EXPERIMENTAL STUDIES

FUNCTIONAL ACTIVITY FEATURES OF LACTOFERRIN-FUCOIDAN COMPLEXES IN MODEL SYSTEMS *IN VITRO*

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Fucoidan, an anionic polysaccharide from brown algae, demonstrates anticoagulant, antioxidant, anti-inflammatory, antitumor, and antiviral activities. It can form polyelectrolyte complexes with various proteins, including the therapeutically important protein lactoferrin. The aim of this study was to investigate the physicochemical and functional properties of a fucoidan-lactoferrin complex formed by mixing their solutions at physiological pH. The complex, detected using atomic force microscopy, had a negative charge and a hydrodynamic diameter of 382 nm. Interaction with lactoferrin changed the IR spectrum of fucoidan in the absorption band in the range of 1220–1260 cm^{-1}, corresponding to vibrations of the sulfate group. It increased the total antioxidant activity of biopolymers in the Fenton reaction and reduced the anticoagulant activity of fucoidan, assessed by determining the activated partial thromboplastin time. Fucoidan reduced luciferase activity in a luciferin-luciferase model system, and complex formation with lactoferrin attenuated the inhibitory capacity of fucoidan. These results demonstrate the possibility of targeted influence on the functional activity of biopolymers during complex formation and prospects for using fucoidan and lactoferrin as a complex in the development of new drugs and drug delivery systems.

Keywords: lactoferrin; fucoidan; polyelectrolyte complexes; antioxidant activity; anticoagulants; luciferin-luciferase

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INTRODUCTION

The formation of polyelectrolyte complexes of proteins with polysaccharides is considered as a promising approach to increase protein stability in aqueous environments [1] and to produce nano- and microsized containers for drug delivery [2, 3]. Intermolecular interactions have a significant impact on the physicochemical properties of biopolymers, which can affect their functional activity [4, 5].

Fucoidan is an anionic polysaccharide from brown algae; it primarily consists of sulfated fucopyranose residues with 1→3 and 1→4 linkages with inclusions of galactose, mannose, xylose, and glucuronic acid. Fucoidan is highly soluble in water, nontoxic, and highly biocompatible. Fucoidan solutions have low viscosity. Due to its anti-inflammatory, antiviral, antitumor, antioxidant, and anticoagulant activities, confirmed by numerous studies, fucoidan can serve not only as a structural component of delivery systems [6], but it also exerts a therapeutic effect [7]. The antioxidant activity of fucoidan is often associated with the polyphenols present in its preparations due to difficulties in their removal during purification [8, 9].

During development of new approaches to the treatment of inflammatory bowel diseases, particular attention is paid not only to fucoidan [7], but also to lactoferrin [10], a cationic glycoprotein (p*I* 8.0-9.0) prone to aggregation in aqueous solutions and sensitive to changes in pH. Complexes with fucoidan preserve the spatial structure of lactoferrin and improve its stability and bioavailability [11, 12].

In the process of the development of medicinal products and their delivery systems, it is important to understand the advantages of using biopolymer complexes. In this study, we have investigated the physicochemical and functional properties of a fucoidan-lactoferrin (F-L) complex at physiological pH values. To this end, we have investigated the antioxidant activity of these biopolymers in the Fenton reaction, the anticoagulant effect of fucoidan, and its ability to inhibit luciferase activity.

For analysis of F-L complex formation, dynamic light scattering (DLS), atomic force microscopy (AFM), fluorescence, and infrared (IR) spectroscopy were used.

MATERIALS AND METHODS

Reagents

The following reagents were used in the study: recombinant human lactoferrin isolated from the milk of transgenic goats (branded "Caprabel"; produced at the Belarusian State University and the Scientific and Practical Center for Animal Husbandry of the National Academy of Sciences of Belarus); fucoidan of 20–200 kDa from *Fucus vesiculosus*, ATP, luminol, hydrogen peroxide, ferrous sulfate, tris(hydroxymethyl)aminomethane (Tris), 2,2′-azino-bis-(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS) (Sigma-Aldrich, USA); firefly luciferin-luciferase mixture (Lumtek, Russia); highly oriented pyrolytic graphite (NT-MDT, Russia); Coagulo-test (PG-6) and Plasma N (KM-1) reagent kits (Renam, Russia).

Preparation of Fucoidan Lactoferrin Complexes

To assess the interaction between fucoidan and lactoferrin in polyelectrolyte complexes, the biopolymers were mixed in 50 mM Tris buffer (pH 7.1 or pH 7.4) so that their mass concentrations were equal, unless otherwise stated in the text, and incubated for 30 min at room temperature.

