Applied Rheology | DOI: 10.3933/APPLRHEOL-24-35190 | WWW.APPLIEDRHEOLOGY.ORG

Rheological and Electrical Properties of Polymeric Nanoparticle Solutions and their Influence on RBC Suspensions

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Received: 5.11.2013, Final version: 13.2.2014

Abstract:
Rheological and electrical properties of polymeric nanoparticle solutions and their influence on the rheological and electrical properties of red blood cell (RBC) suspensions have been studied. Poly(acrylic acid) macromolecules of different architecture and molecular weight were used: (i) a new core-shell type star polymer whose interior forms hyperbranched polystyrene bearing arms of poly(acrylic acid) with molecular weight M_n = 56 920 Da and (ii) linear polyacrylic chains with average molecular weights M_n = 6000, 20000, and 225000 Da. The polymers dissolved in physiological solution with weight concentrations 1 mg/ml and 0.2 mg/ml were used for the experiments. Under physiological conditions the star-shaped macromolecules present spherical nanoparticles while the linear poly(acrylic acid)s adopt an extended chain conformation close to rod-like particles. The apparent viscosity of the nanoparticle solutions and RBC suspensions in the presence and absence (the control) of nanoparticles were measured using a rotational viscometer Contraves Low Shear 30 (LS 30) at a steady flow at shear rates from 0.0237 to 94.5 s^{-1} and temperature 37° C. A method, based on the measurement of dielectric properties of dispersed systems in Couette viscometric blood flow was applied. A concurrent measurement system and data acquisition system implied into the Contraves LS 30 were used to quantify the electrical conductivity. The main advantage of this technique is that blood is subjected to a uniform shearing field in a Couette rheometric cell as well as the information about the mechanical and electrical properties of the fluid is obtained in parallel. The results show that rheological and electrical properties of the nanoparticle solutions and RBC suspensions, namely their electrical conductivity and apparent viscosity, are dependent on the shear rates, shape, concentration and molecular weight of the polymers.

Key words:
Nanoparticles and RBC suspensions, poly(acrylic acid), rheology, electrical conductivity

1 INTRODUCTION

A new core-shell nanocarrier was designed by Kowalchuk et al. [1] for delivery of cisplatin through systemic administration. The macromolecules have star geometry with a highly branched core and covalently attached linear arms. This architecture combines key features for drug conjugation, such as hydrophilic shell with high density of functional groups – carboxylate ions that are able to exchange revesibly ligands with cisplatin and therefore to regenerate the agent at physiological salt concentrations. A high drug payload was achieved – higher than the one obtained with the linear homopolymers and alternating copolymers, or dendrimer macromolecules [1]. In vitro studies revealed lower cytotoxicity of the conjugates consistent with the sustained release of the agent and slower cellular uptake of the conjugated drug compared to that of free cisplatin. Nevertheless, the intracellular levels of platinum (II) complexes indicate that a considerable fraction of the nanoconjugates were endocytosed [1].

Many studies are dedicated to the evaluation of RBC suspensions in the presence of nanoparticles [2–5]. When nanoparticles are injected into the blood for drug delivery or drug detoxification, detrimental interaction of these particles with blood constituents must be avoided. However, the uptake of other blood constituents, such as inorganic blood electrolytes, by particles and the dispersion/coagulation characteristics of these particles in the blood stream have not

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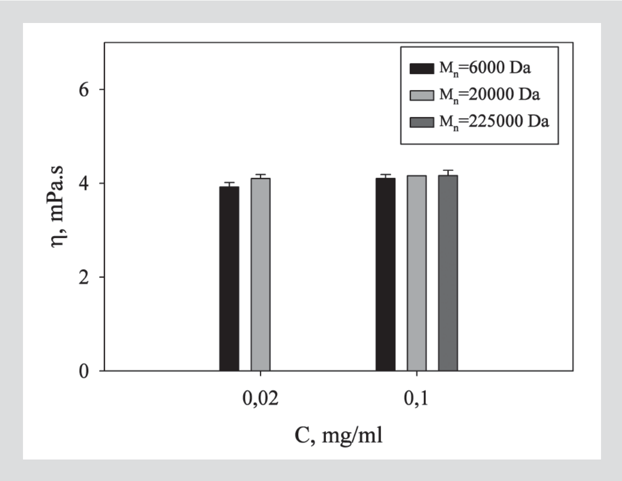

