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EXPERIMENTAL ARTICLES

Mechanisms of Interaction between DNA and Chemical Analogues of Microbial Anabiosis Autoinducers

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Abstract—The alkylhydroxybenzene (AHB) autoregulatory factors d_1 (fd_1) of microorganisms have been found to directly interact with highly polymeric DNA. This circumstance results in changes, related to alterations in the topology of this macromolecule, in DNA physicochemical properties. The physicochemical properties of DNA in the presence of chemical analogues of microbial AHBs (methylresorcinol; hexylresorcinol; and 2-(4-hydroxyphenyl)ethane-1-ol, also known as tyrosol) were investigated using adsorption spectrophotometry, fluorometry, heat denaturation, viscosimetry, and electrophoresis in agarose gel. A number of concordant effects pointing to DNA–AHB interactions were revealed that manifest themselves in the hypochromic properties of the resulting complexes, an increase in their melting temperature and viscosity, a decrease in their electrophoretic mobility, and a change in the fluorescent properties of AHBs upon complexation with DNA. Such alterations were particularly significant in the presence of hexylresorcinol, which possessed the maximum alkyl radical length among the fd_1 analogues tested. Using atomic force microscopy, we visualized the micelle-like DNA structures forming in the presence of AHBs. The results obtained provided the basis for developing a hypothetical model of the interaction between the biopolymer macromolecule and low-molecular-weight AHBs that takes into account the differences in the hydrophobicity of individual AHB homologues functioning as ligands. In terms of our model, we discuss AHB involvement in the stabilization of DNA and alteration of its topology, i.e., in the process related to intragenomic rearrangements, which account for the intrapopulational variability of bacteria, including dissociation processes.

Key words: alkylhydroxybenzenes, alkylresorcinols, tyrosol, DNA complexation, physicochemical properties of DNA, DNA topology.

Recently, considerable attention has been given to microbial autoregulatory d_1 (fd_1) factors, which function as anabiosis autoinducers and control the transition of microbial cells to hypometabolic (stationary phase) or anabiotic (dormant) states. In chemical terms, they are alkylhydroxybenzene (AHB) derivatives such as alkylresorcinols and tyrosol [1, 2]. These substances have received a great deal of attention in studies conducted during the last decade. The first mechanism pertaining to the effect of AHBs on the metabolic activity and physiological state of bacterial cells described in the literature involved interactions with membrane lipids, resulting in an increase in their microviscosity, polycrystallization of the lipid stroma of the membranes, and changes in the functional activity of the lipids [3]. Subsequently, we established the AHB capacity to complexate with enzyme proteins. AHBs behave as low-molecular-weight chemical chaperons: they modify the structure of macromolecules, resulting in their stabilization and a change in catalytic activity [4]. It was revealed that the direction of activity changes (stimulation or inhibition) varies depending on the structure and concentration of the AHB ligand [4, 5]. At the cell level, AHB interaction with biopolymers and supramolecular structures controls metabolic processes, which is exemplified by a considerable inhibition of metabolism, the induction of the formation of cystlike dormant cells in microorganisms [6], and an increase in the cell resistance to stress factors [7, 8].

Importantly, the transition to an anabiotic state and increase in cell stress resistance implicate stabilization of the genetic-information-carrying cell DNA, which becomes resistant to the deleterious effects of a wide variety of abiotic and biotic factors. AHBs are characterized by various hydrophobicity and polarity degrees and produce different regulatory effects on the bacterial cell genome [8–11] and on the elastoviscosity of DNA supramolecular complexes [12]; furthermore, they are likely to be involved in relevant alterations in DNA topology. However, only small amounts of data have been obtained up to now concerning the possibility that AHBs interact with DNA. Therefore, the goal of this study was to investigate changes in the physicochemical properties of DNA in in vitro systems containing alkylresorcinols and tyrosol, chemical analogues of microbial autoregulators that differ in relation to their

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chemical structure, hydrophobicity degree, and biological activity.

MATERIALS AND METHODS

The following chemical analogues of bacterial autoregulatory d_1 factors [1] were used: (i) methylresorcinol (MR, molecular weight 124) and hexylresorcinol (HR, molecular weight 194), with a purification degree of 99.9%, and (ii) the structurally and functionally similar compound 2-(4-hydroxyphenyl)ethane-1-ol, also known as tyrosol (T, molecular weight 138), which operates as autoregulatory factor d_1 in the yeast *Saccharomyces cerevisiae* [2]. The working concentrations of these substances in the tested solutions were 10^{-3}, 10^{-4}, and 10^{-5} M.