IR Spectroscopy

IR spectra were recorded on a Tensor 27 Fourier Transform IR spectrometer (Bruker, Germany) equipped with a liquid nitrogen-cooled MCT detector and a thermostat (Huber, USA). Measurements were performed in a thermostated BioATR-II cell (Bruker) using a single-reflection ZnSe crystal at 22°C and a constant flow rate of dry air through the system using a Jun-Air apparatus (Gast Manufacturing Inc., USA). An aliquot (50 μl) of sample was applied to the crystal cell, and the spectrum was recorded three times in the region from 4000 cm^{-1} to 950 cm^{-1} with a resolution of 1 cm^{-1}. The spectrum was scanned 70 times and averaged. The background without sample application was recorded similarly. Spectra were analyzed using Opus 7.0 software (Bruker), including background subtraction, baseline correction, and atmospheric compensation. Savitsky-Golay smoothing was used, where necessary, to remove white noise. Absorption band positions were determined using the standard Bruker procedure. The Amide I absorption band was deconvoluted.

Measurement of ζ-Potential and Hydrodynamic Diameter

The ζ-potential of fucoidan, lactoferrin, and their complex, as well as the hydrodynamic diameter of the complex, were analyzed using a Zetasizer Nano ZS system (Malvern Instruments, Germany) by measuring electrophoretic and dynamic light scattering (ELS and DLS, respectively). Biopolymer solutions (1 mg/ml) were used for the analysis.

AFM

The experiments were performed on an atomic force microscope with an Ntegra Prima controller (NT-MDT), using a protocol for high-spatial-resolution AFM studies of individual molecules and a highly oriented pyrolytic graphite surface modified with N,N′-(decane-1,10-diyl)bis(tetraglycidamine) (GM) [13]. A drop of a freshly prepared aqueous solution of 0.01 mg/ml GM was placed on the surface of freshly cleaved graphite for 5–7 min, and then excess liquid was removed from the surface with a nitrogen stream. For control experiments, a fucoidan solution was applied to the surface of modified graphite for 2–5 s. A drop of bidistilled water (100× volumes) was carefully placed on the drop of the sample solution for 10 s and then removed from the surface under a nitrogen stream. AFM experiments were performed in tapping mode with a typical scan rate of 1 Hz and a typical free amplitude of several nm. All measurements were performed in air using ultrasharp silicon cantilevers with a tip diameter of approximately 1 nm. The repulsion mode was used to obtain the highest possible AFM resolution during the work with ultrasharp cantilevers. Standard AFM image smoothing algorithms (including quadratic surface subtraction and row averaging) were used. FemtoScan Online software (Advanced Technology Center, Russia) was used to filter, analyze, and present the AFM data.

Fluorimetry

Fluorescence spectra of lactoferrin tryptophan residues were recorded on an CM 2203 spectrofluorimeter (Solar, Belarus) using an excitation wavelength of 280 nm and recording the emission spectrum in the range of 330–420 nm. The results are presented as fluorescence intensity (I) at 334 nm, expressed in relative units.

The Fenton Reaction

In order to analyze the ability of biopolymers and their complexes to scavenge hydroxyl radicals, 25 μl of the test sample and H_2O_2 to a concentration of 44.1 mM were added to a luminometer cuvette containing 0.2 mM luminol in 50 mM Tris buffer, pH 7.4. The reaction was initiated by adding 17.9 mM $FeSO_4$ and chemiluminescence (CL) was recorded continuously. The sample volume was 250 μl. The maximum intensity of the CL response was assessed and expressed as a percentage of the control sample containing 25 μl of Tris buffer instead of the biopolymers.

Interaction with the ABTS Cation Radical

The ABTS cation radical ($ABTS^{\bullet+}$) was prepared and its reaction with fucoidan and lactoferrin was performed according to the procedure described in [14] with minor modifications. The $ABTS^{\bullet+}$ formation reaction was carried out by mixing aqueous solutions of ABTS and potassium persulfate (final concentrations

of 7.0 mM and 2.45 mM, respectively) and incubating the mixture in the dark at room temperature for 16–17 h. The resulting $ABTS^{\bullet+}$ solution was then diluted with 50 mM Tris buffer (pH 7.4) so that the absorbance at 734 nm in the control sample was 0.70±0.02. The ability of fucoidan and lactoferrin to react with $ABTS^{\bullet+}$ was assessed by assaying the decrease in absorbance at 734 nm, with measurements performed 10 min, 20 min, and 30 min after mixing the reagents.

