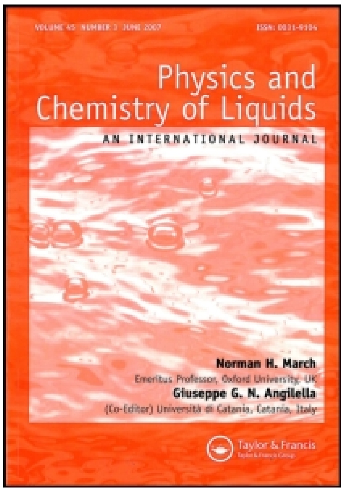

Physics and Chemistry of Liquids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713646857

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Online publication date: 27 October 2010

To cite this Article Mikusinska-Planner, A. , Gagalska, J. , Raczkowska, E. and Rafalont, A.(2003) 'Human Blood Serum X-Ray Diffraction Patterns of Cancer Patients and Pregnant Women', Physics and Chemistry of Liquids, 41: 2, 155 — 160
To link to this Article: DOI: 10.1080/0031910021000061583
URL: http://dx.doi.org/10.1080/0031910021000061583

Physics and Chemistry of Liquids
2003, Vol. 14, No. (2), pp. 155–160

HUMAN BLOOD SERUM X-RAY DIFFRACTION PATTERNS OF CANCER PATIENTS AND PREGNANT WOMEN

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(Received 20 September 2002)

Human blood serum samples coming from healthy subjects, cancer patients and pregnant women were studied by X-ray diffraction and compared with the diffraction patterns obtained for pure water. It has been established that the changes in blood serum related to the disease or pregnancy are manifested directly in X-ray diffraction patterns. The diffraction patterns of blood serum of pregnant women have been found similar to those of the blood serum of cancer patients and different from the pattern for pure water. This result indicates that cancer or pregnancy stimulate an increase in the concentration of non-specific proteins or appearance of other factors destroying the structure of water in the blood serum. The changes in the structure of water, making about 92% of the blood serum are manifested directly in the diffraction patterns of the samples by the disappearance of the maximum characteristic of the pattern of pure water in the angular range $8.5^\circ \geq \Theta \leq 10^\circ$. Therefore, the X-ray diffraction method can be an effective tool in early diagnostics of neoplasmic changes, but not in pregnant women.

Keywords: X-ray diffraction patterns; Angular intensity distributions; Human blood serum; Cancer patients; Pregnant women

INTRODUCTION

The article reports the results of an X-ray diffraction study of serum samples from cancer-recognised patients, who were the subjects of an earlier study [1,2]. The diffraction patterns obtained for healthy subjects were comparable to those of pure water, whereas significant differences were observed between the diffraction patterns of cancer patients and those of pure water.

As the blood serum of pregnant women contains the same type of protein which is characteristic of cancer patients [3–5], also samples from this group were studied. This article reports the first results of X-ray diffraction study of serum samples from pregnant women.

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ISSN 0031-9104 print: ISSN 1029-0451 online
DOI: 10.1080/0031910021000061583

Human blood serum is the human blood plasma devoid of fibrin. From the chemical point of view, because of a large content of water (92%) [6] the samples are diluted water solutions of proteins.

Because of its polar character, each water molecule can be linked with four other molecules forming an unstable tetrahedral lattice characteristic of the structure of ice [7–9]. The ordering influence of non-polar groups on the water structure has been discussed in [8–11]. Thus, it can be expected that if in blood serum there are protein macromolecules with nitrogen or oxygen molecules (on the specific bordering surface) in such a position that they fit the water lattice, the ordering of water molecules can be similar to the structure of ice.

The chemical composition of blood serum from cancer patients differs from that of healthy subjects but is similar to that of pregnant women. The samples from cancer patients and pregnant women contain an elevated level of acute phase proteins [3], immunological proteins produced in the organism as a protective response against a foreign tissue (neoplasmic changes of foetus) and foetal or neoplasmic antigens [3,5]. Blood serum of pregnant women contains also high levels of certain neoplasmic markers such as carcino-embrional antigen (CEA) [4,12], AFP (glycoproteid), in the amounts of 125 μg/L in the first trimester, 250 μg/L in the second and 500 μg/L in the third trimester, and HCG (glycoprotein) produced in the amount of 26 mg/day. These markers are characteristic of the following neoplasmic changes [12]: AFP – ovarian cancer, liver and testicles cancer; CEA – breast cancer, cancers of the pancreas, colon, rectum, stomach, lungs; HCG – ovarian cancer and cancer of the testicles. In physiological blood serum from healthy subjects the marker indices are much lower: CEA −10 μg/L, AFP – 2−20 μg/L, HCG 10 IU/L.

EXPERIMENT

Diffraction patterns were recorded on a typical X-ray diffractometer equipped with a special cell for liquid samples [13,14]. A layer of the liquid studied restricted by mica windows was placed between the source of monochromatic X-rays MoKα and a counter probe. The pulses were counted within 120 s, in the angular range $2^\circ \leq \Theta \leq 40^\circ$, with an accuracy of $0.005^\circ \leq \Delta\Theta \leq 0.1^\circ$.