The main series of experiments used a commercial preparation of highly polymeric linear DNA isolated from bovine spleen and purified to homogeneity (the optical density ratio $D_{260/280}$ was 1.8). The techniques of electrophoresis in agarose gel and atomic force microscopy employed a commercial preparation of *Hin*dIII–cleaved λ phage DNA (Sibenzim, Russia). The DNA concentration in the tested solutions was 10^{-4} M (in terms of nucleotide content), and the DNA–AHB molar ratios were 1 : 10, 1 : 1, and 10 : 1 in various samples. The DNA + AHB mixtures were preincubated for 1, 2, 3, 4, and 5 weeks at 4°C. Individual DNA or AHB samples with the same concentrations and preincubated under the same conditions were used as controls.

The absorption and emission properties of the AHB solutions and DNA + AHB mixtures were investigated using a Flyuorat-02 Panorama spectrofluorometer (Lyumeks, Russia). The measurements were carried out in 1-cm quartz cuvettes within the 210–300 nm and the 280–350 nm ranges for absorption and fluorescence spectra, respectively; the wavelength of the exciting light was 270 nm. The hypochromic effect (HC) resulting from the DNA–AHB interaction was estimated from the ratio $(D_{mix} - D_{AHB})/D_{DNA}$, where D_{mix} is the optical density of the DNA + AHB mixture at λ = 260 nm, and D_{AHB} and D_{DNA} are the optical densities of solutions containing the same AHB and DNA concentrations and measured at the same wavelength.

Thermal denaturation (melting) of the intact DNA and DNA–AHB mixtures was performed by heating the samples from 30 to 95°C at a rate of 1°C/min, with the optical density values being monitored at λ = 260 nm. The quantitative characterization of the DNA melting process included calculating its start (T_s) and finish (T_f) temperatures; the 50% heat denaturation temperature (T_{50}); the transition zone width (ΔT), in the form of the T_s–T_f difference; and the melting increment (ΔH), from the difference between the control and experimental hyperchromism values.

The viscosity of the intact DNA solutions and DNA–AHB mixtures was measured using an Ostwald viscosimeter with a working capillary diameter of 0.86 mm. The relative viscosity values were determined from the t/t_0 ratio, where t is the flow time of the tested solution and t_0 is the flow time of distilled water.

Electrophoresis was carried out in 0.8% agarose gel with 0.5 μg/ml ethidium bromide at a current of 100 mA and an electrical field strength of 5 V/cm. The DNA migration after 2 h of electrophoresis was estimated using a transilluminator (Vilber Lourmat, France), and the digital pictures obtained were processed using the ImageJ software.

Atomic force microscopy of the DNA and DNA + AHB samples was performed by placing the samples on a fresh mica fracture surface and incubating them in this system until complete desiccation was achieved. The samples were scanned with a SMM-2000T probe microscope (Zelenograd, Russia) in contact with the air and employing a cantilever with a needle radius of 15 nm.

Each of the three series of experiments was performed in at least three replicates. The data obtained were treated statistically using standard mathematical methods and the SPSS for Windows software. The complex method we used to estimate the parameters reflecting the physicochemical changes occurring in DNA in the presence of AHBs included the factor analysis procedure.

RESULTS AND DISCUSSION

The insignificant distance between the spectral maxima of the tested compounds (260, 277, 280, and 278 nm for DNA, MR, HR, and T, respectively) set limits for measurements of the optical density of the DNA, AHBs, and DNA + AHB mixtures. At the beginning of the incubation time, the absorption spectra of the DNA + AHB mixtures were additive with respect to the individual contributions of the components involved; however, a hypochromic effect was observed after 2 weeks of incubation (Fig. 1). This phenomenon occurred in the DNA–tyrosol mixture (with the hypochromic coefficient decreasing to 0.83), and it was particularly significant in the DNA–hexylresorcinol mixture (with the hypochromic coefficient decreasing to 0.67). The hypochromic effect increased with an increase in the AHB concentration, resulting in a negative correlation between the relative absorption value of the DNA–AHB complex and the AHB concentration (the correlation coefficients were –0.708 and –0.861, respectively; $P < 0.01$). It was suggested that development of the hypochromic effect is due to the formation of a more ordered DNA structure resulting, e.g., from the interaction of intercalating molecules with DNA [13]. However, in view of the manifest relationship between the effect and the length of the alkyl radicals, which accounts for the structural differences between the tested AHBs (their polar heads being of the same type), an alternative hypothesis concerning the mechanism of DNA–AHB complexation was necessary.

