



## CHANGES IN THE STRUCTURAL ORDERING OF HEMOGLOBIN UNDER EXTREME CONDITIONS OF THE ARCTIC REGION

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### ABSTRACT

*The structure of hemoglobin (Hb) was examined by UV and IR Fourier spectroscopy. The electronic characteristics of the  $\pi$ -conjugated (aromatic) prosthetic group of heme and the content of the secondary structure elements of globin in Hb were studied. Heme and globin are connected to each other by Van der Waals forces. A 8-10 nm short-wave shift of the heme absorption band at  $417\pm 0.5$  nm was revealed for the residents of the Arctic Region in different latitudes (the Yamal Peninsula, 64 and 70° North) as compared to the residents of middle latitudes (Novosibirsk, 55° North). This indicates that the ordering of heme structure increases with the latitude of human residence. The IR Fourier spectroscopy study of the content of the secondary structure elements showed that the ordering of hemoglobin in the Arctic residents increases with latitude. The study has demonstrated that affinity of Hb for oxygen in the residents of the Arctic Region is higher than in the residents of middle latitudes. Changes in the structure of Hb and its affinity for oxygen in the Arctic residents can be attributed to heliophysical factors.*

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### 1. INTRODUCTION

Extreme conditions of the Arctic Region are determined by an increased magnetic field strength, frequent magnetic storms, high ionization of the atmosphere, high electric field strength, long polar nights and low temperatures in comparison with the middle latitudes. The effect of heliophysical factors on the human body has been discussed in many works [1-4]. Results of the studies suggest that all the indicated factors can change with the latitude and longitude of the coordinates for a region under consideration. The spatial structure of protein is maintained by a set

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of various physical forces, which determine the principles of structural organization of protein and the hierarchy of interactions. The ordering of a macromolecule should be compensated by its internal energy primarily due to the hydrogen bonds, hydrophobic and Van der Waals interactions and side radicals [5, 6]. The ordering of heme and globin in hemoglobin determines its affinity for oxygen [7]. In addition, it was found that hemoglobin binds to the erythrocyte membrane; so, this interaction can affect the membrane structure. Changes in hemoglobin structure alter the membrane, and conversely, alteration of the membrane structure produces changes in Hb. Investigation of the structure and oxygen transport functions of hemoglobin in erythrocytes in dependence on the geographical place of human residence and heliophysical factors is a topical problem. Our study of the residents of middle and high latitudes, 70 and 64° (Arctic Region, Yamal Peninsula, Tazovsky district, and forest-tundra, Kharampur, Purovsky district), has revealed changes in the ordering of hemoglobin (Hb), which were attributed to the effect of heliophysical factors. In particular, these latitudes are characterized by an increased magnetic field strength, frequent magnetic storms, high ionization of the atmosphere, long polar nights and low temperatures in comparison with the middle latitudes (Novosibirsk, 55° of latitude). Radically new characteristics of Hb inherent in indigenous and alien residents of the Arctic Region, in distinction to the residents of middle latitudes, have been found. These characteristics make it possible to propose an alternative interpretation of structural changes in erythrocytes (spherocytosis) and erythropoiesis (cell and body aging) under the North conditions. The goal of the study was to investigate the structure of hemoglobin under extreme conditions of the Arctic Region in dependence on the latitude of human residence.

## 2. MATERIALS AND METHODS

Blood samples were obtained from indigenous and alien residents who have spent at least 10 years on the Yamal Peninsula. Blood samples were supplemented with EDTA for anticoagulation and then frozen at minus 20°C. At this temperature the samples were delivered to a laboratory. Blood was centrifuged at 6000 rpm during 60 min at a temperature of 4°C ( $\varphi_{\text{rotor}} = 15$  cm), all the dispersed particles were sedimented, and hemoglobin was taken for the study. Hb solutions were examined by UV spectrometry (Evolution 300, Thermo Scientific, USA) and IR Fourier spectrometry (Nicolet 6700, Thermo Scientific, USA). A solution of hemoglobin was prepared with an isotonic phosphate buffer, pH 7.35. The optical density for UV spectroscopy did not exceed 3.5 units at a temperature of 22-23°C. The volume of Hb solution for IR Fourier spectroscopy was 10 microliters. The secondary structure of Hb was studied by decomposition of the absorption band at 1600-1700  $\text{cm}^{-1}$  into components by taking the 2<sup>nd</sup> and 4<sup>th</sup> derivatives with the use of Savitzky-Golay algorithm [8, 9]; an appropriate program was incorporated in the Nicolet 6700 device (the OMNIC system).