Coagulometry

The anticoagulant properties of fucoidan were determined by an increase in the activated partial thromboplastin time (APTT). For this purpose, 10 µl of an aqueous solution of the test compounds were added to 40 µl of human plasma, the mixture was heated for 1 min at 37°C, then 50 µl of a cephalin-kaolin mixture was added, and the mixture was incubated for 2 min at 37°C. After adding 50 µl of a 0.025 M calcium chloride solution heated at 37°C, the time of fibrin clot formation was recorded. Measurements were performed using an APG4-03-Ph optical-mechanical coagulometer (EMCO, Russia) and Renam reagent kits (Russia).

Luciferin-Luciferase Reaction

ATP was added to a 1:50 dilution of the prepared luciferin-luciferase mixture in 50 mM Tris-buffered saline with 5 mM $MgCl_2$ (pH 7.8) to a final concentration of 1 µg/ml, and CL recording was started in continuous mode; the sample volume was 250 µl. Then, 25 µl of fucoidan solution or a mixture of fucoidan and lactoferrin at various concentrations, pre-incubated for 30 min at room temperature, were added, and their effects were assessed based on the degree of CL reduction versus the control (an appropriate aliquot of Tris buffer added instead of the biopolymer solutions).

RESULTS

Structural Features of the Fucoidan-Lactoferrin Complex

According to the AFM data, fucoidan represented branched chains of 1.0±0.3 nm in height (Fig. 1A), while lactoferrin formed protein globules of 2.7±0.6 nm in height (Fig. 1B). Their size distribution is shown in Figures 1D,E. In the case