A subsequent stage of our research on the physicochemical properties of DNA in the presence of AHBs was based on the fluorometric method, since illuminating the aromatic ring in the AHB molecule with a wavelength close to its absorption maximum results in its fluorescence at an emission wavelength that increases in the following sequence: methylresorcinol (301 nm) ⟶ tyrosol (304 nm) ⟶ hexylresorcinols (312 nm). These differences between the fluorescence wavelengths of various AHBs are due to the different length of their alkyl radicals, which influence the intramolecular distribution of electron density and, therefore, the distance between the energy levels of excited and unexcited AHB molecules [14]. A DNA molecule does not emit light per se under normal conditions. This fact enabled the monitoring of polymeric DNA-induced changes in the spectral parameters of the AHB fluorescent probe and, therefore, made it possible to obtain information concerning alterations in the properties of the DNA microenvironment surrounding the fluorophore.

The changes we revealed included a gradual blue shift in the AHB fluorescence maximum in the presence of DNA and a concomitant increase in the quantum yield. This effect was directly proportional to the length of the alkyl radical, and it was particularly significant for hexylresorcinols (Fig. 2), suggesting DNA–AHB complexation. The resulting wavelength value of the fluorescence maximum approached 301 nm and, therefore, tended to become identical to that of the methylresorcinol fluorescence maximum. Methylresorcinol displayed no significant changes in the fluorescence spectrum under the same experimental conditions. Interestingly, a maximum effect was observed at low and intermediate resorcinol : DNA molar ratios, whereas high DNA concentrations decreased the effect, which may be due to saturation of the binding sites responsible for the DNA–AHB interaction and masking of the spectrum of the hexylresorcinols–DNA complex by the fluorescence spectrum of unbound excess AHB. We showed an analogous dependence of changes in the AHB fluorescence spectrum in protein–AHB complexes on protein–AHB ratios in our studies of RNase–hexylresorcinol complexation [4]. Apparently, this dependence reflects general patterns of AHB–biopolymer interactions, which are accompanied by changes in the physicochemical properties of the macromolecules in the resulting complexes.

The results obtained can be explained on the basis of the idea that the emission spectra of a large number of fluorophores (especially if they contain polar substituents in their aromatic ring) vary depending on the properties of the microenvironment. It is traditionally assumed that a blue shift in the fluorescence maximum accompanied by a quantum yield increase results from a decrease in the polarity of the fluorophore-enclosing "cell" [14, 15]. Accordingly, we can suggest that the interaction of AHB with hydrophobic parts of the DNA causes a partial dehydration of the AHB alkyl radicals, which lose polar solvent (water) molecules. The ensuing intramolecular redistribution of electron density and the corresponding increase in the distance between energy levels result in an increase in the energy of emitted quanta, which, nevertheless, does not exceed the maximum value obtained with methylresorcinol, whose alkyl radical has a minimum length.

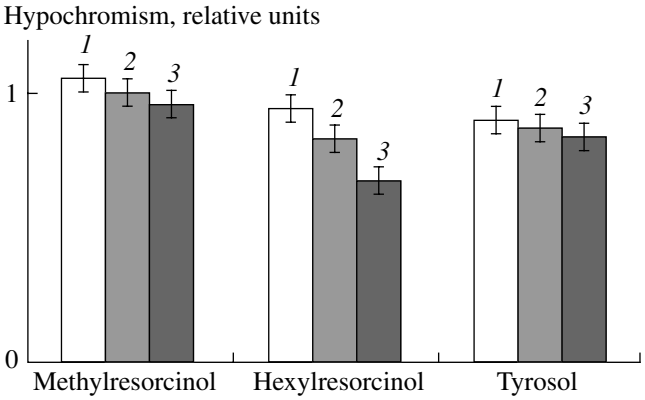

Fig. 1. DNA hypochromism upon complexation with various alkylhydroxybenzenes: OD_{260} values relative to the control system (intact DNA) at the AHB : DNA nucleotides ratios of (*1*) 1 : 10, (*2*) 1 : 1, and (*3*) 10 : 1.

The insignificant length of the alkyl radical in the methylresorcinol molecule could be one of the reasons why no large-scale redistribution of electron density occurs in its molecule. Therefore, we could not record major shifts in the fluorescence spectrum, although, according to the physicochemical changes in the DNA we observed (see below), DNA–methylresorcinol complexation actually occurred. Importantly, the induction of chromosome aberrations by alkylresorcinols is enhanced, in a biological test system, by increasing the length of the alkyl radicals, which provides indirect evidence for hydrophobic interactions between AHB and DNA [16]. This is consistent with our results.

