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Antibacterial Films of Composite Materials Based on the Biocompatible Metal–Organic Framework MOF-5 and Hydrocolloids

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Abstract—The preparation of a new type of packing for food products using biocompatible functional materials is based on the quality control and safety of food products. Composite films of the hydrocolloid matrix including kappa carrageenan and hydroxypropyl methylcellulose with particles of the biocompatible metal-organic framework MOF-5 bearing the antibacterial agent (sodium benzoate) immobilized in the pores are prepared. The manifested resistance of the prepared films to potentially pathogenic microorganisms provides wide prospects for manufacturing antimicrobial composite materials of food packing.

Keywords: biocompatible metal–organic framework, functional package, hydrocolloids, composite materials, powder X-ray diffraction

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INTRODUCTION

Package of food products plays the fundamental role in the protection of food products from physical damages and negative effects of external factors. Materials for the so-called functional [1, 2] (or "active" [3] and "smart" [4, 5]) packing became especially popular in the recent time. The task of this package is an increase in the shelf life and safety of products in the usage compared to the traditionally used inert packing [6]. One of the variants of fulfilling these functions by the functional package is the controlled release of antioxidants [7] and antimicrobial [8] or indicating [9] agents during probable bacterial contamination [10], putrefying processes [11, 12], or prolong staying of food products under unfavorable conditions [13].

An important characteristic of this packing related to a prolong contact with food products is the full biocompatibility of all components [14]. Natural hydrocolloids have a longstanding history of the use in food industry [15–17] as safe components of both food products (in the form of emulsifiers, stiffeners, stabilizers, etc.) and materials for their package [18], including functional packing [19]. However, the direct functionalization of the hydrocolloid matrix has a number of drawbacks: the separation of hydrophobic active agents (as a rule, natural extracts safe for human and environment) from the hydrophilic composite component and no control of their release [20]. In addition, any modification of the hydrocolloid composition with water-soluble substances can worsen the gelation properties of the starting polymers, which can impede the preparation of films with desirable mechanical characteristics and long-term stability.

Metal–organic frameworks (MOF) [21] form a unique class of crystalline materials with a periodic three-dimensional structure [22]. Their pores of various size can be controlled by choosing appropriate metal-containing nodes and organic linkers [23]. The pores impart unsurpassed sorption properties to the MOF [24] and form a basis for their practical use [25], for example, in medicine [26]. Biocompatible MOF are applied in the target delivery of therapeutic agents [27], including those acting as organic linkers [28], and in tissue engineering [29], protein separation [30], and biocatalysis [31]. In addition, this class of crystalline materials has recently been proposed for the preparation of a functional food packing [32, 33] due to the uniform distribution of particles of the MOF capable of controlled releasing active agents in the polymer matrix.

The corresponding materials for the functional packing were obtained in this work on the basis of the product SB-MOF-5 prepared by the absorption of the antibacterial agent (sodium benzoate) into pores of the previously described [34] biocompatible metal-organic framework MOF-5 ($\{Zn_4O(BDC)_3\}_n$, where BDC is the terephthalate anion) distributed in the

