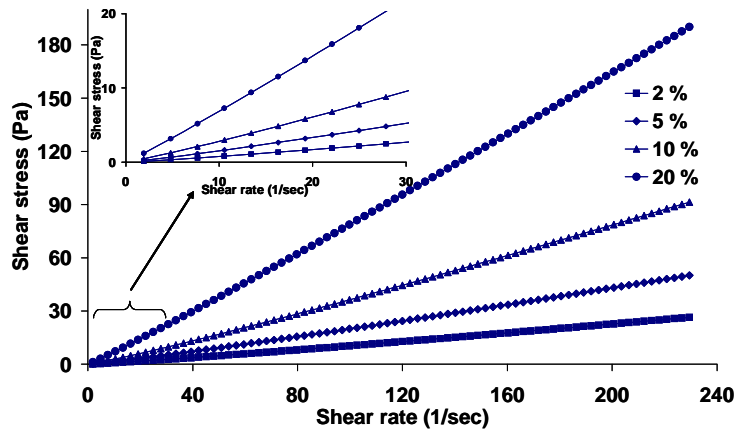


Fig. 1. Shear stress–shear rate plot of dextran sulfate solutions with different concentrations (2, 5, 10 and 20%) at 25 °C.

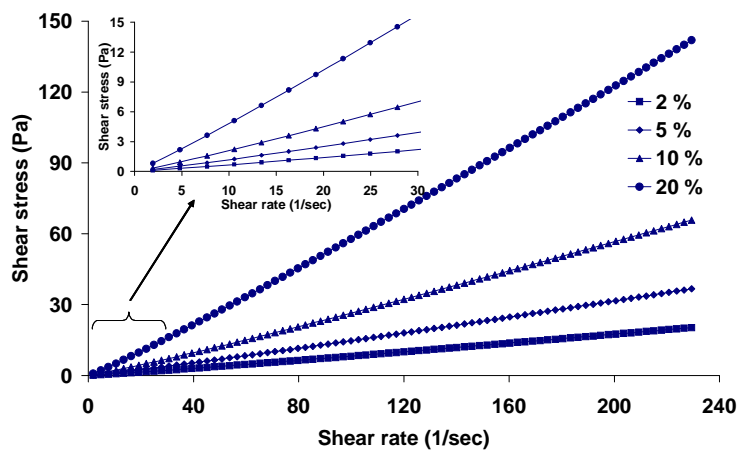


Fig. 2. Shear stress – shear rate plot of dextran sulfate solutions with different concentrations (2, 5, 10 and 20%) at 40 °C.

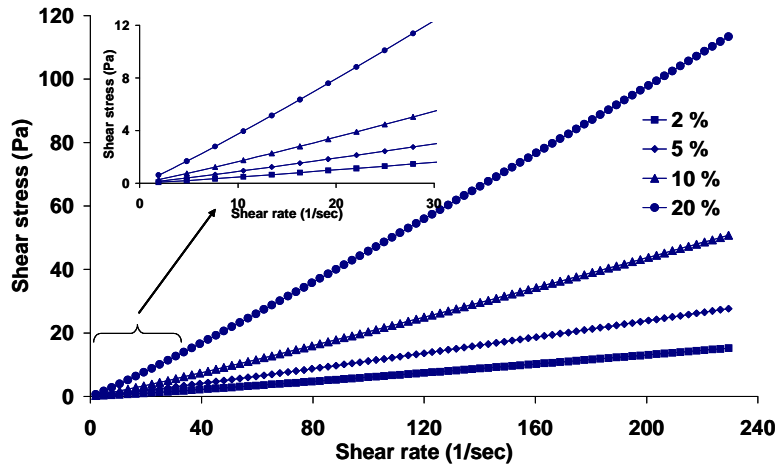


Fig. 3. Shear stress – shear rate plot of dextran sulfate solutions with different concentrations (2, 5, 10 and 20%) at 60 °C.

Shear stress-shear rate data were used to calculate the consistency (K) and flow behaviour (n) indices of dextran sulfate solutions of different concentrations. Power Law equation was used to calculate the indices. Temperature and concentration both had significant effects on consistency indices of the solutions. As seen in Table 1, consistency index (K) increased with concentration, for example consistency indices of 2, 5, 10 and 20% solutions of dextran sulfate at 25 °C were 5.84, 12.00, 21.90 and 59.80 mPa.s, respectively. As expected, consistency index was also affected and decreased by temperature, for example for a 10% solution of dextran sulfate at 25, 40 and 60 °C, it was 21.90, 16.65 and 13.20 mPa.s, respectively.