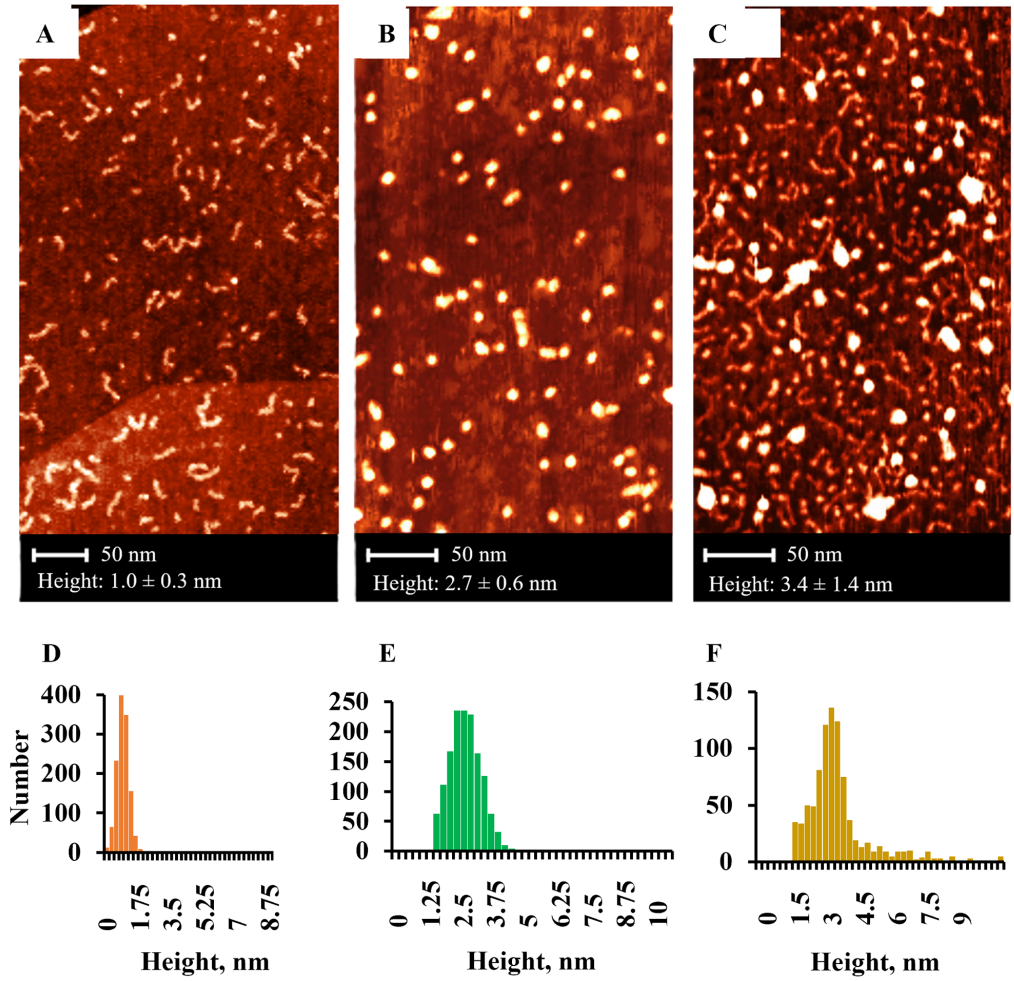

Figure 1. AFM of fucoidan (**A**), lactoferrin (**B**), and their F-L complex (**C**), and height distribution diagrams for fucoidan (**D**), lactoferrin (**E**), and their F-L complex (**F**). The concentration of the aqueous solution of fucoidan and/or lactoferrin before application on the sample carrier was 0.01 mg/ml.

of fucoidan-lactoferrin (F-L) complexes (Fig. 1C), the globule height increased to 3.4±1.4 nm (Fig. 1C), and globules higher than 4 nm also appeared (Fig. 1F).

Table 1 shows the results of measuring the ζ-potential and hydrodynamic diameter for fucoidan, lactoferrin, and the F-L complex, obtained by mixing solutions of the biopolymers at equal mass concentrations in water adjusted with NaOH to pH 8.0. It should be noted that in solutions of fucoidan and the F-L complex, the final pH of the solutions changed towards neutral values (from pH 8.0 to pH 7.0).

The resulting soluble F-L complexes had a hydrodynamic diameter of 382 nm and a negative ζ-potential close to that of fucoidan; this could be explained by the fact that the polysaccharide was mainly located on the surface of the complexes, while lactoferrin was located predominantly in the internal region [11].

For further characterization of changes in the fucoidan structure, a band at 1200–1300 cm^{-1}, which corresponds to vibrations of the sulfate group, has been selected [2]. Figure 2 shows a shift in the fucoidan peak from 1249 cm^{-1} to 1251 cm^{-1} observed in the complex with lactoferrin.

At the same time, according to IR spectroscopy data, the formation of the F-L polyelectrolyte complex did not change the content of α-helices, β-sheets, β-turns, or disordered structures in lactoferrin (Supplementary Materials, Fig. S1) thus indicating preservation of the protein structure.

Table 1. Characteristics of fucoidan, lactoferrin and their F-L complex in water with pH 8 (according to ELS and DLS data)

Sample	ζ-potential, mV	Diameter, nm
Fucoidan	-59.5±4.9	—
Lactoferrin	-4.8±1.8	—
F-L	-48.5±3.3	382±20

The concentration of each component was 1 mg/ml.

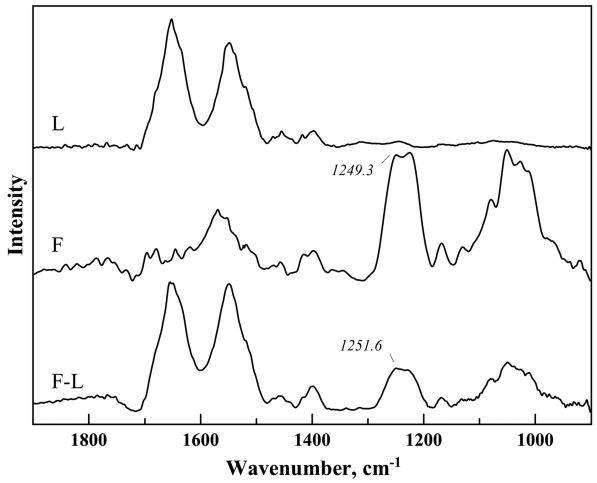

Figure 2. IR spectra of lactoferrin (L), fucoidan (F), and their F-L complex. The concentration of each component in 50 mM Tris-HCl buffer, pH 7.4 was 2.5 mg/ml.

For further analysis of the lactoferrin structure in F-L complexes, we have used the fluorescence of tryptophan residues. Fluorescence was measured in the initial lactoferrin solution and after its incubation with fucoidan for 30 min in 50 mM Tris buffer, pH 7.4. No differences in the fluorescence spectrum were detected that would indicate a change in the lactoferrin structure as a result of its complex formation with fucoidan: the fluorescence intensity was 1.15±0.09 relative units for the lactoferrin solution (0.05 mg/ml) and 1.14±0.11 relative units for the F-L complex with the same concentration of each component (Supplementary Materials, Fig. S2). Apparently, the formation of the F-L complex is accompanied by structural changes in the fucoidan molecules, but not in lactoferrin.