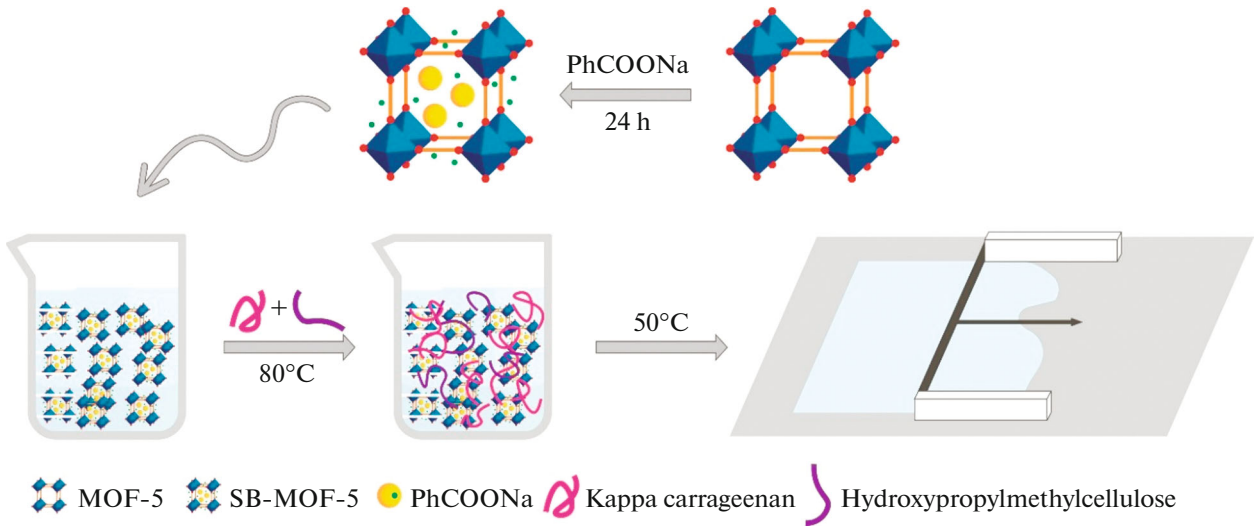

Fig. 1. Scheme of the preparation of the composite films with the MOF particles.

hydrocolloid matrix of kappa carrageenan and hydroxypropyl methylcellulose (Fig. 1). In this case, the role of MOF was the encapsulation of antibacterial agent molecules in order to retard their release to the external medium. The prepared materials demonstrated good resistance to potentially pathogenic microorganisms.

EXPERIMENTAL

All procedures associated with the synthesis of MOF and preparation of composite films were carried out in air using commercially available organic solvents and reagents. Analysis to the carbon and hydrogen contents was conducted on a CarloErba microanalyzer (model 1106).

Synthesis of MOF-5. A solution of zinc acetate dihydrate (80 mmol, 17.6 g) in distilled water (100 mL) was added dropwise with stirring to a solution of terephthalic acid (60 mmol, 10 g) and sodium hydroxide (120 mmol, 5.8 g) in water (200 mL). The reaction mixture was stirred at room temperature for 30 min. The resulting precipitate was filtered off, washed with water and ethanol, and dried under reduced pressure. The yield of the product was 9.685 g (46%).

For $C_{24}H_{12}O_{13}Zn_4$		
Anal. calcd., %	C, 23.69	H, 1.99
Found, %	C, 23.53	H, 2.11

Synthesis of SB-MOF-5. The product MOF-5 (5 g) was activated by drying at 140°C in vacuo for 5 h and placed in a saturated solution of sodium benzoate in methanol. The reaction mixture was kept with stirring for 24 h. The precipitate was filtered off, washed with methanol, and dried under reduced pressure. The yield of the product was 5.076 g. The content of sodium benzoate in SB-MOF-5 was 0.3 mmol/g.

Preparation of composite films. The products MOF-5 or SB-MOF-5 were added in different amounts (5, 15, and 30 wt % of the total weight of hydrocolloids) to a solution of glycerol (0.16 g) and KOH (0.004 g) in distilled water (20 mL). The mixture was stirred using an ultrasonic bath for 3 min and then heated to 80°C. A mixture of kappa carrageenan (0.32 g) and hydroxypropyl methylcellulose (0.08 g) was introduced with stirring to obtain a homogeneous suspension, which was cooled to 50°C with stirring. The resulting solution was poured onto the glass heated to 50°C, leveled with a blade device (blade height 3 mm), and left on the heated support to complete drying. The prepared film was separated from the glass and stored at room temperature in a dry place.

Scanning electron microscopy (SEM). SEM images of the prepared films placed on a 25-mm aluminum stage and fastened with a conducting carbon ribbon were obtained in the secondary electron mode with an accelerating voltage of 5 kV under low vacuum conditions on a Hitachi TM4000Plus bench electron microscope. The film thickness was measured with a micrometer at 10 random sites.