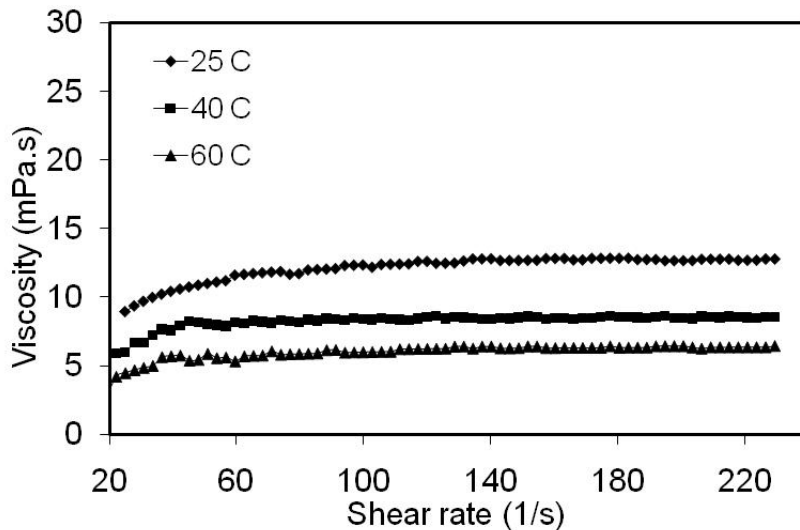


Fig. 4. Viscosity versus shear rate of a 2% dextran sulfate solution at 25, 40 and 60 °C.

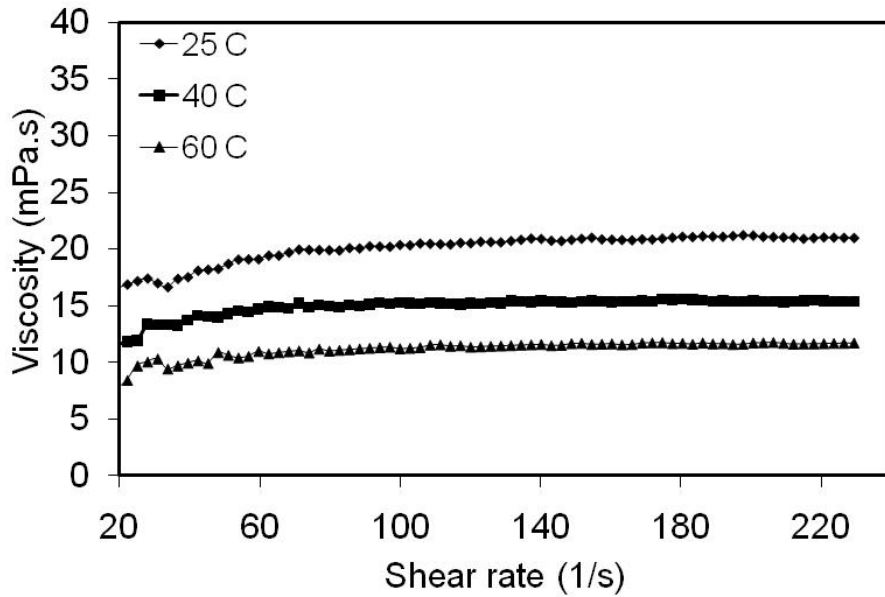


Fig. 5. Viscosity versus shear rate of a 5% dextran sulfate solution at 25, 40 and 60 °C.