Functional Features of Fucoidan-Lactoferrin Complexes

Antioxidant activity. Evaluation of the hydroxyl radical scavenging capacity of polysaccharides is a widely used approach for analysis of their antioxidant properties [8]. The Fenton reaction is typically used as the source of the hydroxyl radical:

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + {}^{\bullet}OH + OH^-$$

Radical formation is assessed using spectrophotometry [15], luminol-dependent CL [16], or EPR spectroscopy [17]. According to various researchers, the effects of fucoidan are detected at concentrations as low as 0.1 mg/ml [18].

Fucoidan and lactoferrin reduced CL in the Fenton reaction in a dose-dependent manner (Fig. 3). The concentration causing 50% inhibition of CL (IC_{50}) for fucoidan was approximately 0.07 mg/ml, while for lactoferrin it was approximately 0.4 mg/ml (Fig. 3A).

The antioxidant effect of the F-L complex in the Fenton reaction was more pronounced than in the case of separate addition the biopolymers at the same concentration (Fig. 3B). Since lactoferrin at a concentration of 0.06 mg/ml did not reduce the CL response, the increase in antioxidant activity upon complex formation could be explained by changes in fucoidan resulting from intermolecular interactions.

Another widely used indicator of antioxidant activity is the scavenging capacity of biopolymers for the ABTS cation radical ($ABTS^{\bullet+}$) [8, 9]. At a concentration of 0.5 mg/ml, lactoferrin reduced the absorbance of $ABTS^{\bullet+}$ by 44±3% over 30 min, as did the F-L complex, which decreased this parameter by 42±2% (Supplementary Materials, Fig. S3). The effect of fucoidan at this concentration (0.5 mg/ml) did not exceed 8±1%.

A comparison of the results obtained by both methods suggests that complex formation increases the antioxidant activity of fucoidan, but not lactoferrin.

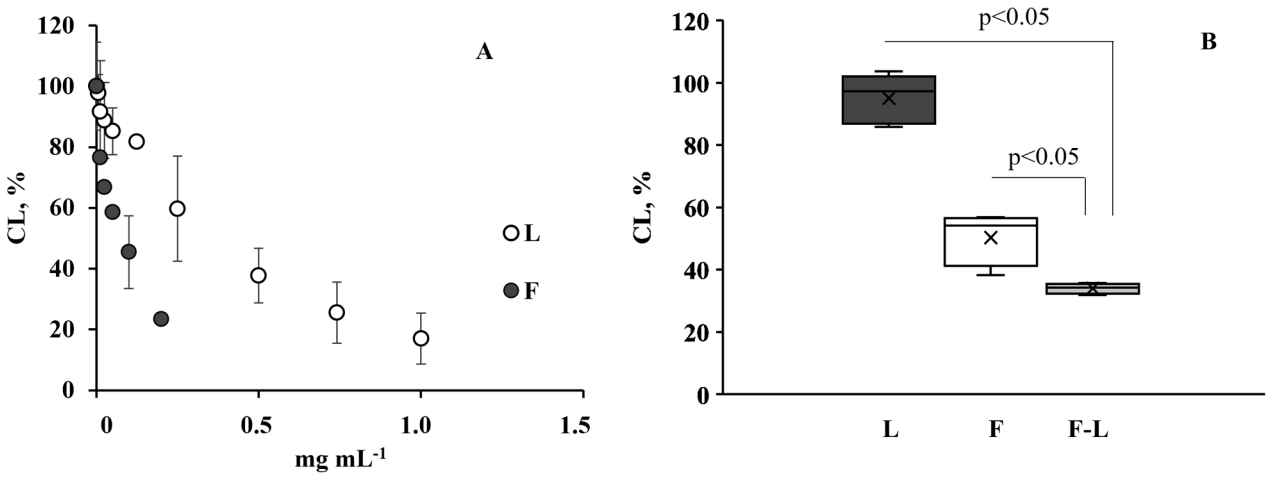

Figure 3. A decrease in the magnitude of the luminol-dependent CL response in the Fenton reaction: **A** – dependence on the concentration of fucoidan (F) or lactoferrin (L); **B** – the effect of 0.06 mg/ml lactoferrin (L) or fucoidan (F), separately and in their complex (F-L). Measurements were performed in 50 mM Tris-HCl buffer, pH 7.4. Samples without biopolymers served as controls. Results are presented as % of control values.

