Interactions Between Biomarkers and Main Blood Proteins

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Abstract. This article is devoted to main blood proteins (albumin and γ-globulin) while adding gadopentetic acid. Main idea of this investigation is to check whether there is interaction between proteins and different biomarkers. At this work as biomarker was chosen gadopentetic acid. Molecules of gadolinium and gadopentetic acid have gadolinium-containing chelate structures that are used in magnetic resonanse tomography (MRT) to enhance the contrast of images [*Zubarev et al,* 2003]. That's why it becomes interesting and useful to investigate such system as blood and its components, especially albumin and γ-globulin. So we studied the concentration dependence of the scattering parameter cH/R_{90} for γ-globulin and albumin water solutions without the addition of gadopentetic acid and with its addition by static light scattering (SLS).

Introduction

At this work we study water solutions of albumin and γ-globulin while adding gadopentetic acid. Gadopentetic acid [*Murphy et al*, 1996] is a paramagnetic contrast agent for MRI:

1) for enhancing picture contrast;
2) for the detection of tumors, including small and bad visualized,
3) is used to assist imaging of blood vessels and of inflamed or diseased tissue where the blood vessels become "leaky."

Serum albumin's main function in the organism is transport, γ-globulin determines the immune properties of the organism [*Neurath & Bailey*, 1983].

In this regard we investigate intermolecular interactions between them which are connected with 2nd virial coefficient — B. Average scattering intensity is a function of the (particle) molecular weight and the 2nd virial coefficient. All investigations were made by SLS. A detailed study of the properties of the scattered light provides information about the structure of molecules and molecular systems. In experiments on SLS is observed the average (over time) scattering intensity. The analysis of the angular and concentration dependences provides information about the size of the scattering centers: molecular weight and molecular interaction coefficient B.

Detailed study of the properties of scattered light allows obtaining information about molecules structure and molecular systems, about the nature of the intermolecular and intramolecular forces and make qualitative and quantitative analysis of various compounds.

Light scattering in pure fluid is caused by the fluctuations of the density in volumes, small compared with the cube of the wavelength of light. In the solutions to this is added scattering by fluctuations of the concentration of the dissolved substance. In this case, the rate of excess scattering is determined by the difference between the intensity of scattering of a solution and a solvent. The nature of the scattering depends on the relationship between the wavelength of the light and the size of the scattering particles. If the linear size is $l < \lambda / 15$, the scattering is called Rayleigh scattering [*van de Hulst*, 1981].

Theory Of Rayleigh-Debye

Determination of the molecular weight of the scattering particles. Scattering equation allows, in principle, to determine the molecular weight of the small noninteracting particles:

$$M = \left(\frac{cH}{R_{90}} \right)^{-1},$$

where M — molecular weight, R_{90} — Rayleigh ratio [*Debye*, 1947], c — concentration, H — optical constant.

$$B = \frac{\nu_0 N_A}{2M^2},$$

where B — 2nd virial coefficient, N_A — Avogadro's number, ν_0 — excluded volume, i.e., volume of the molecule which supersedes all other. B is a thermodynamic property describing the interaction strength between the molecule and the solvent. For samples where B > 0, the molecules tend to stay in solution (protein molecules prefer contact with buffer). When B = 0, the molecule-solvent interaction strength is equivalent to the molecule-molecule interaction strength — the solvent is described as being a theta solvent. When B < 0, the molecule will tend to fall out of solution or aggregate.

Experimental results

To check interaction between gadopentetic acid and main blood proteins were made several experiments on "Photocor Complex" [http://www.photocor.com/dls-theory/] parameters of laser: wavelength — 647 nm, power P = 25 mW, the conditions of experiment: T = 20 °C, pH ≈ 7.0, I ≈ 0.01 mol/L, angle — 90°. The concentration of gadopentetic acid doesn't change during the experiment.

In the experiments we studied the coefficient of intermolecular interaction. The results showed that in pure albumin water solutions dependence of scattering parameter has a positive slope (Fig. 1a). For albumin water solutions with the addition of gadopentetic acid the slope becomes negative (Fig. 1b).

In the experiments with γ-globulin water solutions dependence of scattering parameter has a positive slope (Fig. 2a). For γ-globulin water solutions with the addition of gadopentetic acid the slope becomes negative (Fig. 2b).