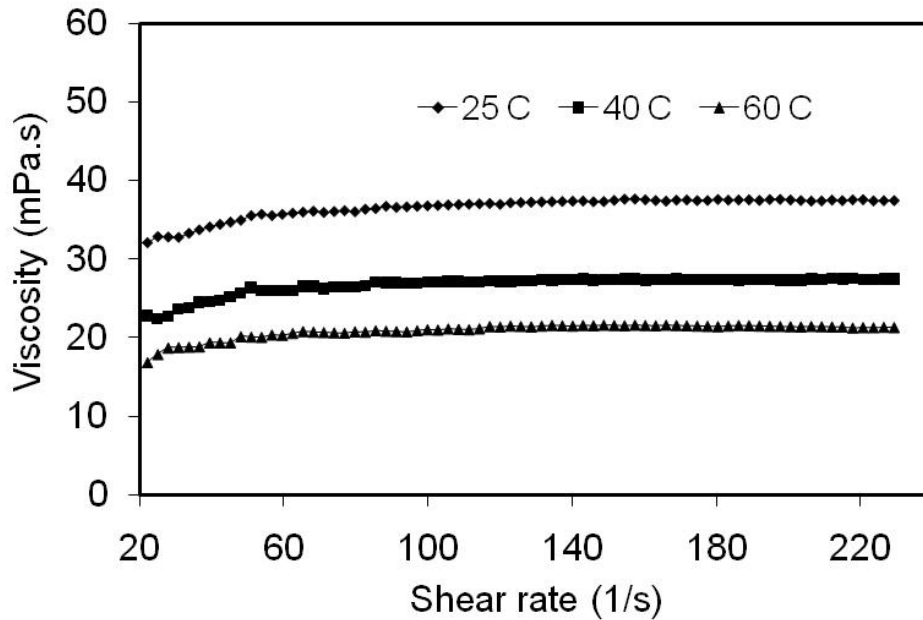


Fig. 6. Viscosity versus shear rate of a 10% dextran sulfate solution at 25, 40 and 60 °C.

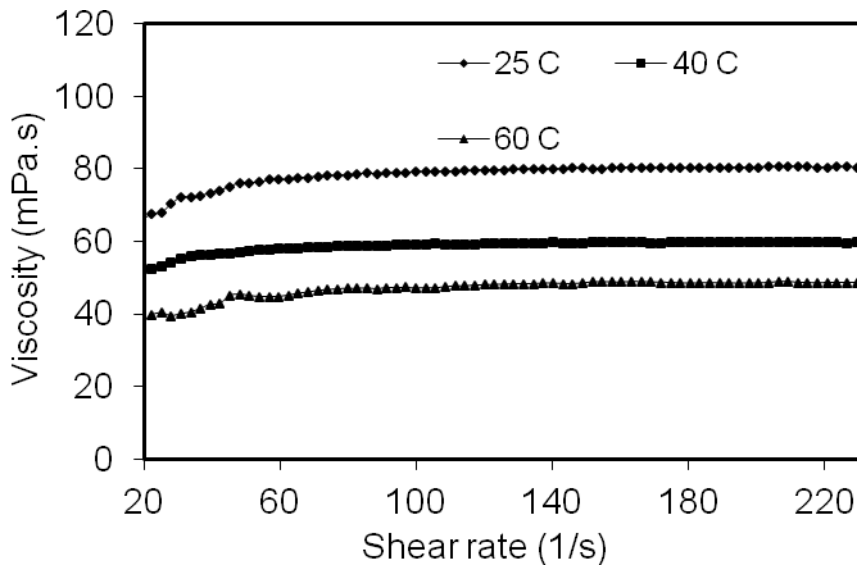


Fig. 7. Viscosity versus shear rate of a 20% dextran sulfate solution at 25, 40 and 60 °C.

Flow behaviour index is an important criterion which is the indication of viscosity changes of a polymer solution when subjected to a range of shear rates. Viscosities of solutions of different concentrations of dextran sulfate at a wide range of shear rates (8-230 1/s) at 25, 40 and 60 °C are presented in Figures 4-7. For all concentrations and temperatures the viscosity of the solutions was almost unchanged with shear rate, i.e. when the rate of mixing increases the recorded viscosity was also constant, in other words the fluid does not get thicker or thinner. Although there were some slight increases of viscosity with shear rate, the flow behaviour indices remained in the Newtonian range. Slight increases of viscosity with shear rate was observed at the lower range of the shear rates applied (i.e. up to 20-50, 1/s) which in turn it eliminates the possibility of effect of turbulent flow on the recorded viscosities. The flow behaviour indices of the dextran sulfate solutions calculated from fitting shear stress–shear rate data into the Power Law equation presented in Table 1, show that all dextran sulfate solutions had Newtonian or slight shear thickening behaviour with the n values of between 1.060 and 1.105. There was not any significant difference between the n values of DS solutions as a function of concentration or temperature.