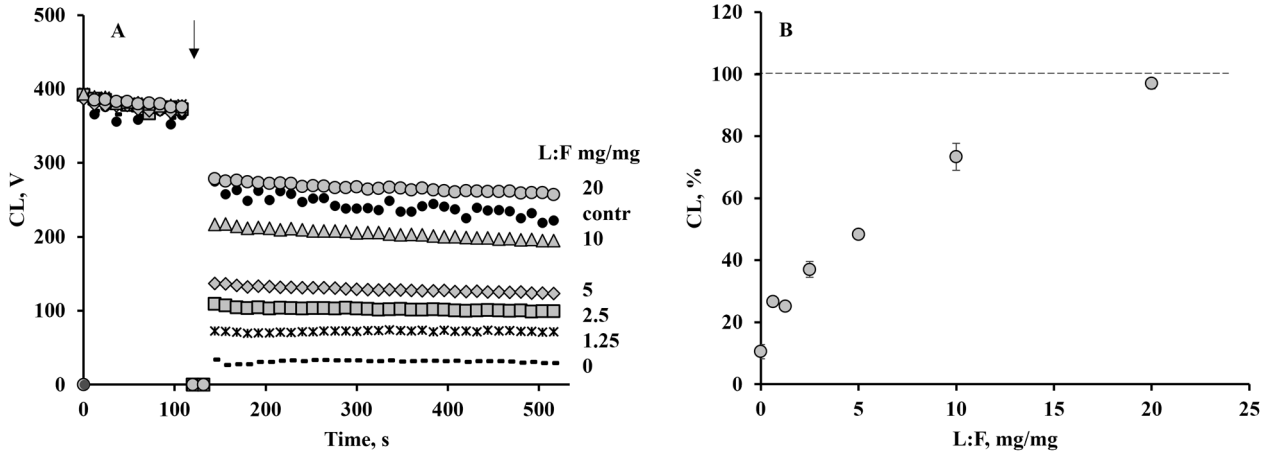

Figure 4. The CL response of luciferin-luciferase to ATP depending on the lactoferrin:fucoidan ratio (L:F, mg/mg) in the F-L complex at a fucoidan concentration of 0.2 mg/ml: **A** – CL kinetics (the moment of mixture addition is indicated by an arrow); **B** – CL as percent of the value at the moment before mixture addition. Lactoferrin-fucoidan mixture was pre-incubated for complex formation for 30 min at room temperature. The sample without the addition of lactoferrin and fucoidan served as a control.

Inhibition of the luciferin-luciferase reaction. Fucoidan interaction with proteins can lead to changes in their functional activity in various systems. For example, binding of the complement protein C1q to fucoidan prevents lysis of this protein by trypsin and thereby inhibits activation of the classical complement pathway [19], while binding of low-molecular-weight fucoidan to the cationic peptide melittin attenuates the hemolytic effect of this peptide [20]. Based on a preliminary study, firefly luciferase (p*I* 6.2–6.3) was selected for analysis of the effects of the F-L complex. It produces a stable CL signal in the presence of luciferin after ATP addition [21].

The CL signal was induced by adding ATP to a luciferin-luciferase mixture in 50 mM Tris buffer with 10 mM $MgCl_2$ (pH 7.4) and then we added fucoidan solution or the pre-prepared F-L complex (with the L:F ratio ranged from 1.25 mg/mg to 20 mg/mg at a fucoidan concentration of 0.2 mg/ml) (Fig. 4A).

Fucoidan itself reduced CL in a concentration-dependent manner (IC_{50} ≈0.05 mg/ml); in a complex with lactoferrin, its inhibitory effect weakened as the protein concentration increased. As can be seen from the curve presented in Figure 4B, at the L:F ratio of 20 mg/mg, the inhibitory effect of fucoidan was absent. Apparently, as the number of lactoferrin molecules bound to the polysaccharide increased, the availability of fucoidan for interaction with luciferase decreased. It can be hypothesized that fucoidan interacts with lysine residue located in the luciferase active site [22], as in the case of the complement protein C1q [23], leading to inhibition of enzyme activity, while lactoferrin binding to fucoidan, shields the sites and groups of the polysaccharide involved in this interaction.

Anticoagulant activity. The anticoagulant activity of fucoidan (Fig. 5A) and its complex with lactoferrin (Fig. 5B) was determined by their effect on APTT. It is known that the anticoagulant activity of fucoidan is associated not only with direct binding to thrombin but also with its interaction with antithrombin III (AT III), a natural thrombin inhibitor. Thus, in the presence of AT III, the inhibitory activity of fucoidan against thrombin increases [24]. In our experiments, fucoidan (0.01–0.1 mg/ml) dose-dependently increased plasma clotting time (Fig. 5A), while lactoferrin in the concentration range of 0.025–0.25 mg/ml did not have any significant effect on APTT (Fig. 5B).