Figure 6: Comparison of the mean apparent viscosity of RBC suspensions in nanoparticle solutions of linear polyacrylic chains with average molecular weight M_n = 6000, 20000, and 225000 Da and 0.1 and 0.02 mg/ml volumetric concentrion at the shear rate 20.4 s^{-1} (H = 40%, T = 37° C, Contraves LS30).

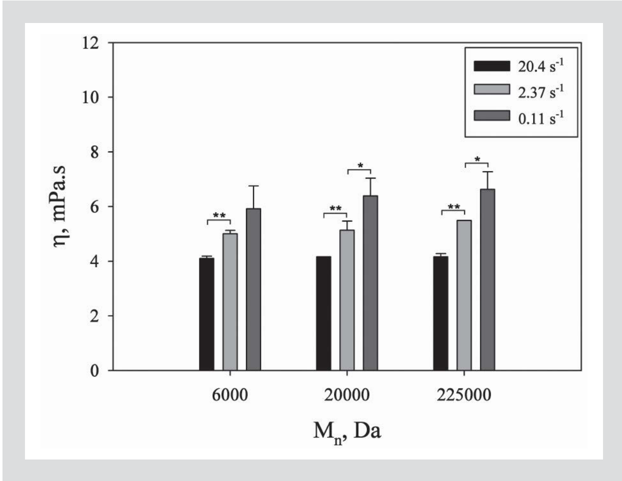

*Figure 7: Mean apparent viscosity of normal human RBCs in solution of PAA with different molecular weights and concentration 0.1 mg/ml at shear rates 0.1102, 2.37, and 20.4 s^{-1} (H = 40%, T = 37° C, Contraves LS30, * $p < 0.01$, ** $p < 0.001$).*

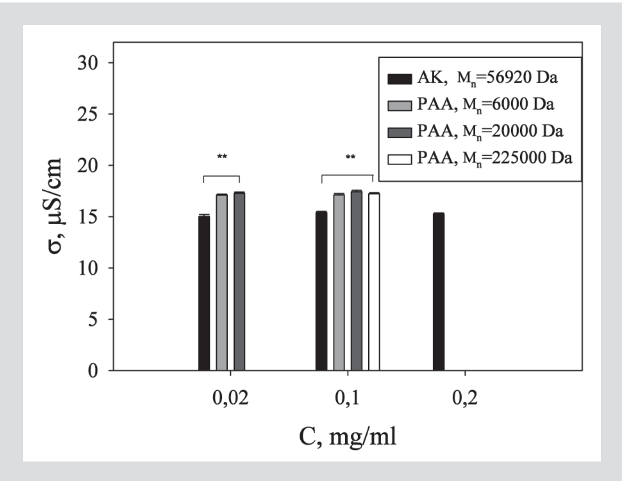

*Figure 8: Comparison of the mean values of the conductivity of RBC suspensions in both type of nanoparticle solutions AK and PAA at a shear rate 94.5 s^{-1} and 0.02, 0.1, and 0.2 mg/ml volumetric concentrations (T = 37° C, Contraves LS30, ** $p < 0.001$).*