The values of intensity obtained in the experiment are expressed in relative units. Their conversion to the absolute values, the so-called electronic units (eu) must be performed before a comparison of the experimental curves of intensity distribution since each of them is recorded at different time. In order to do that the normalisation coefficient is found. When it is taken into account, the course of the experimental curve of intensity distribution coincides with the corresponding course of the theoretical curve for large scattering angles. The theoretical grounds for the normalisation of the experimental curve are given in [15]. Figure 1 presents the experimental curve for pure water normalised with respect to the theoretical curve denoted by the dotted line.

The error in the measured values of intensity for water and the plasma studied is $\Delta I_{eu}/N = \pm 0.4$ electronic units (eu). It is marked on the curve in Fig. 1(a).

The calculation of the theoretical curve requires the knowledge of the atomic composition of the smallest structural unit – a molecule. For liquids, we can also

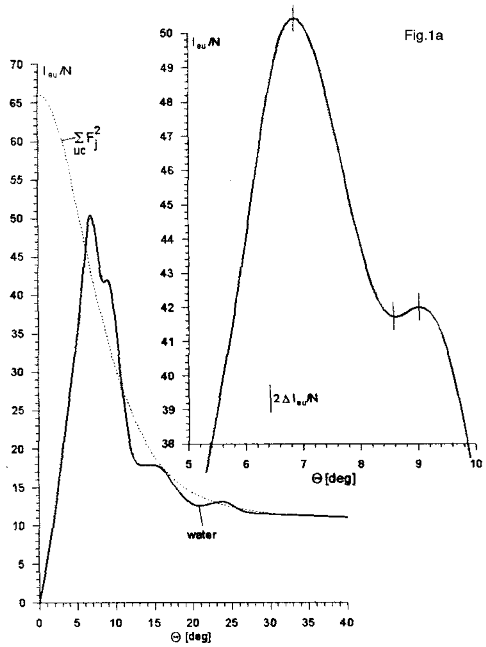

FIGURE 1 Distribution of experimental $I_{eu}(\Theta)/N$, per one structural unit, and theoretical ΣF_j^2 (broken line [15]), the theoretical scattering on atoms of one structural unit, for intensity for pure water. The error is marked in the insert $\Delta(I_{eu}/N) = \pm 0.4$ eu, Fig. 1a.

calculate the so-called mean molecule, if the atomic composition of molecules of the substance studied is known exactly. Determination of the mean molecule for blood plasma is theoretically possible, although much more complex as its atomic composition depends on the individual and his/her health status. Therefore, we have assumed as a standard theoretical curve the angular distribution of independent scattering calculated for water, see the dotted line in Fig. 1. The experimental curves of intensity distribution of the blood plasma samples were normalised with respect to this curve. This procedure has no effect on the course and position of the experimental curve maxima. It can only cause a small parallel shift of the experimental curves with respect to the axis of ordinates towards lower values of intensity, since the normalisation coefficients are somewhat lower because of a great molecular weight of blood plasma relative to that of pure water. Thanks to the normalisation with respect to water it is possible to compare the angular dependencies of intensity obtained for blood plasma and water since the numerical values of intensity have the same independent units.

The samples of blood plasma from blood donors were obtained from centrifuged blood, characterised by standard analytical procedures [16]. Pure water was three times distilled, while the samples of serum were defrosted prior to the measurement.

The study was performed for 200 samples of human blood serum collected from pregnant women and cancer patients. The samples from the pregnant women were tested for the presence of CRP (so-called acute phase proteins) [3], roseola and toxoplasmosis. For all samples studied the results of the tests were negative.

RESULTS

Figures 2 and 3 present a comparison of the mean angular distribution of the X-ray radiation scattered by a sample of pure water (broken line) with the distributions obtained for blood serum of healthy subject (Fig. 2, Curve 1), pregnant women (Fig. 2, Curves 2–6) and cancer patients (Fig. 3, Curves 7–9). The angular distributions of X-ray scattered radiation intensity were normalised to electron units $I_{eu}/N \pm 0.4$ (eu) per one molecule relative to pure water [7]. For the clarity of the picture, subsequent curves are vertically shifted by $20\, I_{eu}/N$. The main maxima of the curves from Fig. 2 correspond to the angles from the range $6.6° \leq \Theta_{max} \leq 7.5°$. The side maxima corresponding to the angles Θ in the range $8.5° \leq \Theta \leq 10°$, broken line and