In the case of complexes obtained by mixing fucoidan (0.05 mg/ml) and lactoferrin at increasing concentrations (from 0.025 mg/ml to 0.25 mg/ml), a dose-dependent decrease in APTT was observed (Fig. 5B). It can be suggested that, unlike free fucoidan, fucoidan molecules in a complex with lactoferrin have shielded sites involved in interaction with enzymes of the blood coagulation system. Similar results were obtained when measuring prothrombin and thrombin times (Supplementary Materials, Fig. S4).

DISCUSSION

The development of new multifunctional drug delivery systems includes the study of the mutual influence of biologically active components and the specific features of their interactions. For example, the stability and bioavailability of lactoferrin in various environments can be increased by forming complexes with both anionic polysaccharides (carrageenan and xanthan gum) and neutral ones (locust bean gum). In the former case, electrostatic interactions are involved in the formation of protein-polysaccharide complexes, while in the latter case hydrophobic interactions are involved [12].

Fucoidan, exhibiting a wide range of effects in biological systems, is negatively charged at physiological pH values, unlike lactoferrin, thus allowing formation of soluble complexes and nanoparticles by mixing these biopolymers [11]. The authors of [11] explain the negative charge of these structures by the fucoidan location on the surface of the F-L complex and the lactoferrin location inside it; this is consistent with our results. According to the authors, particles obtained from fucoidan and lactoferrin at pH 3 and a 1:1 mass ratio reached the size of 248±1.3 nm, i.e., they were 1.3 times smaller than those in our study (Table 1).

According to [12], the intermolecular interaction of lactoferrin with polysaccharides at pH 7–8 does not affect the protein structure at a lactoferrin-to-polysaccharide mass ratio greater than 1. This is confirmed by the IR spectroscopy and fluorimetry data obtained in the present study for the F-L complexes with the mass ratio of 1:1.

At neutral pH values, fucoidan and lactoferrin carry opposite charges, which contribute to the formation of a more stable polyelectrolyte complex than the complex of fucoidan with luciferase having a p*I* of 6.2–6.3.

There are no data revealing a direct relationship between the structural features of fucoidan and its activities, primarily its antioxidant and anticoagulant effects [8, 24]. Apparently, the distribution of sulfate groups and the overall configuration of the molecule, as well as the presence of impurities in the polysaccharide molecule, play an important role [25]. At the same time, the antioxidant activity of lactoferrin in the reaction with the radical $ABTS^{\bullet+}$ was preserved in the complex with fucoidan, which could be explained by the absence of significant conformational changes in the structure of the protein in the complex with fucoidan. Since the greatest contribution to the reaction with $ABTS^{\bullet+}$ is made by tyrosine, tryptophan, and cysteine [26], the obtained result is consistent with

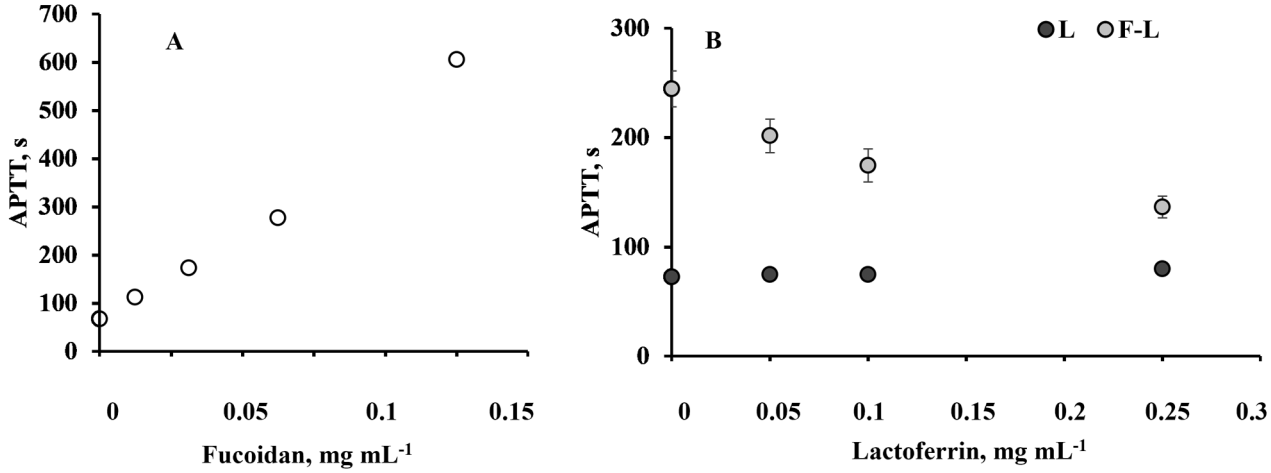

Figure 5. Changes in activated partial thromboplastin time (APTT) induced by: **A** – different concentrations of fucoidan (F), **B** – different concentrations of lactoferrin (L) added either separately or in complex with 0.05 mg/ml fucoidan (F-L).

the data on the absence of changes in the fluorescence of tryptophan in the lactoferrin molecule in the presence of fucoidan.