The issue to be raised concerns the mechanisms of DNA–AHB complexation, which results in shifts in the fluorescence spectra of AHB. It seems likely that, in addition to interactions between AHB and the relevant parts of polymeric DNA molecules, AHB molecules directly interact with each other (while attached to the DNA) and form supramolecular structures. This suggestion is consistent with the fact that they exhibit high radical-quenching activity and the capacity for multistage oxidation and polymeric condensation of oxidized AHB forms via the formation of polyhydroxyphenolic intermediates [17]. The products generated in polymeric condensation of AHBs retain and even enhance their biological activity [7]. Of special interest in this context is the fact that the physicochemical changes in DNA upon complexation with AHB increase with an increase in the incubation time of the DNA–AHB mixtures under aerobic conditions.

An alternative technique used by us to investigate DNA–AHB interactions was based on thermal denatur-

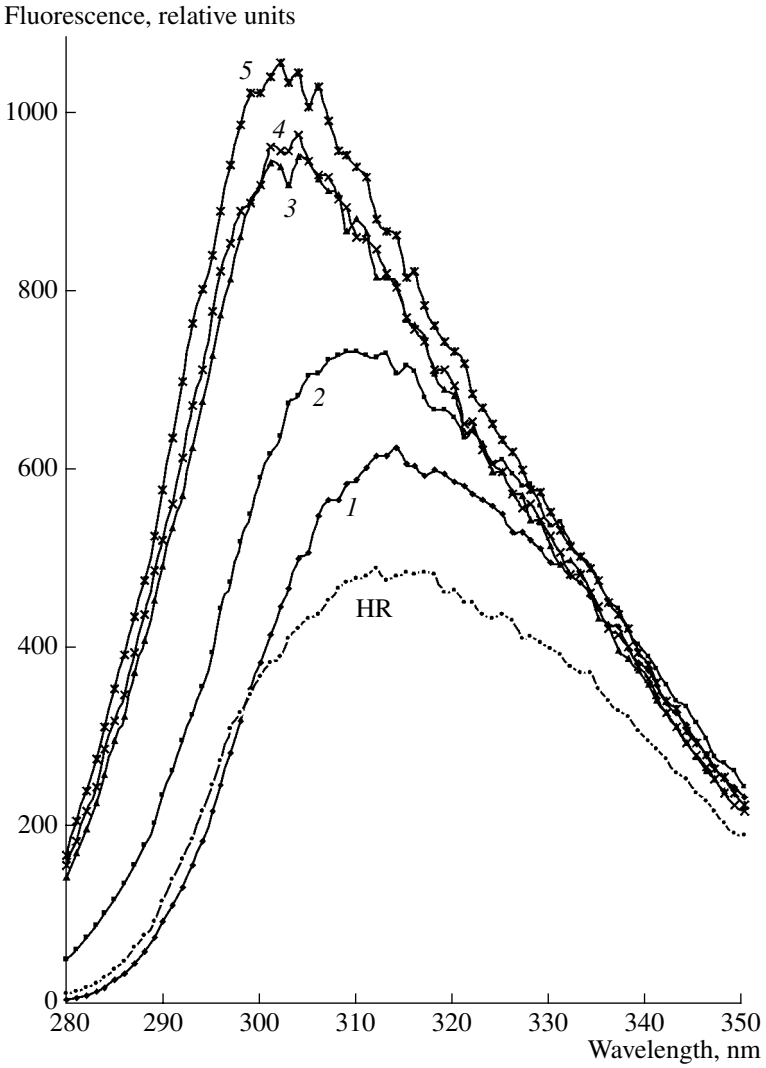

Fig. 2. Fluorescence spectra of hexylresorcinol (HR) and its complexes with DNA after incubation for (*1, 2, 3, 4, 5*) 1, 2, 3, 4, and 5 weeks.

ation (melting) of the DNA macromolecule. This process resulted in unstacked complementary bases and conversion of the double-stranded helix DNA into a single-stranded coil, which manifested itself in an increase in its optical density. It is widely accepted that low-molecular-weight substances function as "ties" that stabilize the DNA structure and change the parameters of the melting process. A large number of low-molecular-weight ligands (ions of divalent metals, acridine dyes, and, more importantly, organic solvents) have been shown to raise the DNA melting temperature [18].

Spectrophotometric studies on thermal denaturation of DNA in the presence of AHBs and tyrosol revealed the following general pattern. Melting curves shift toward higher temperatures, and the T_s, T_{50}, and T_f values increase, but no statistically significant ΔT change occurs. However, we noted a difference between the control and experimental hypochromism values (ΔH). The effect of AHBs on DNA was analogous to that of other low-molecular-weight ligands and is indicative of stabilization of the DNA double strand, which is achieved, in part, by blocking the negative charges of its phosphate groups [19]. The melting temperature of the DNA–AHB complexes increased with an increase in the length of the alkyl radical of the AHB. Accordingly, the above changes were particularly prominent in the system in which DNA complexated with hexylresorcinols (Fig. 3). In contrast, if tyrosol was used, only some of the melting parameters were affected; methylresorcinol caused statistically insignificant changes.

