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MACROMOLECULAR CHEMISTRY AND POLYMERIC MATERIALS

Surface Modification of Polypropilene by Gentamicin

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Abstract—A possibility of the immobilization of gentamicin on the surface of the polypropylene materials activated by the aqueous solution of hydrogen peroxide is studied. The polymers modified by biologically active materials are mainly the polymers of medical designation. Their basic function is exerting a complex of therapeutic actions in all phases (inflammation, regeneration and epitalization). Such materials in essence are used for preparing surgical seam threads, ambulance means, fixing bandages, prostheses of internal organs and tissues, etc.

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The scope of medicines for admitting the biological (in particular, bactericidal) activity to polymer carriers is quite limited. Such means should be searched first of all among the chemotherapeutic preparations, antibiotics and antiseptics. One group of this type of preparations includes gentamicin.

Polypropylene (PP) is characterized by high mechanical durability and chemical stability, and it can be used as the medical material of the multifunctional action: as structural and shielding material and as a carrier and a donor of therapeutic and preventive pharmacological means. However owing to its inertness it requires the surface activation by applying chemical reagents, which leads to formation on the surface and in the thin near-surface layer of the polymer of the required functional groups practically without a change in the volumetric and strength properties of the initial material. This form of surface activation makes it possible grafting the medicinal substances bearing active functional groups on the periphery of bioactive molecules to the polymer carrier.

The strength of the binding antimicrobial substances on the polymer carrier can be regulated by the inclusion of the corresponding functional groups in polymer and medicines. Thus, it is possible the creation of the materials with prolonged action that most actual now [1–3].

The purpose of this work was the surface modification of polypropylene with gentamicin and creation on this basis of the materials of medical designation. The activation of the polypropylene surface for the immobilization of gentamicin was conducted by action of aqueous solution of hydrogen peroxide.

EXPERIMENTAL

The work up by the solution of hydrogen peroxide in the presence of Fe(II) salts is effective enough for the activation of the polymer surface.

In the work were used the films of isotactic polypropylene with thickness of 20 μ (biaxially oriented) and non-woven polypropylene material of the type "Spanbond" with specific density 40 g m^{-2}.

The surface activation of polypropylene materials was carried out by the following procedure. The samples of PP with the area of 20 × 65 mm^2 were placed into the weighing bottles with the 37% aqueous solution of hydrogen peroxide, and two drops of the aqueous solution of iron(II) sulfate was added. Then weighing bottles were kept in a thermostate at 60°C for 2-h activation duration. At the end of the activation the weighing bottle were taken from the thermostat and cooled in air to room temperature.

The chemical composition of the surface layer of the initial and the activated PP was investigated by the method of infrared spectroscopy in the version of repeatedly disrupted total internal reflection (MIR). Measurements

were carried out on an Avatar 360 FT-IR Fourier spectrometer of firm "Nicolet". A prism of crystalline zinc selenide was used. The angle of ray incidence on the media interface was 45°, number of reflections 12. The spectra were registered with the accumulation of the signals of 32 scans. The assignment of bands in the spectra was carried out in accordance with the data of work [4]. Measurements were conducted in the range of the wave numbers of 400–4000 cm^{-1}.

The IR MIR spectra showed that the activation of polypropylene with hydrogen peroxide leads to the appearance on the material surface of the functional oxygen-containing groups of different structure, such as –OH, –C=O, –COOH, which are formed in the primary processes of activation. In Fig. 1 is represented the differential IR MIR spectrum of the chemically activated PP film and PP comparison sample. According to the spectrum the activation leads to the appearance of absorption bands, characteristic of OH groups. This is indicated by the appearance of the absorption bands in the region of 3000–2800 cm^{-1}, which correspond to the intramolecular stretching vibrations of hydroxyl groups. Furthermore, increases the intensity of absorption bands in the regions of 1750–1700 and 1580–1560 cm^{-1}, which correspond to the stretching vibrations of double bonds C=O in the compositions of different functional groups (carbonyl and carboxyl). In the region of 1400–1300 cm^{-1} appear the absorption bands which are identified as stretching vibrations of –COO– in carboxylic groups. In the region of 1200–1100 cm^{-1} appears an absorption band, which corresponds to the stretching vibrations of group C–O in the primary alcohol groups. Also is observed the formation of double bonds, to which correspond the absorption bands in the regions of 1100–930 and 880–800 cm^{-1} corresponding to deformation vibrations of C–H bond in –CH=CH– group [5].