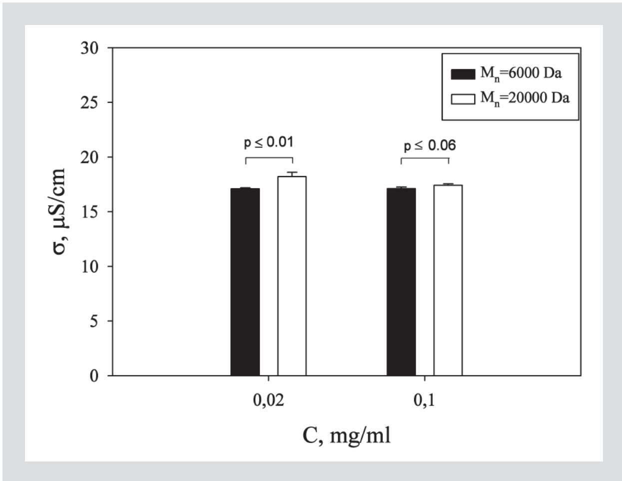

Figure 9: Comparison of the mean values of the conductivity of RBC suspensions in nanoparticle solutions of linear polyacrylic chains with average molecular weights M_n = 6000 and 20000 Da and 0.1 and 0.02 mg/ml volumetric concentration at the shear rate 94.5 s^{-1} (T = 37° C, Contraves LS30).

and temperature 37° C. Poly(acrylic acid)s with different architectures of the macromolecules were used. The star polymer of a molecular weight M_n = 56920 Da was compoused of a hyperbranched polystyrene core bearing ten arms of poly(acrylic acid). The other polymers presented linear polyacrylic chains of average molecular weights M_n = 6000, 20000, and 225000 Da. Both types of polymers possess one and the same functional groups, i.e. carboxylic groups that are dissociated under physiological conditions, therefore, the stars and the linear chains are negatively charged.

The star-shaped nanoparticle solutions exhibit higher apparent viscosity and lower conductivity in comparison to the solutions of the linear PAA. The enormous negative charge of the macromolecules is concentrated in the small spherical nanoparticles. They attract strongly the low molecular counter ions that affect the conductivity of the solutions. Because of their architecture, the macromolecules cannot undergo deformation and orientation under shearing. The two types of macromolecules, the stars and the linear ones, possess hydration shells which increase their hydrodynamic radius and influence the rheological properties of their solutions. Probably, the measured higher apparent viscosity at low shear rates is a consequence of structuring of the polymer solutions – macromolecular anions with a layer of counterions and hydration shells firmly attached to the macromolecules by hydrogen bonds and dipol interactions. Upon increasing the shear rate the network of hydrogen bonds is destroyed and the apparent viscosity decreases. This effect is clearly seen for the solutions of the linear poly(acrylic acid) chains which adopt extended conformation under physiological conditions (Figure 2).

It was found that RBC suspension in nanoparticle solutions have a non-Newtonian rheological properties which depend on the shape of the nanoparticles and the range of shear rates. The shape of the nanoparticles influences also the electrical conductivity of these solutions. No significant effect of the molecular weight of PAA nanoparticles on the apparent viscosity and conductivity of RBC suspensions was observed. Probably, it is due to a low concentration of PAA. The polymer concentration range was chosen with respect to the concentrations of polymer careers used in therapy. It is worth mentioning that RBC suspension in the star-shaped nanoparticles solutions (AK) has significantly higher apparent viscosity and lower conductivity in comparison to the RBC suspension in the presence of linear poly(acrylic acid)s. The ability of the linear chains to undergo conformational changes under external forces or variations of the solution characteristics results in a certain decrease of the apparent viscosity of the RBC suspension. On the other hand, the star macromolecules, possessing high density, negative charge and spherical shape lead to increase of the apparent viscosity of the RBC suspension over the whole range of shear rates applied. The effect of macromolecular architecture is clearly illustrated by the data presented in Figure 5 and Figure 8. Altogether our results show that rheological and electrical properties of nanoparticle solutions and RBC suspensions are dependent on the shear rates of the flow.

In summary, the addition of polymers to the blood even at very low concentrations could influence the rheological and electrical properties of the system. Moreover, not only the molecular weight and concentration of the polymer but also the shape of the nanoparticles is an important factor and should be taken into account when polymer drug delivery system is applied in therapy or diagnostics via systematic administration.

ACKNOWLEDGEMENTS

The Ministry of Education and Science of Bulgaria supported the study by the Operational Programme "Human Resources Development" within the Project No. BG051PO001-3.3-05/0001, regimen "Science-Business" and by the Grant No. DO2-164/2013. The work was also supported by the cooperation program between the Bulgarian Academy of Sciences and the Academy of Sciences of the Czech Republic.

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