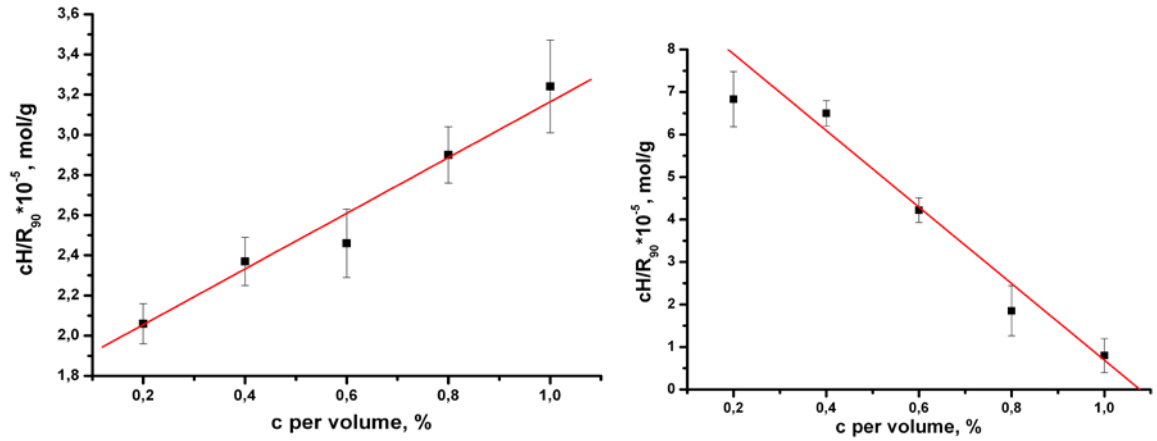

Figure 1. The concentration dependence of the scattering parameter cH/R_{90} for albumin water solutions: (a) without the addition of gadopentetic acid, b) with the addition of gadopentetic acid.

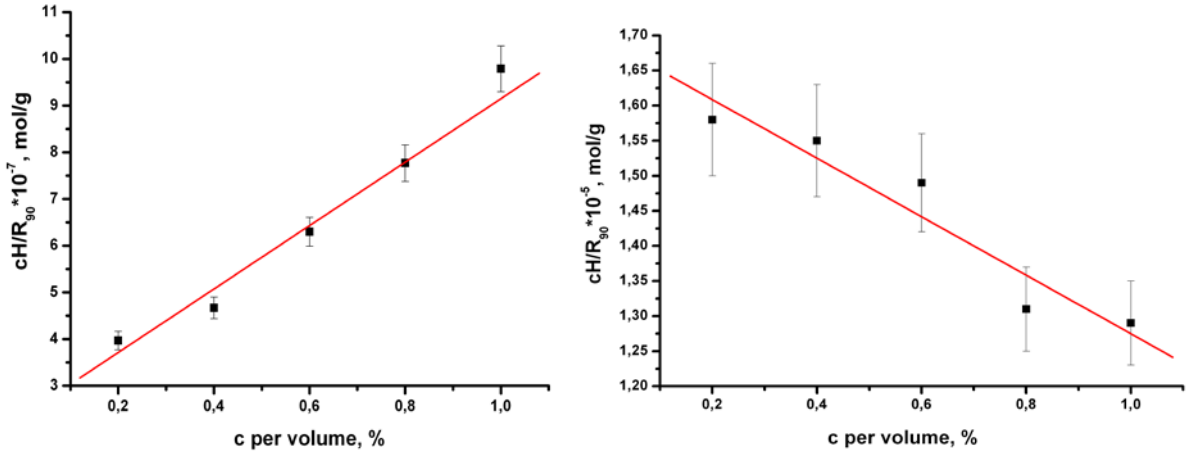

Figure 2. The concentration dependence of the scattering parameter cH/R_{90} for γ-globulin water solutions: (a) without the addition of gadopentetic acid, (b) with the addition of gadopentetic acid.

Discussion

From the obtained data probably follows that there is interaction between proteins and gadopentetic acid, resulting in a change of the sign of the coefficient of intermolecular interaction B and in changing of slope to the opposite. Perhaps, one of the reasons why the slope changes, is associated with protein conformation. Probably the addition of gadopentetic acid may cause the change of protein structure from globular to secondary. So the molecular weight changes that leads to the new kind of interaction or to the replacement of surface charge of the molecules. As a slope is negative we can't discuss the molecular-weight of investigated systems. Photocor Complex provides an opportunity to measure dynamic light scattering as well, so in our previous proceeding for ALT 2012 [https://bop.unibe.ch/ALT-Proceedings/issue/view/25/showToc] we have done such experiments on albumin water solutions containing gadolinium ions. We showed that the coefficients of D_t in albumin water solutions containing gadodiamide greatly reduces, so the hydrodynamic radius increases.

Conclusion

Since the slope of a line is associated with the tangent of the angle, the coefficient of intermolecular interaction can be considered as one of the key parameters for early diagnostics of changes which are connected with main blood proteins and be useful for medicine investigations.

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