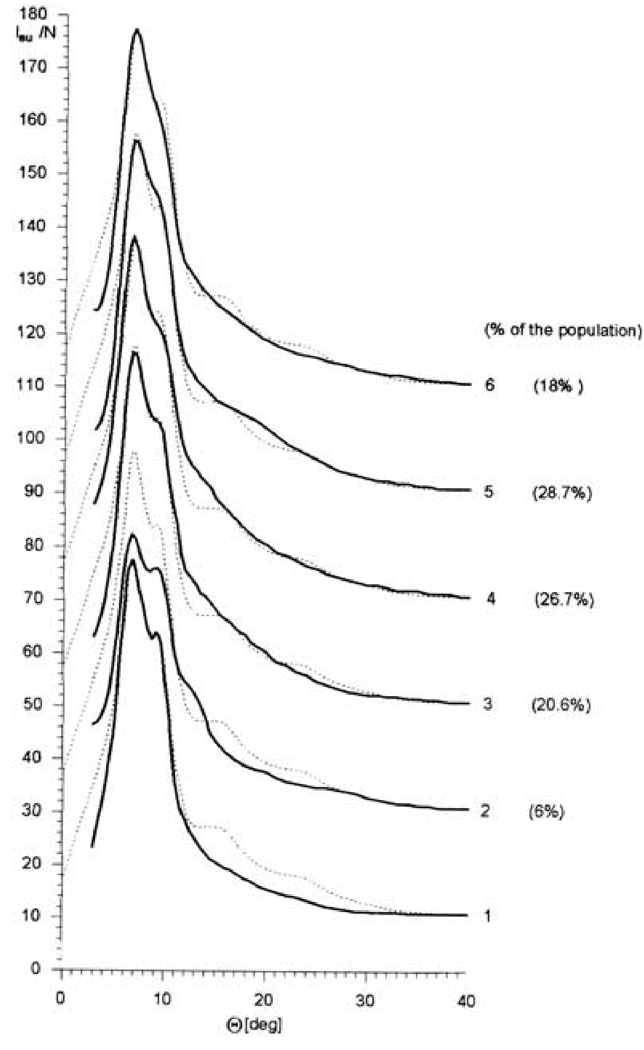

FIGURE 2 The mean angular distributions of X-ray scattered radiation intensity I_{eu}/N in electron units for pure water (broken lines) and for human serum from healthy subjects (Curve 1) and pregnant women (Curves 2–6).

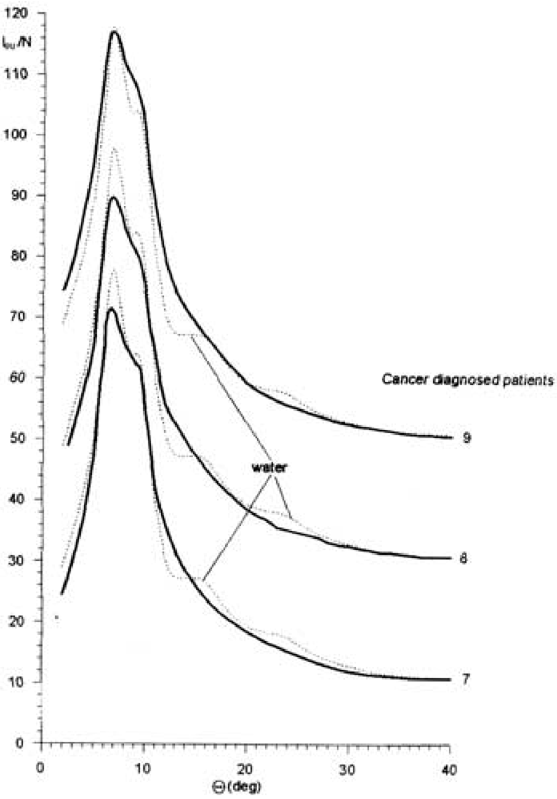

FIGURE 3 The mean angular distributions of X-ray scattered radiation intensity I_{eu}/N in electron units for pure water (broken lines) and neoplasmic patients (Curves: 7 – stomach cancer, 8 – rectar cancer, 9 – breast cancer).

curves 1–4 in Fig. 2, are related to the characteristic tetrahedral arrangement of water molecules. For the other samples the Curves 3–9, [Figs. 2 and 3], did not reveal side maxima, that is the main and the side maxima were fused in one maximum of different shape.

CONCLUSIONS

For 73.4% (Fig. 2) of the samples studied, the character of the curves obtained was different from that of the curve for pure water. The character of the curves recorded for pregnant women is very similar to that obtained for cancer patients (Fig. 3, Curves 7–9). This result is quite understandable because of an increased level of antigens in blood serum of pregnant women. The samples contain carcino-embrional antigens, proteins of acute phase and neoplasmic markers [3–5,12]. These substances are proteids, proteins, glycoproteins or glycoproteids [3]. The appearance or increase in the concentration of such substances can have destructive effect on the structure of water. The side polar chains of the amine acids localised on the surface of the globule interact through hydrogen bonds with the water molecules and the anions, which can have destructive effect on the water structure [16,17]. This destructive effect is illustrated by the curves from 3 to 9, in Figs. 2 and 3. Destruction of the tetrahedral structure of water is manifested by disappearance of the side maximum θ_{side} on the angular distribution of scattered radiation. The most important phenomenon in the X-ray study of blood serum is that the structure of water reflects the changes taking place in the other components of blood serum and that these changes can be directly observed in the diffraction patterns. It has been shown that the diffraction patterns of blood serum can be an important diagnostic tool of neoplasmic diseases, however, as shown by this study, this method is unreliable for pregnant women.

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