INTRODUCTION

Studies in recent decades have shown that low intensity non-ionizing millimeter electromagnetic waves (MMEWs) without causing a significant increase in temperature in the tissues and cells, promote activation of a number of physical and chemical processes taking place in biological systems. Therefore MMEWs currently are widely used in several fields, including biology and clinical medicine [1]. In particular, in recent years, due to the combined use of MMEWs with anticancer drugs, it became possible with experimental animals in vivo in a number of test systems to observe the formation of an external aggregate complex with DNA [6]. The aim of this work is to identify the factors of interaction of antitumor drug DX with DNA isolated from sarcoma-45 tumor pre-irradiated by resonant frequencies of oscillations of molecular water structures.

EXPERIMENT

In our experiments DNA samples were used, which were isolated from liver of healthy white rats (hDNA) and from tumor of affected with sarcoma-45 tumor in buffer solution at temperature of 300 K. During titration doxorubicin concentration remains constant, equal to C

\( C_0 \)

= 10⁻⁸ mol/L, then DNA concentration varies from zero (1) to 10⁻³ mol/L. The irradiation of DNA by millimeter waves at the power density of 50 W/cm² results in the irradiation of DNA in the range of 48.3 GHz to 50.3 GHz, which corresponds to the resonant frequency of oscillations of water structures in the tissues and cells, promote activation of a number of physical and chemical processes taking place in biological systems.

RESULTS and DISCUSSION

Table 1 shows the values of the DNA melting parameters during irradiation with resonant and non-resonant coherent millimeter waves. As seen from the Table, when irradiated with resonant frequencies similar regularities of changes of the melting parameters are observed, however T

\( M \)

, greatest change occurs during irradiation with frequency of 64.5 GHz, which coincides with the resonant frequency of oscillations of water structures.

It is known that the resonant frequencies of DNA absorption are within 2±9 GHz range. Therefore, summarizing the literature and our experimental data, it can be assumed that DNA isotachnostability growth by irradiating with resonant frequencies of oscillations of the water molecular structures probably is caused by indirect influence of millimeter waves on DNA, namely, by affecting the water, waves cause quantitative and qualitative changes of water associated with DNA [9].

It is known that in the process of malignation (neoplastic transformation) the content of 5-methylcytosine significantly increases in DNA extracted from solid tumors [8]. Relatively recently it has been shown [9] that the cytosine methylation contributes to the binding of a number of antimycobacteria to DNA. Because a combination of anticancer drugs with radiation increases the effectiveness of drugs action [3,4], we can assume that the interaction DX with DNA can to some extent be changed and be selective if DNA was prior irradiated with resonant frequencies of the water molecular structures.

The experimental data shows that, starting from a certain value of the relative concentration of C

\( C_0 \)

/C

\( C_1 \)

(where C

\( C_0 \)

is a molar concentration of DNA for base pairs, and C

\( C_1 \)

is a molar concentration of DX) the absorption spectra of the complex DX-DNA in the visible region no longer are changed, which means that all DX molecules in the solution are in bound state. From the absorption spectra of DX-DNA complexes the values of the basis quantitative parameters characterizing the complex were determined: binding constant (K) and a parameter determining the complex stoichiometry at saturation of the interaction (n). The absorption spectra were obtained for unirradiated and irradiated complexes of hDNA-DX and tDNA-DX for three different temperatures.

At in vitro irradiation of DNA solutions certain structural changes occur in DNA molecules (due to the partial dehydration of DNA caused by irradiation), which are stronger in tumor DNA, owing to which the irradiated DNA molecules form more stable complexes with an anticancer drug Doxorubicin (DX). When DNA is irradiated with millimeter waves the binding constant (K) increases. Doxorubicin forms a stable complex with DNA. For a DNA irradiated with resonant for water molecular structures frequencies of 64.5 GHz and 50.3 GHz the coefficient of binding K to DX is almost an order of magnitude more than for the non-irradiated DNA. With irradiated and non-irradiated tumor DNA anticancer drug forms more stable complexes, and when tumor DNA is irradiated with 64.5 GHz and 50.3 GHz frequencies DX forms much stronger spectrophotometric (for irradiated at 64.5 GHz frequency of 48.3 GHz) absorption spectra, as compared with unirradiated complexes.

Table 1. The values of the parameters thermal denaturation of DNA exposed to the millimeter waves for 90 minutes

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>n</th>
<th>K (±0.1)</th>
<th>M (±0.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>300</td>
<td>2</td>
<td>8.9±1</td>
<td>3.1±0.1</td>
</tr>
<tr>
<td>305</td>
<td>2</td>
<td>11.9±1</td>
<td>3.6±0.1</td>
</tr>
<tr>
<td>310</td>
<td>2</td>
<td>15.9±1</td>
<td>4.0±0.1</td>
</tr>
</tbody>
</table>

CONCLUSION

Summarizing the experimental data can be said that at in vitro irradiation of DNA solutions certain structural changes occur in DNA molecules (due to the partial dehydration of DNA caused by irradiation), which are stronger in in-DNA, owing to which the irradiated DNA molecules form a more stable complex with DX. Increase in the thermodynamic binding parameters (K, ΔH) in in vitro complexation of anticancer drug DX with irradiated DNA indicates to the prospects of development of the millimeter therapy complex with anticancer drug for clinical oncology in the treatment of malignant tumors.

REFERENCES