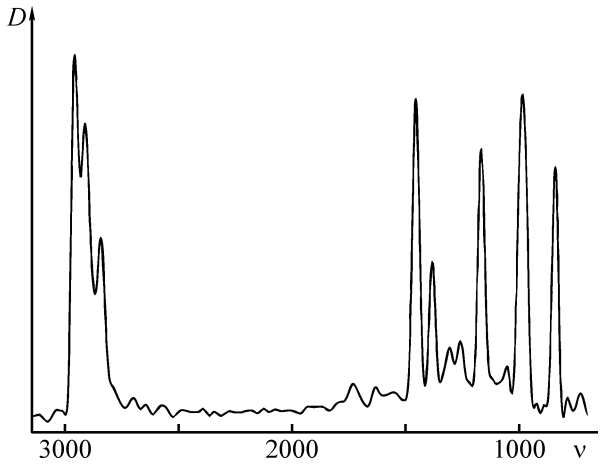
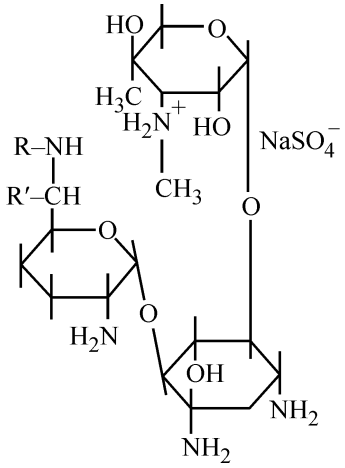


Fig. 1. Differential IR MIR spectrum (PP activated with hydrogen peroxide minus PP not activated) in the region of 3500–900 cm^{-1}. *D* is absorption, ν is wave number (cm^{-1}); the same for Fig. 2.

The presence of the active oxygen-containing functional groups on the surface of polymer carrier makes it possible to accomplish its surface modification with a medicine preparation.

As the medicinal substance is used gentamicin (sulfate sodium salt) [6] of the general formula $C_{29}H_{53}N_5O_7(SO_4Na–)$



where R = CH_3, R' = H (gentamicin C_2); R = R' = H (gentamicin C_{1A}); mp(decomp.)= 107–124°C (for C_2 and C_{1A}). The immobilization of gentamicin on the initial and activated PP was carried out by keeping the samples (film or "Spanbond") in 1.5% aqueous solution of gentamicin at room temperature 18 ± 2°C for 3–72 h or at a temperature of 60°C for 3 h. As a result of interaction of gentamicin with the activated molecules of polymer occur both the physical absorption and its durable binding with the surface of polypropylene.

The aqueous solution of gentamicin does not absorb electromagnetic vibrations in UV and visible regions of spectrum. Therefore the results of its immobilization were controlled by the IR MIR spectra. Comparison of the IR spectra of pure gentamicin and of the PP superficially modified by gentamicin was carried out.

The presence of gentamicin on the surface of the polypropylene carrier, activated by chemical method, is also confirmed by the method of microscopy on a BIOLAM microscope of LOMO firm. All measurements were conducted with zoom 40.