The antioxidant effect of lactoferrin in the Fenton reaction is due to the direct scavenging of hydroxyl radicals by so-called "sacrificial amino acids", such as histidine, lysine, arginine, and others [17, 27]. This may result in rapid damage to protein molecules and, as a result, a less pronounced effect in the Fenton reaction than that of fucoidan, including its complex with fucoidan.

Our results suggest that the formation of F-L complexes at a 1:1 mass ratio provides certain conformations to achieve detectable effects. Conformational changes in fucoidan upon binding to lactoferrin are confirmed by a shift in the peak corresponding to sulfate groups (from 1220 cm^{-1} to 1224 cm^{-1}) [2]. It has been demonstrated that the negatively charged sulfate groups of fucoidan react with positively charged sites of protein molecules, such as arginine residues [4]. Furthermore, the authors substantiate the involvement of tyrosine hydroxyl groups in the formation of hydrogen bonds with hydrogen bond acceptors in the sulfate groups of fucoidan [4].

The ability to control the anticoagulant activity of fucoidan by forming complexes with lactoferrin would expanded the use of fucoidan-containing preparations in inflammation, for example, in cases of thinning of the gastrointestinal mucosa and the risk of ulcerous lesions [28].

CONCLUSIONS

A soluble polyelectrolyte complex of fucoidan with lactoferrin (F-L), obtained at the F:L mass ratio of 1:1 at neutral pH, exhibits higher antioxidant activity in the Fenton reaction than free fucoidan. In the complex with lactoferrin, the anticoagulant effect of fucoidan and its inhibitory activity against luciferase in a model system reduced. The obtained results suggest that the formation of a fucoidan-lactoferrin complex could be a way to develop delivery systems with controlled biological activity.

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COMPLIANCE WITH ETHICAL STANDARDS

This article does not contain any research involving humans or the use of animals as objects.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

Supplementary materials are available in the electronic version at the journal site (pbmc.ibmc.msk.ru).

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ФУНКЦИОНАЛЬНЫЕ ОСОБЕННОСТИ КОМПЛЕКСОВ ЛАКТОФЕРРИНА И ФУКОИДАНА В МОДЕЛЬНЫХ СИСТЕМАХ *IN VITRO*

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Фукоидан — анионный полисахарид из бурых водорослей, проявляющий антикоагулянтную, антиокислительную, противовоспалительную, противоопухолевую и противовирусную активность — способен образовывать полиэлектролитные комплексы с различными белками, включая терапевтически важный лактоферрин. Целью данного исследования было изучение физико-химических и функциональных особенностей комплекса фукоидана и лактоферрина, образующегося при смешивании их растворов при физиологических значениях pH. Комплекс, регистрируемый с помощью атомно-силовой микроскопии, имел отрицательный заряд и гидродинамический диаметр 382 нм. Взаимодействие с лактоферрином приводило к изменениям в области ИК-спектра фукоидана в полосе поглощения в диапазоне 1220–1260 $см^{-1}$, соответствующем колебаниям сульфатной группы, увеличивало суммарную антиокислительную активность биополимеров в реакции Фентона и снижало антикоагулянтную активность фукоидана, оцениваемую по данным определения активированного частичного тромбопластинового времени. Фукоидан снижал активность люциферазы в модельной системе люциферин-люцифераза, а образование комплекса с лактоферрином ослабляло ингибирующую способность фукоидана. Полученные результаты свидетельствуют о возможности направленно влиять на функциональную активность биополимеров при включении их в комплекс и о перспективности использования фукоидана и лактоферрина в виде комплекса при разработке новых препаратов и средств доставки лекарств.

Полный текст статьи на русском языке доступен на сайте журнала (http://pbmc.ibmc.msk.ru).

Ключевые слова: лактоферрин; фукоидан; полиэлектролитные комплексы; антиокислительная активность; антикоагулянты; люциферин-люцифераза

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