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Interaction of netropsin with double-stranded nucleic acids irradiated with non ionizing athermal millimeter electromagnetic waves

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The our studies show that binding constant (K) of netropsin with irradiated DNAs changes: almost by one order for B-form DNA and is tripled in case of A-form DNA. The changes of enthalpy (ΔH) and entropy (ΔS) for binding process were calculated by Van't Hoff analysis, from the dependence of K on the temperature. As a result of irradiation with resonant frequencies, the absolute values of ΔH and ΔS increase.The increase in the thermodynamic binding parameters (K, ΔH, ΔS) at complexing of anticancer drug netropsin in vitro with irradiated double-stranded nucleic acids indicates of prospects of development of the complex millimeter therapy with anticancer drug for clinical oncology in the treatment of malignancies.

The anticancer drug netropsin is widely used in chemotherapy due to its efficacy in fight against a wide range of cancers such as carcinomas, sarcomas and hematological cancers. Despite extensive clinical utilization, the mechanisms of action of netropsin remain under intense discussions [1, 2]. The binding of netropsin with natural and synthetic double-stranded nucleic acids was investigated. Nucleic acids were irradiated with non-thermal coherent millimeter electromagnetic waves, with resonant (64.5 and 50.3 GHz) and non-resonant (48.3 GHz) frequencies of water structures for 90 min. As a source of millimeter wave radiation the generators G4-141 and G4-142 (Russian made) were used. The incident power density at the location of object was about 50 $\mu W/cm^2$.The spectra of the absorption of the non irradiated and irradiated for 90 minutes calf thymus DNA and synthetic polyribonucleotides poly (A) poly (U) with netropsin has been obtained. Experiments show that the absorption spectra of the complexes and the nature of their change in the titration are almost identical to the non-irradiated and irradiated nucleic acids. From the absorption spectra concentration of free and bound netropsin in solution was considered and binding isotherms are constructed according to the method described in [3].The calculated value of parameters K and n for complexes netropsin with calf thymus DNA (B-form) and a synthetic double stranded polyribonucleotide poly (A) poly (U) (A-form) at different temperatures are shown in Table. 1.As can be seen from Table 1, K is almost 4 times more than when bound to the B-form than with the bound to A-form: netropsin is hydrated more stable complex with B-forms, than with A-hydrated form. For DNA complexes netropsins $n\approx6$, and for RNA complexes netropsins $n\approx8$. Most likely, the difference of the values of n and K, obtained for DNA-netropsin and RNA - netropsin, is due to the fact that under the same external conditions DNA was stored in B-form, and RNA in A-form, which significantly differ in the helix geometry and hydration . In addition, the uracil is replaced by thymine in RNA, which greatly affects on stability of the double helix. The values of parameter K and n are consistent with those of other authors [4,5] obtained for netropsin binding to DNA.For irradiated with resonant structures forwater64.5 and 50.3GHz frequencies, the binding constant, which characterizes the strength of the complexes exposed nucleic acids with netropsins almost an order of magnitude greater for the B-form, and 3 times for A-form (Table 2).When irradiation of solutions of calf thymus DNA and poly (A) poly (U) with non resonance frequency (e.g., 48.3 GHz), the thermodynamic parameters characterizing the complexation of double-stranded nucleic acids with netropsin within experimental error of the calculated values are constant (Tables 1 and 2).In [6,7], in explaining the experimental data, it was assumed that the irradiation of the resonant frequencies of structures for water decreases hydration present in the solution of Na+ and bases pairs double-stranded DNA. Consequently, most of all, when irradiated nucleic acids resonant 50.3 and 64.5 GHz frequencies in a hydrated B-forme is much severe dehydration, whereby, netropsin settling in a narrow groove, is able to more tightly bind a positively charged NH_2 groups to negatively charged phosphate groups nucleotides, which leads to an increase in the binding constant.As can be seen from Table 3, the irradiation with resonant frequencies increases(ΔH)and(ΔS), which is more pronounced when the binding netropsin with calf thymus DNA

(B-form). Irradiation of the natural and synthetic double-stranded nucleic acids with a non-resonant frequency (48.3 GHz), enthalpy (ΔH)and entropy (ΔS) binding within the error do not change. Studies demonstrate that absorption curves of the complexes and the character of change during titration process are the same for irradiated and non-irradiated nucleic acids. The results show that binding constant (K) of netropsin with irradiated nucleic acids changes: almost by an order for B-form DNA (extracted from calf thymus) and is tripled in case of A-form RNA (poly (A) poly (U)). The changes of enthalpy (ΔH) and entropy (ΔS) for binding process were calculated by Vant Hoff analysis, from the dependence of K on the temperature. As a result of irradiation with resonant frequencies, the absolute values of ΔH and ΔS increase, while in case of non-resonant irradiation these values practically remain constant.