Water vapor permeability (WVP) was measured by the gravimetry method according to the ASTM E96-80 standard [35]. For this purpose, a film sample was tightly fixed on a glass vial filled with anhydrous silica gel to maintain 0% relative humidity, and the cell was placed in a desiccator with a saturated solution of NaCl to maintain 75% relative humidity and left at room temperature (25°C) for 2 h. The weight of water vapors passed through the film was determined from a change in the vial weight with silica gel by weighing at an interval of 2 h for 10 h. The WVP was determined using the equation

$$\mathrm{WVP} = \frac{A\Delta x}{(p_1 - p_2)S},$$

where A (g/h) is the slope of the linear regression of the weight in time, Δx (mm) is the film thickness, $(p_1 - p_2)$ (kPa) is the difference in partial pressures inside and outside the cell, and S (m^2) is the surface area of the film.

Powder X-ray diffraction (XRD). All XRD studies were carried out on a Bruker D8 Advance diffractometer equipped with a system of automated slits for monochromatization and focusing ($\lambda_{\mathrm{Cu}K_\alpha} = 1.5418$ Å) and a LynxEye position sensitive detector in an angular range of 4°–50° with an increment of 0.02° for the 2θ range using transition geometry. The calculations were performed using the EVA [36] and TOPAS 4.2 programs [37].

NMR spectroscopy. A weighed sample of SB-MOF-5 was placed in D_2O for 7 days, stirred using an ultrasonic bath for 15 min, and centrifuged at a velocity of 6000 rpm for 5 min. The solution was decanted, and a weighed sample of the internal standard (sodium citrate) in D_2O was added. ^{1}H NMR spectra were recorded on a Bruker Avance 300 instrument with the Larmor proton frequency 300.15 MHz.

The resistance of the composite films to infection with microorganisms was studied by storing film samples 4 × 4 cm in size at room temperature and 75% relative humidity for 10 days.

RESULTS AND DISCUSSION

The chosen MOF-5 has a low stability in the presence of water [38] and, hence, this MOF is traditionally prepared in highly polar organic solvents (DMF, DEFA) [39, 40]. However, the possibility of synthesis in aqueous solutions is known for MIL-53(Al) when using sodium terephthalate as the organic linker source [41]. Using this approach we obtained a microcrystalline powder of MOF-5 in a high yield by the direct precipitation from an aqueous solution of zinc acetate and sodium terephthalate in a ratio of 1.5 : 1. The synthesis was carried out at room temperature for 30 min. The formed crystalline product was washed with distilled water and ethanol, filtered off, and dried under reduced pressure. The incorporation of the antimicrobial agent (sodium benzoate) into the MOF-5 pores was carried out after thorough drying. The content of sodium benzoate in SB-MOF-5 was determined using NMR spectroscopy by the internal standard method.

A mixture of kappa carrageenen and hydroxypropyl methylcellulose in a ratio of 4 : 1 was chosen as a hydrocolloid matrix for the preparation of composite films with MOF-5 or SB-MOF-5 particles containing sodium benzoate [42]. The mixture was molded by the doctor blade method using a blade type membrane coating machine [43]. Glycerol (40 wt % of the total weight of hydrocolloids) was added as a plasticizer to the film forming solution to improve the mechanical properties of the films. The addition of KOH (1 wt % of the total weight of hydrocolloids) as the source of potassium ions decreasing the repulsion between the sulfate groups of the kappa carrageenan molecules was used to form an elastic gel [44]. The uniformity of the MOF particle distribution was provided by stirring a suspension of MOF-5 or SB-MOF-5 in an aqueous solution for 3 min before the addition of the hydrocolloids to the mixture indicated above. The hydrocolloid film (KcHm) containing no MOF particles served as the control sample.