Special emphasis should be placed on the following feature of thermal denaturation of DNA–AHB complexes. The hyperchromic effect (ΔH) observed is clearly dose-dependent. It decreases with an increase in AHB concentration, i.e., the AHB molar percentage in the complex (Fig. 3a). These changes are consistent with the dose-dependent DNA hypochromism resulting from complexation with AHB (see above) and similar

to the effects produced by interactions of DNA with cationic amphiphilic N-trimethylalkyl compounds that resemble AHBs in terms of their chemical structure [20]. These phenomena are regarded as consequences of light scattering by the micellelike structures forming on DNA molecules [20].

Importantly, statistically significant changes of only the initial part of the melting curves (reflecting a T_m increase without appreciable changes in the other melting parameters) occur at low AHB : DNA molar ratios, i.e., in a relatively ligand-deficient system (Fig. 3b). Because the process of thermal DNA denaturation starts at AT-rich sites, the results obtained suggest site-specific (nucleotide sequence-specific) binding of AHB to a polymeric DNA molecule. This is characteristic of cationic amphiphiles (see above) [19, 20]. Nevertheless, this process is only relatively site-specific, becoming nonspecific upon an increase in AHB concentration or in the DNA–AHB interaction time. This fact, along with the above data on the fluorescence of AHB–DNA mixtures, suggest that stable complexes gradually form under aerobic conditions.

The fact that DNA–AHB complexes melt at a high temperature is consistent with the earlier data on (i) the protective role of AHBs, which enhance cell stress resistance [7, 8, 21] and (ii) the high thermal resistance of cystlike dormant forms of microorganisms, whose generation is induced by an increase in the AHB level [6]. In addition, the data obtained enable us to include an additional biopolymer, i.e., DNA, into the list of macromolecules whose thermal resistance is subject to regulation by AHBs.

Additional information on the physicochemical changes occurring in DNA in the presence of AHBs was obtained using capillary viscosimetry of the DNA solutions. Alkylresorcinols caused a moderate, but statistically significant, increase in the η value; the magnitude of this effect varied depending on the chemical structure of the tested AHB. In analogy to the above studies, the most drastic changes were found in the presence of hexylresorcinols, which increased the η value 1.15 fold (compared to the control). This effect can be considered as evidence of the formation of complexes involving the tested molecules, and it is correlated with the elastoviscosity changes in supramolecular DNA–AHB complexes that we earlier revealed [12].

Based on our concepts concerning polymer molecular weight–viscosity interrelationships, we made an attempt to quantitatively estimate AHB binding to DNA. We proceeded from the assumption that the viscosity changes resulting from DNA–AHB complexation are mainly due to an AHB binding-dependent increase in the molecular weight of the DNA. To a lesser extent, they are conditional on possible changes in the rigidity of the linear polymer. From our calculations, it follows that the average molecular weight of DNA–hexylresorcinol complexes (5406 kDa) exceeds that of the polymer per se (4465 kDa) by approximately

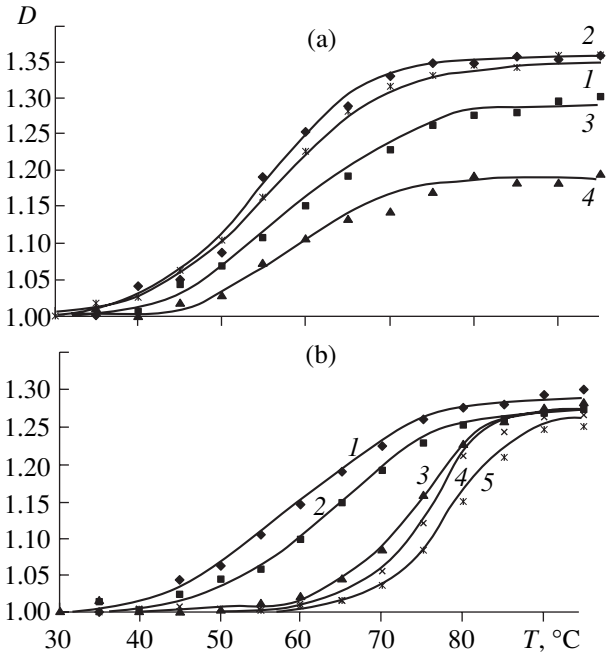

Fig. 3. Melting curves of DNA–hexylresorcinol complexes (a) at AHB : DNA nucleotides ratios of (*1*) 0, (*2*) 1 : 10, (*3*) 1 : 1, and (*4*) 10 : 1 and (b) at a 1 : 1 ratio after incubation for (*1, 2, 3, 4, 5*) 1, 2, 3, 4, and 5 weeks.