## 3. RESULTS

The analysis of UV spectra has revealed a 10 nm shift of the absorption maximum wavelength for heme (417±0.5 nm) in the indigenous and alien population of middle latitudes (Novosibirsk,

55.1° North, Long 82.56° E). Indigenous population of the Yamal Peninsula, Tazovsky district (69°72' North and Long 78°43' E) had  $\lambda_{\max} = 407.0 \pm 0.1$  nm, while the alien population showed  $\lambda_{\max} = 407.7 \pm 0.1$  nm. Examination of the indigenous population of Purovsky district (64° 20', the Yamal Peninsula) has revealed an increase in the wavelength up to  $409 \pm 0.1$  nm. Thus, our study has demonstrated that the wavelength of the Soret absorption band of hemoglobin (417 nm) decreases with increasing the geophysical latitude. The following dependence was observed: 1. Novosibirsk, 55.1° North, Long 82.56° E,  $\lambda_{\max} = 417 \pm 0.5$  nm > 2.  $\lambda_{\max} = 409 \pm 0.1$  nm in the population of Purovsky district, 64°20' (the Yamal Peninsula) > 3.  $\lambda_{\max} = 407.7 \pm 0.1$  nm in the alien population of Tazovsky district (69°72' North) > 4.  $\lambda_{\max} = 407.0 \pm 0.1$  nm in the indigenous population of Tazovsky district (69°72' North) (Table 1).

**Table-1.** Absorption maxima of the HbSoret band in residents of different latitudes

No.	Place of human residence	$\lambda_{\max}$
1.	Novosibirsk, 55.1° North, Long 82.56° E	417±0.5 nm
2.	Purovsky district, 64° 20 North (the Yamal Peninsula)	409±0.1 nm
3.	Alien population of Tazovsky district, 69° 72' North (the Yamal Peninsula)	407.7±0.1 nm
4.	Indigenous population of Tazovsky district, 69° 72' North (the Yamal Peninsula)	407.0±0.1 nm

The IR Fourier spectroscopy study of Hb has revealed a higher ordering of globin in the residents of the Arctic Region as compared to the residents of middle latitudes. In the Arctic population, hemoglobin had a higher total content of the ordered elements in the secondary structure of  $\alpha$ -helices and  $\beta$ -structures (Table 2) and a lower content of tangles. The spatial structure of  $\alpha$ -helices and  $\beta$ -structures in Hb is maintained by the hydrogen bonds.

**Table-2.** Content of Hb secondary structure elements in the residents of middle latitudes and Arctic Region (1. Novosibirsk, 55° North 2. The Yamal Peninsula, 64° North; 3-4. The Yamal Peninsula, 70°North;)

No.	Secondary structure elements	$\alpha$ -helices, %	$\beta$ -structure,%	Tangle, %
1	Novosibirsk	58.0±5.0	20.5±4.0	12.8±3.0
2	Yamal Peninsula (Pur.)	57.4±5.0	21.8±4.0	9.5±3.0
3	Yamal Peninsula (Rus.)	59.4±5.0	24.5±4.0	7.5±3.0
4	Yamal Peninsula (nenets)	56.9±5.0	28.4±4.0	4.5±3.0

One heme group binds to globin by Van der Waals forces in 60 points. This suggests that the increased ordering of globin is caused by an increased ordering of heme [10], which affects the  $\pi$ -conjugated bond of the heme group, shifts the d-electron levels of iron atom ( $\text{Fe}^2$ ), and decreases the wavelength of the Soret absorption band. In our opinion, an increase in Hb ordering is related to a higher strength of electric and magnetic fields in the Arctic Region, magnetic storms, and paramagnetic features of the  $\text{Fe}^2$  atom in Hb. However, the contribution of other factors, in particular cold, long nights, stress and alimentary pattern, cannot be ruled out [1, 3, 10].

An increase in Hb ordering enhances its affinity for oxygen; thus, indigenous residents of the Arctic Region have a higher affinity for oxygen as compared to the residents of middle latitudes.

This observation correlates with the data on dissociation of oxyhemoglobin in the Arctic residents. The indicated dependencies have a more pronounced S-shape exactly for the residents of the Arctic Region in comparison with the residents of middle latitudes [1], which points to a stronger cooperativity of Hb.

Thus, in the residents of the Arctic Region, hemoglobin has a more ordered structure than in the residents of middle latitudes; Hg ordering depends on the latitude of human residence, which increases the affinity for oxygen and efficiency of its delivery to the tissues. Changes in the ordering of hemoglobin structure and erythrocyte shape (microspherocytosis and spherocytosis) occur most likely during erythropoiesis in the red bone marrow.

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