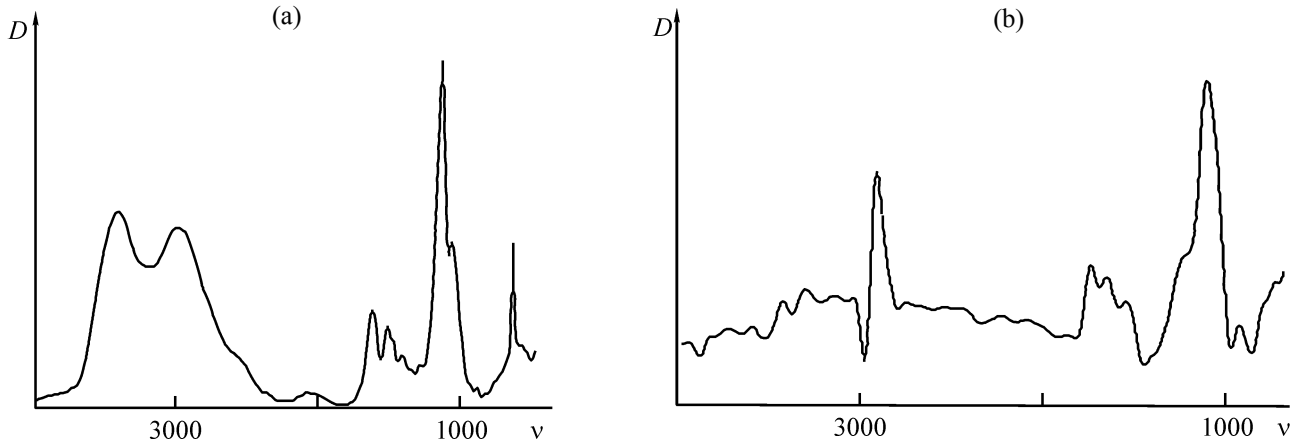
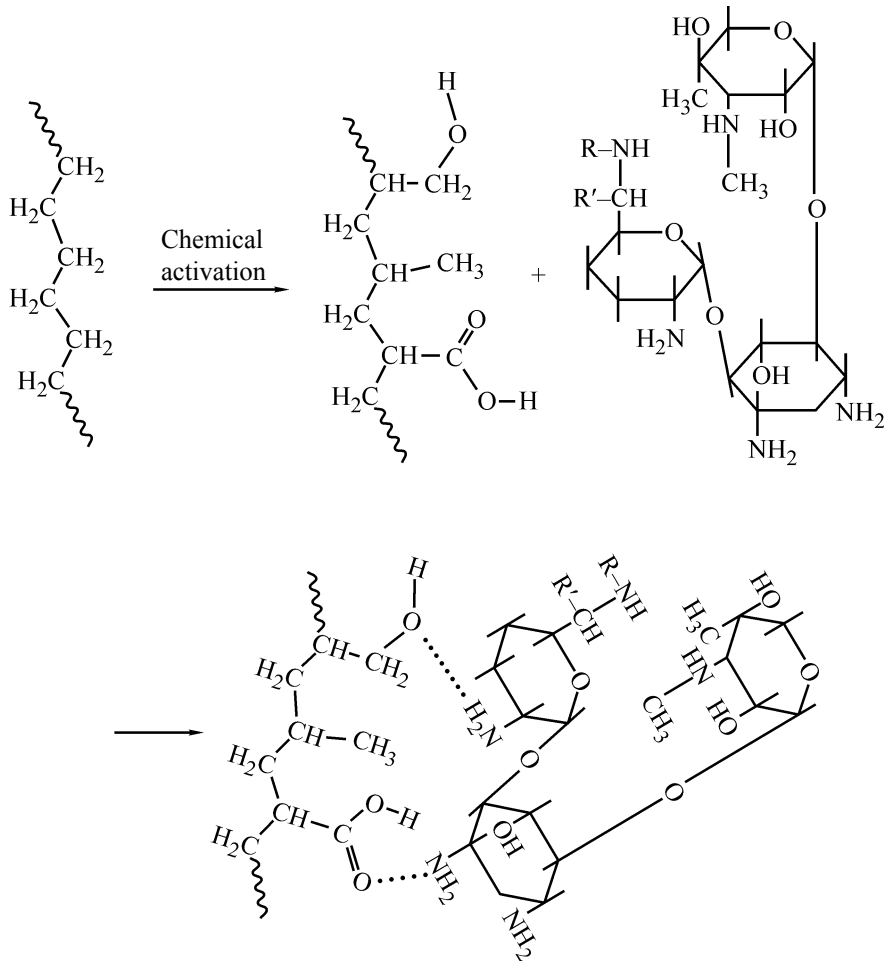