20%, corresponding to the binding of ca. 1500 (1492) hexylresorcinol molecules to a 1000-bp-long DNA fragment. Taking into account possible changes in the biopolymer's rigidity, we regard the values obtained to be underestimates.

Similar results were obtained by calculating the molecular weights of the DNA and DNA–AHB complexes on the basis of their electrophoretic mobility in agarose gel in the presence of an array of DNA molecules with varying molecular weights (*Hin*dIII–degraded phage λ DNA, Fig. 4). From the 4th or the 5th week of incubation onwards, we noted an appreciable decrease in the electrophoretic mobility of the DNA–hexylresorcinol complexes in comparison to the intact DNA. This result suggested an increase in their average molecular weight value to 6432 kDa in contrast to a control value of 4217 kDa. Calculations based on this difference indicate that over 1500 (1670) hexylresorcinol molecules can bind to 1000 bp in a polymer DNA molecule. This result of our calculations was slightly above the value obtained by analyzing the viscosity–molecular weight dependence, which may result from an increase in the hexylresorcinols–DNA binding parameters over time. However, the decrease in the electrophoretic mobility of the DNA–AHB complexes could be partly due to ligand binding to the DNA surface, which results in blocking and neutralizing the negative charge of phosphate groups. As a consequence, the binding parameters may be somewhat overestimated.

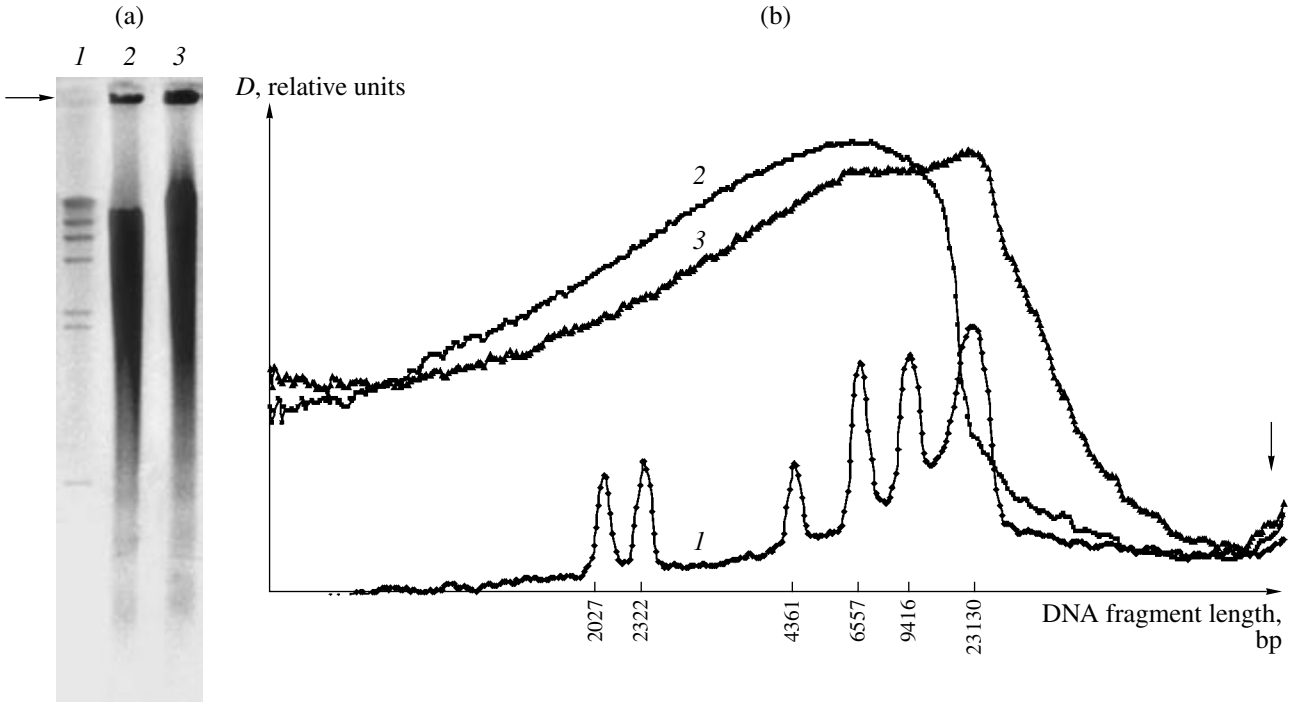

Fig. 4. Electrophoretic mobility of DNA complexated with hexylresorcinol: (a) photograph of the gel and (b) optical density profiles. (*1*) DNA molecular weight markers (λ/*Hin*dIII), (*2*) DNA from bovine spleen, and (*3*) DNA–hexylresorcinol (10 : 1). The arrows indicate the starting point.