Power Law equation: Shear stress (Pa)= $K(\text{Pa}\cdot\text{s}) \cdot \text{Shear rate (1/s)}^n$
(Equation 1)

Dextran is a neutral polysaccharide with high water solubility and the viscosity of its solutions does not depend on shear, i.e. to a very high concentration (30%) dextran solutions of different molecular weights show

Newtonian flow behaviour. The viscosity of dextran solutions does not depend on pH or salts. Tirtaatmadja, Dunstan and Boger (2001) pointed out that dextran molecules are less stiff than most carbohydrates and are highly branched, so that the molecules are in a highly compact configuration in aqueous solutions.

Table 1. Consistency (K) and flow behaviour (n) indices of dextran sulfate solutions of different concentrations at 25, 40 and 60 °C. Power Law equation was used to calculate K and n indices. The fitting was performed using the software “Rheocalc” developed by the Brookfield Engineering (USA)

Concentration (w/v)	Temperature (°C)					
	25		40		60	
	K	n	K	n	K	n
2 %	5.84 a B	1.105 b N.S.	5.27 a B	1.095 n.s. N.S.	3.64 a A	1.110 n.s. N.S.
5 %	12.00 b C	1.110 b N.S.	9.29 b B	1.100 n.s. N.S.	7.20 b A	1.095 n.s. N.S.
10 %	21.90 c C	1.110 b N.S.	16.65 c B	1.100 n.s. N.S.	13.20 c A	1.095 n.s. N.S.
20 %	59.80 d C	1.060 a N.S.	40.05 d B	1.080 n.s. N.S.	30.30 d A	1.090 n.s. N.S.

Morris, Cutler, Ross-Murphy, Rees and Price (1981) studied the viscosity of commercial dextran (Pharmacia T2000) of nominal molecular weight of 2×10^6 , as a function of concentration and found the critical concentration, for the transition from dilute to semi-dilute region to be approximately 8% w/v. In addition, the rheology of some of dextran derivatives has also been studied. Nomura, Koda and Hattori (1990) studied the viscosities of aqueous solutions of methyl cellulose, dextran, and their carboxymethyl derivatives as functions of molecular weight and concentration. Furthermore, effects of ionic group and added salt on the viscosity of aqueous solutions of carboxymethyl derivatives were investigated. The viscosities of dextran and carboxymethyl dextran solutions did not show any shear stress dependence, but methyl and carboxymethyl cellulose solutions showed strong shear thinning behavior even at low concentrations. Newtonian flow behaviour of carboxymethyl dextran solutions was related to the more expanded conformation of the polymer.

Dextran sulfate sodium salt is prepared by sulfating a selected fraction of dextran with a known mean molecular weight followed by careful purification. Each glucose unit in the dextran chain has approximately two sulfate groups, located normally at C₂ and C₄ of the glucose units. The high density of negative charges of this polyanionic biopolymer makes it different from the neutral molecule of dextran. This could lead to different behaviours of dextran sulfate in solution. Having rather high charge density regions on all glucose units of a dextran sulfate molecule can make the polymer molecules stiff in a way in which their movement in every angle is limited and prohibited

by the repulsive forces of negative charges on each unit. When the shear rate applied on a solution of dextran sulfate increases the molecules are forced towards each other but the repulsive forces on all molecules cause them to move away resulting in more collision and therefore more friction between the dextran sulfate molecules occur. This phenomenon could result in non-shear thinning flow behavior of dextran sulfate solutions. The presence of negative charges of dextran sulfate molecules may indicate that the viscosity of these solutions would be affected by the presence of salts as well as pH changes.

4 Conclusions

Overall, unlike the shear thinning behaviour of most polysaccharides such as starch, carboxymethyl cellulose, xanthan, tragacanth gum, dextran sulfate solutions showed Newtonian (shear rate-independent) behaviour at all temperatures and concentrations studied. This would have practical applications in the use of dextran sulfate in pharmaceuticals formulations and processing of foods and nutraceuticals. More research is needed on rheology of dextran sulfate solutions under different conditions e.g. in terms of ionic strength, pH and presence of different salts.

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