Thus prepared composite films (Fig. 2a) were characterized by transparency and elasticity that decreased with an increase in the MOF concentration. An analysis of the corresponding XRD patterns (Fig. 3) confirmed the presence of the crystalline phase corresponding to MOF-5 (except for the control sample). The observed minor amounts of another crystalline phase of unknown nature can be ascribed to the partial hydrolytic decomposition of the MOF. The SEM data (Figs. 2c, 2d) indicate a change in the character of the film surface associated with the aggregation of particles of the latter, which are 30–44 nm in size according to the powder XRD data. The difference observed in the morphology of the MOF-5 and SB-MOF-5 particles can be attributed to the formation of crystallization centers of sodium benzoate on the surface of the SB-MOF-5 particles after their partial hydrolysis.

The easiness of moisture penetration through the prepared composite films was estimated by measuring the WVP. The WVP increases along with an increase in the film thickness as the concentration of MOF particles increases (Table 1), which can probably be attributed to the hydrophilicity of MOF-5 that performs the function of a channel for water vapor migration. The insertion of sodium benzoate into the MOF-5 structure leads to a still greater increase in the WVP of the composite material.

The prepared films exhibited an appreciable antimicrobial activity in model experiments. Being higher polysaccharides, kappa carrageenan and hydroxypropyl methylcellulose represent an excellent nutrient medium for the development of potentially pathogenic microorganisms. When a sample of the KcHm hydrocolloid film was placed in a warm and wet medium, the indications to infection with microorganisms (Fig. 2) in the form of musty colonies appeared already in 24 h. The presence of the MOF-5 particles in the film elongates its shelf time to 3–4 days, after which pathogens begin to grow. The antimicrobial activity of the MOF in the absence of sodium benzoate can be due to its slow decomposition accompanied by the release of terephthalic acid characterized by weak antibacterial properties. On the contrary, the composite films with the particles of SB-MOF-5 containing sodium benzoate remained