In toto, the data obtained suggest that a number of concordant physicochemical changes in DNA occur in the presence of alkylresorcinols and tyrosol, which indicates that DNA interacts with these molecules. Using a multidimensional statistical assay (the main component method), we established that a major factor existing in the tested system determines the types of effects of structurally different alkylhydroxybenzenes. The maximum factor contribution (FC) was attained with hexylresorcinol (0.718), in contrast to negative FC values with methylresorcinol (–0.522). Therefore, a sufficient length of the alkyl radical is essential for securing efficient interactions between AHB and DNA. This crucial factor included the following components (with the FC value increasing in the sequence given below): hypochromism of DNA–AHB complexes (FC = 0.299), an increase in their viscosity (FC_η = 0.424) and melting temperature (FC_{T50} = 0.406 and FC_{Ts} = 0.47), and a decrease in electrophoretic mobility.

The results obtained provided no evidence for concluding that the AHB mechanism of action is analogous to that of any familiar group of low-molecular-weight DNA ligands, whether intercalating between base pairs arranged in parallel or binding to the major or minor furrow on the DNA molecule. In the latter case, the formation of DNA–AHB complexes can proceed, in part, via hydrophobic interactions between AHB and DNA-bound lipids [22]. Studies aimed at proving the existence of such lipids are currently in progress.

The final stage of our work used atomic force microscopy to visualize complexes forming in DNA–hexylresorcinol mixtures (Fig. 5). Both the control system and the DNA–AHB mixture at their early incubation stages contained 125- to 23130-bp-long linear DNA fragments (Figs. 5a, 5b) that resulted from *Hin*dIII–catalyzed cleavage of phage λ DNA. During the 2nd and the 3rd week of incubation, spherical structures with a diameter of ca. 200 nm (with 150 to 250 nm spaces separating them) formed in the DNA–hexylresorcinol mixtures on the basis of linear DNA molecules (Figs. 5c, 5d). No structures of this kind formed in the DNA solutions per se or in the DNA–methylresorcinol mixtures. A further increase in the incubation time resulted in the formation of thickened branched strand-like structures in the DNA–hexylresorcinol mixtures. These structures exceeded the original DNA restricts in terms of their length and width. At the intersection points, they were connected to one another via nanostructures (see above) that tended to increase in size up to 1 μm. They assumed an irregular shape and were located at the branching points of the DNA molecules (Figs. 5e, 5f). The structural changes in the DNA occurring with hexylresorcinol resembled the changes associated with nucleoid compactization in cystlike dormant bacterial cells [6, 12].

The data obtained enabled us to put forward a hypothesis concerning the mechanism of DNA–AHB (hexylresorcinol) interactions. Presumably, they undergo three main stages. At the first stage, lasting for