Fig. 2. IR MIR spectra in the region of 3500–900 cm^{-1}. (a) pure gentamicin, (b) gentamicin on the chemically activated PP film (differential spectrum).

Nature of the binding of medicinal substance by the activated polypropylene is of interest. It is very probable that gentamicin is fixed due to the formation of hydrogen bonds between the amino groups and the surface carboxylic and hydroxyl groups, and also due to dispersion interactions of the large gentamicin molecule with the polymer.

On the basis of the data obtained, it is possible to propose the following hypothetical scheme of the processes, which lead to the binding of medicinal substance with the chemically activated PP surface:



It is significant that the grafted gentamicin is removed only partially at the washing the film with water or alcohol. This indicates the formation of the sufficiently durable bonds of the polymer carrier with the immobilized substance. But the version of the formation of covalent amide bonds is excluded, in the first place, because the conditions of grafting are soft enough, and in the second place because gentamicin is completely washed off from the surface of the activated polypropylene film by the 1–5% solution of hydrochloric acid.

At the development of the materials of medical designation modified by gentamicin, which possesses antipyretic and bactericidal action, there was no purpose of the removal of the preparation connected by unspecific interactions. Its quantity can be 5–10 times higher than that of strongly bound substance. It is obvious that weakly bound gentamicin relatively rapidly penetrates the tissue. As a result, the therapeutic action of preparation will be manifested immediately after operation.

The preparation grafted by a combination of two hydrogen bonds is chipped off slowly and that provides its prolonged action.

The bactericidal activity of the samples of the polypropylene materials modified by gentamicin was determined by the method "paper disks" [7] with respect to the following forms of microorganisms: *Staphylococcus aureus* and *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*).

In Table 1 are listed the averaged data characterizing the bactericidal activity of the obtained PP materials.

In parallel was carried out a number of experiments regarding the prolonged action of the chemically activated polypropylene materials grafted with gentamicin. For this purpose the PP experimental samples were kept in the buffer solution at pH 7.4 (imitation of the human blood). The data obtained are listed in Table 2.

As can be seen from the Tables 1 and 2, the modified by gentamicin PP samples possess good bactericidal activity, and also have the prolonged action.

Table 1. Bactericidal activity of the polypropylene samples modified by gentamicin with respect to the pathogenic microorganisms

Sample	Temperature of gentamicin immobilization	Diameter[a] of the zone of the test-culture growth depression around the sample, mm	
		Staphylococcus aureusi	*Pseudomonas aeruginosa*
Control	40	0	0
	20	0	0
PP film	40	23	21
	20	17	19
"Spanbond"	40	24	22
	20	18	19

[a] Includes the diameter of the zone occupied by the PP film (~10 mm); the same in Table 2.

Table 2. Bactericidal activity of modified polypropylene films, with respect to the pathogenic microorganisms, at keeping the samples in the buffer solution (pH 7.9) for different time

Keeping duration	Diameter of the zone of the test-culture growth depression around the sample, mm	
	Staphylococcus aureus	*Pseudomonas aeruginosa*
0 (control sample)	0	0
30 min	20	18
60 min	18	16
120 min	16	14
4 h	12	14
2 days	14	14

CONCLUSIONS

(1) The proposed method of the surface chemical modification of polypropylene materials by gentamicin (films, non-woven materials) is effective for creating new medical materials of the combined action.

(2) The polypropylene samples possess high bactericidal activity, and also have prolonged antimicrobial action.

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