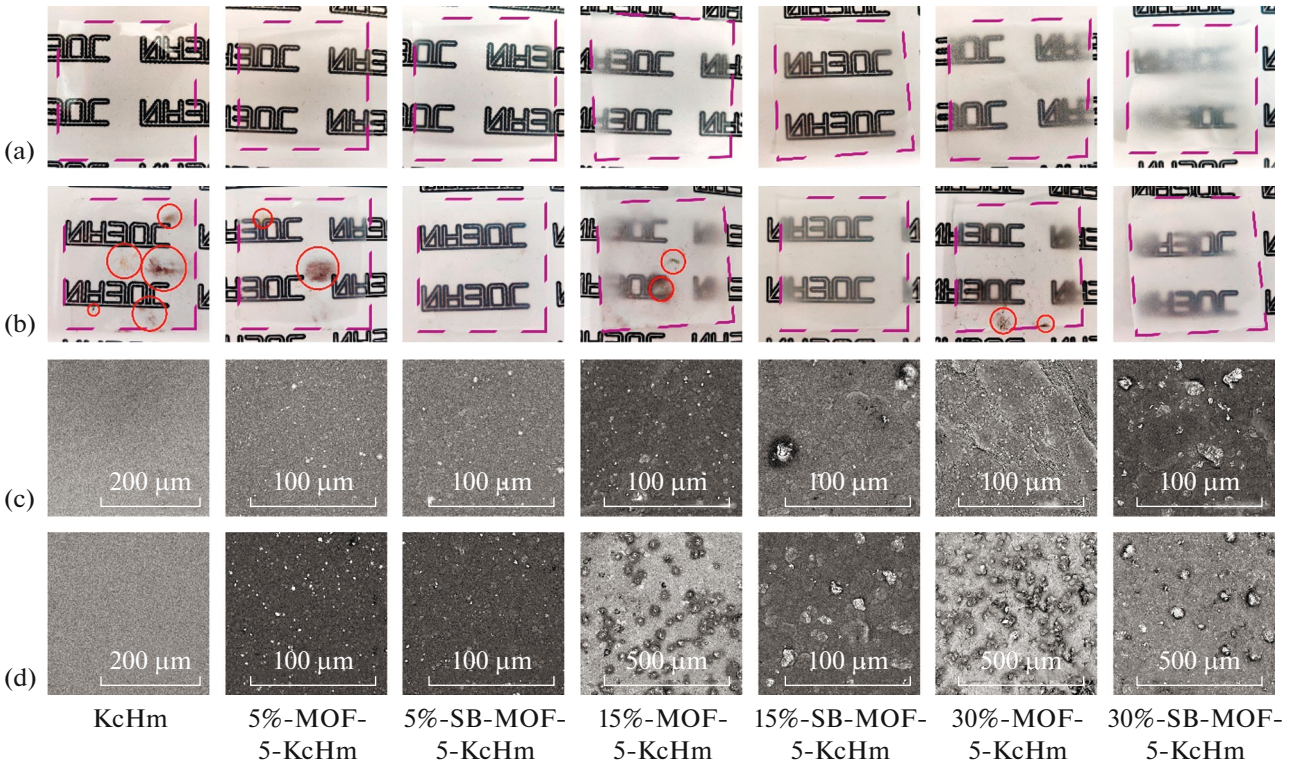

Fig. 2. Photographs of the composite films (a) before and (b) on the 7th day of storage in a wet medium. The centers of microbial insult are encircled with red. (c, d) SEM images of the surface fragments from two sides of the composite films of different compositions obtained immediately after film preparation.

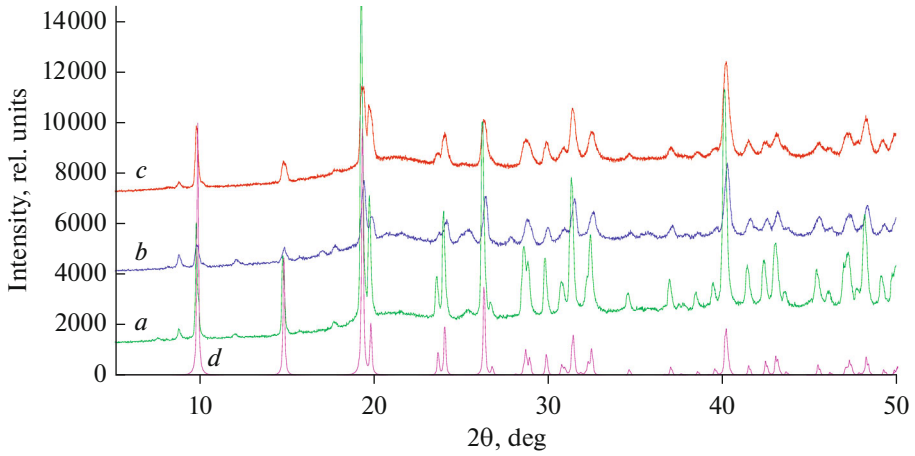

Fig. 3. Powder XRD data for the composite films based on MOF-5 with a MOF content of (*a*) 5%, (*b*) 15%, and (*c*) 30% and (*d*) the theoretical XRD pattern of MOF-5.

unchanged to the end of experiments (after 10 days), which confirms that this antibacterial agent was included into the MOF-5 structure and released gradually to the hydrocolloid matrix. This leads to the efficient inhibition of bacterial or mycotic infection of the corresponding composite films.

Thus, the composite films were prepared using our approach. In these films, a mixture of kappa carrageenon and hydroxypropyl methylcellulose served as the hydrocolloid matrix and sodium benzoate incorporated in pores of the biocompatible metal–organic framework MOF-5 acted as the antibacterial agent.

Table 1. Barrier properties of the composite films

Film	Film thickness, μm	WVP, g mm/(kPa h m^2)
KcHm	32	0.499
5%-MOF-5-KcHm	35	0.545
15%-MOF-5-KcHm	42	0.654
30%-MOF-5-KcHm	65	1.013
5%-SB-MOF-5-KcHm	31	0.598
15%-SB-MOF-5-KcHm	41	0.730
30%-SB-MOF-5-KcHm	79	1.348

The prepared materials were characterized by powder XRD and SEM. The found resistance of the composite films to potentially pathogenic microorganisms provides wide prospects for using similar materials in the production of the functional food packing.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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