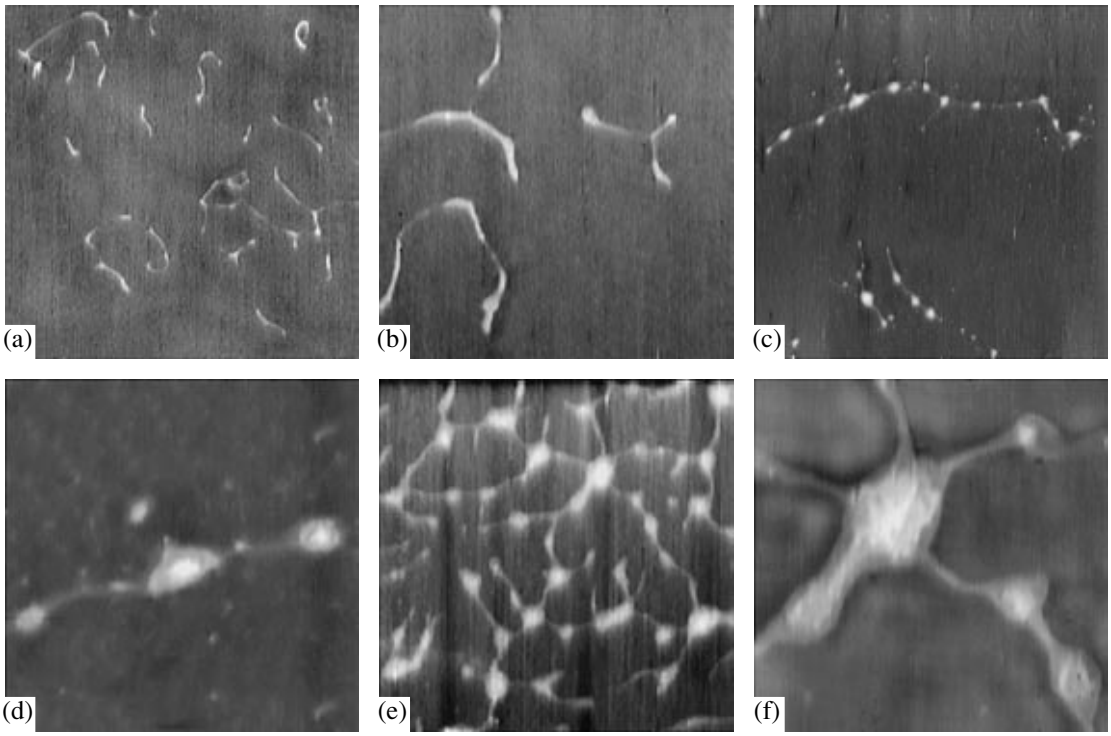

Fig. 5. Results of atomic force microscopy of (a, b) DNA and (c–f) its complexes with hexylresorcinol after incubation for (c, d) 3 weeks and (e, f) 5 weeks. (a, c, e) Scan size, 8×8 μm; (b, d, f) scan size, 2.5×2.5 μm.

several hours or days, DNA complexates with AHB, which is chiefly due to interactions between the alkyl radicals of AHB and the hydrophobic parts of the DNA macromolecule; complexation predominantly occurs at AT-rich sites. It seems certain that intercalating intermolecular links based on hydrogen bonds also form, and they account for interactions between DNA and methylresorcinol/tyrosol.

At the second stage (2–3 weeks of incubation), the system exceeds the micelle formation threshold concentration (MFTC) at the DNA–AHB complexation sites, resulting in the formation of the micellelike nanostructures discernible by atomic force microscopy. Importantly, the capacity to form micelles is a characteristic property of amphiphilic alkylresorcinol molecules [4, 16]. In our system, however, this process did not occur in a solution reaching MFTC; rather, it resulted from supercritical local concentrations at certain sites of a linear DNA molecule, which functioned as a kind of condensation nuclei for AHB molecules.

Changes in the physicochemical properties of DNA upon complexation with alkylresorcinols and the possible mechanisms involved

Effects	Mechanisms
DNA hypochromism	Hydrophobic interactions between AHB alkyl radicals and hydrophobic DNA domains. AHB intercalation into DNA molecules. Light scattering by micellelike structures (at the late stages of incubation)
Blue shift in the AHB fluorescence maximum	Hydrophobic interactions between AHB alkyl radicals and hydrophobic DNA domains. Occurrence of AHB radicals in the hydrophobic environment in the interior of micelles (at the late stages of incubation)
Increase in the DNA melting temperature in the presence of AHB	Stabilization of DNA strands by AHB molecules
Decrease in the magnitude of the hyperchromic effect upon melting (ΔH)	Light scattering by micellelike structures
Increase in the microviscosity of DNA–AHB complexes	Increase in the total molecular mass
Decrease in the electrophoretic mobility of DNA–AHB complexes	Increase in the total molecular weight. Screening of the negative charge of phosphate groups in the DNA molecule

At the last (third) stage, occurring after a long incubation period, the DNA molecules grouped together by low-molecular-weight ligands (AHB) interact with one another, resulting in the formation of thickened elongated structures that consist of a large number of DNA strands arranged in parallel. This phenomenon manifests itself in the DNA compactization seen in micrographs.

In terms of the suggested model, we can sufficiently adequately explain the differences in the patterns of DNA interactions with AHB homologues differing in terms of hydrophobicity (methyl- and hexylresorcinol), which manifests itself in different physicochemical changes in DNA upon complexation with these ligands (table). In addition, this model can help us eliminate the apparent contradictions between (i) the data suggesting that alkylresorcinols produce a mutagenic effect and (ii) the fact that they also possess antimutagenic activity [9, 10, 16]. Selective binding of AHB molecules to AT-enriched DNA domains and subsequent events resulting in DNA compactization (nanostructure formation) can cause changes in the DNA topology and, accordingly, in the replication and transcription processes. This circumstance accounts for intragenomic transitions, which are responsible for the variability of bacterial populations including dissociation processes [10]. However, an increase in DNA stability resulting from DNA–AHB complexation can neutralize the effects of the more powerful mutagens. A large number of such mutagens belong to classical intercalating agents. DNA stabilization can also promote dissipation of the destructive energy generated by photo- or γ-irradiation [7].

Importantly, this study also yielded additional results concerning features of DNA–AHB complexes that manifest themselves during their long-term storage. These data are of special interest in terms of the properties and behavior of DNA in dormant cells of microorganisms. Our forthcoming article will consider these issues.

ACKNOWLEDGMENTS

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