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Figures

T, K	$K \cdot 10^{-8}$, M^{-1}	-ΔG kcal/mol	n
DNA - netropsin			
293	5.0±0.2	11.7±0.2	6.0±0.1
303	3.0±0.2	11.7±0.2	5.9±0.2
313	1.9±0.2	11.9±0.2	6.0±0.2
poly(A)poly(U) – netropsin			
293	1.20±0.02	10.9±0.2	8.0±0.1
303	0.72±0.03	10.9±0.2	8.1±0.2
313	0.44±0.02	11.0±0.2	8.0±0.2

Figure 1. Table 1. Thermodynamic parameters netropsin binding to double-stranded nucleic acids of non-irradiated at several temperatures.

The radiation frequency	T, K	$K \cdot 10^{-8}$, M^{-1}	-ΔG kcal/mol	n
DNA - netropsin				
50.3 GHz	293	36.1±0.3	12.8±0.3	5.9±0.2
	303	21.1±0.2	12.9±0.2	6.0±0.2
	313	12.8±0.3	13.1±0.3	6.0±0.2
64.5 GHz	293	38.4±0.2	12.9±0.3	6.0±0.2
	303	22.3±0.3	13.0±0.2	6.1±0.2
	313	13.0±0.2	13.1±0.3	6.1±0.2
48.3 GHz	293	6.9±0.2	11.9±0.2	6.0±0.3
	303	4.1±0.2	11.9±0.2	6.2±0.3
	313	2.4±0.2	12.0±0.2	6.1±0.2
poly(A)poy(U) – netropsin				
50.3 GHz	293	3.9±0.2	11.5±0.1	8.0±0.2
	303	2.3±0.1	11.6±0.2	8.1±0.3
	313	1.4±0.1	11.7±0.1	8.0±0.2
64.5 GHz	293	4.2±0.1	11.6±0.2	8.0±0.2
	303	2.5±0.1	11.6±0.2	8.0±0.2
	313	1.5±0.1	11.7±0.2	8.2±0.2
48.3 GHz	293	1.71±0.05	11.1±0.2	7.9±0.3
	303	1.02±0.05	11.1±0.3	8.2±0.3
	313	0.63±0.03	11.2±0.2	8.0±0.2

Figure 2. Table 2. Thermodynamic parameters binding netropsin irradiated double-stranded nucleic acids at three temperatures.

Thermodynamic parameters	Non-irradiated	Irradiated, with frequencies (GHz)		
		50.3	64.5	48.3
DNA – netropsin				
$-\Delta H, \frac{kcal}{mol}$	9.1±0.2	9.5±0.2	9.6±0.2	9.2±0.2
$\Delta S, \frac{cal}{mol \cdot K}$	8.6±0.2	11.2±0.2	11.2±0.2	8.9±0.2
poly(A)poly(U) - netropsin				
$-\Delta H, \frac{kcal}{mol}$	9.1±0.2	9.3±0.2	9.3±0.2	9.1±0.2
$\Delta S, \frac{cal}{mol \cdot K}$	5.9±0.2	7.6±0.2	7.6±0.2	6.6±0.3

Figure 3. Table 3. The values of enthalpy (ΔH) and entropy (ΔS) binding netropsin with irradiated and non-irradiated double-stranded nucleic acids.

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The low power electromagnetic millimeter waves influence on the cellular indicators of leucopoiesis

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On the base of our experimental results and the literature data we conclude that the low intensity millimeter waves elevate the functional state of the blood cells, the functional potential of the leukocytes, preparing the cells to resist against other agents.

At the present time, a dramatic change in the human life style has led to restriction of motive activity and to a sedentary lifestyle. Today, the computer technology is evolving into different fields of human activity and is becoming indispensable for work and the learning process. Relative non-motile stages create a stress reaction, the tension of regulatory mechanisms, the movements in the immune system and the reduction of the reserve capacity of the organisms. These processes are responsible for the development of pathologic processes in the organisms. The results of experimental investigations show that in the case of hypokinesia, the concentration of lysozyme, the amount of complimentary lymphocytes and immunoglobulins are decreased. In addition, it was observed that the functional activity of neutrophilsis decreased as well. As a consequence of this theresistance of the organism against various infections and diseases decreases. Therefore, it is important to find means that under the hypomotile conditions will help either to prevent and correct such deviations. The clinical and experimental data of numerous investigations have shown that the electromagnetic waves are considered to be a new, highly efficient method for the treatment of various diseases. They have anti-stress effect on neuroendocrine and immune systems, as well as on the peripheral