

Nadiya Solomko, Olga Budishevskaya and Stanislav Voronov

PEROXIDE CHITOSAN DERIVATIVES AND THEIR APPLICATION

Lviv Polytechnic National University,
12 Bandera str., 79013 Lviv, Ukraine
budish@polynet.lviv.ua

Received: September 12, 2007

Abstract. Peroxychitosanes with ditertiary peroxide fragments were synthesized via radical reactions of chitosan and 5-*tert*-butylperoxy-5-methyl-1-hexen-3-*in*. They can be used as macroinitiators and coemulsifiers for emulsion polymerization of vinyl monomers. It is shown that peroxychitosanes are grafted to the surface of latex particles and impart antibacterial properties to emulsion polymer. Polymeranalogical interaction of chitosan with *tert*-butylperoxymethyl ester of butendicarboxylic acid yields in peroxychitosanes with controlled quantity of primary-tertiary peroxide fragments. New pH-sensitive smart hydrogels with antibacterial properties were created on their basis.

Keywords: chitosan, peroxychitosan, emulsion polymerization, surface modification, macroinitiator-coemulsifier, pH-sensitive hydrogels.

1. Introduction

Recently, the scope of usage of natural biopolymers, in particular chitosan, has been increased in medicine, bioengineering, pharmaceutical, cosmetic and food industries [1]. Chitosan (Chi) poly- β -1,4-(2-deoxy-2-amino-D-glucose) is a product of chitin deacetylation, the second most widely spread natural polysaccharide, and has unique properties – biocompatibility, biodegradability, non-toxicity and polymeranalogical interaction ability. It has been used to obtain gels, composite polymer materials, polymer aqueous dispersions with antibacterial properties [2-6]. However, the possibilities of Chi using are significantly limited by such drawbacks as selective solubility, rigidity, thermodynamic incompatibility with predominant majority of polymers. Therefore, the usage of its various copolymers with synthetic polymers – polyvinylpyrrolidone, polyacrylamide etc. is constantly growing [7].

At the same time, the research of synthesis of heterofunctional polyperoxides and regularities of peroxidation of polymer colloid system interphase, conducted at the Department of Organic Chemistry of Lviv Polytechnic National University allowed to elaborate the principles of polymer layer forming with regulated

content of peroxide groups covalently grafted on the surface [8, 9]. Immobilization of regulated amount of hetero-functional polyperoxides on the interfaces of different colloid systems allowed to obtain disperse filled polymer composites with improved operational properties, to create latexes with “core-shell” particle morphology, forming grafted polymer nanolayers on micro- and macro-surfaces with special properties (biocompatibility and bactericidal action) [10, 11].

One might expect that the incorporation of peroxide groups to Chi structure will allow to receive a new type of Chi derivatives – reactive peroxychitosans, able to participate in the construction of covalently cross-linked polymer frames of gels or to perform the role of reactive polyemulsifiers of latex synthesis and to graft onto polymer surfaces, as well as to impart biocompatible properties and bactericidal action to them.

It should be noted that reactive ability of peroxide fragments depends on their chemical composition. It is known that ditertiary peroxide groups are thermally more steady than primary-tertiary ones [12]. Taking into consideration these facts, the formation of peroxychitosans with peroxide groups of various reactive abilities looks quite interesting.

This report deals with the synthesis methods and the research of peroxychitosans with ditertiary and primary-tertiary peroxide groups.

2. Experimental

2.1. Materials

Styrene (St), vinylpyrrolidone (VP) (Aldrich) were distilled under reduced pressure.

Low molecular weight and medium molecular weight Chi were purchased from Aldrich and used as received.

tert-Butyl peroxide methyl ester of butane dicarboxylic acid (PM) was obtained by acylation of *tert*-butylperoxymethanol (TBPM) by maleic anhydride (MA) in the presence of pyridine.

tert-Butylperoxymethanol was synthesized by the procedure described in [13].

All other chemicals were analytical graded and used as received without further purification.

The degree of deacetylation of low molecular weight Chi was found to be 64 % and medium molecular weight Chi – 70 % by the back titration.

2.2. Viscometric measurement

The molecular weight of Chi was determined by viscometric method using Mark-Houwink equation:

$$[\eta] = K \times M^\alpha \quad (1)$$

The functional relationships for k and a as a function of the deacetylation degrees (DD) [14]:

$$k = 1.64 \cdot 10^{-30} \cdot DD^{14} \quad (2)$$

$$\alpha = -1.02 \cdot 10^{-2} \cdot DD + 1.82 \quad (3)$$

The average molecular weight of the low molecular weight Chi was 32300 Da and medium molecular weight Chi was 53200 Da.

2.3. Synthesis of Chi and VEP grafted copolymers

Grafting of 5-*tert*-butylperoxy 5-methyl-1-hexene-3-in (VEP) onto the Chi backbone was carried out by persulfate-induced free-radical reactions in a 1 % aqueous acetic acid solution at 323 K. Argon was purged into the blend during the polymerization reaction. The reaction time was 4 hours. The copolymer was precipitated by NH_4OH solution and washed with distilled water to remove ammonium persulphate (APS). Then it was extracted with acetone and chloroform to remove VEP monomer and non-grafted homopolymer polyVEP.

2.4. IR measurement

IR spectral measurements were performed using “Specord-80M” spectrophotometer to confirm grafting between Chi and VEP.

2.5. Degradation of Chi backbone by APS

The degradation of Chi backbone was carried out in the presence of APS in a 1 % v/v aqueous acetic acid solution at 323 K. Argon was purged into solution during the whole reaction. The reaction time was 4 hours. The Chi was precipitated by NH_4OH solution and washed with distilled water to remove APS.

2.6. DTA analyses

DTA analyses were performed for Chi, Chi-VEP, polySt using Q-1500 microcalorimeter at the heating rate of 1.25 K/min under the oxygen flow.

2.7. Emulsion polymerization

The emulsion polymerization of St was performed with simultaneous using Chi-VEP as a macroinitiator-emulsifier and cation-active trimethylcetylammiumbromide (MCAB) as a coemulsifier at 333–353 K. The emulsion polymerization was carried out with oleo- and aqueous phases ratio 1:9. The polymerization rate was defined using dilatometric and gravimetric methods. Latex polySt was separated from the latex by freezing-out and washed with aqueous acetic acid solution to remove MCAB and non-grafted Chi-VEP, then it was dried at room temperature.

2.8. Obtaining of Chi-PVP copolymers and hydrogels on their bases

Chi-PVP copolymers were prepared by free radical solution grafted copolymerization of Chi-PM and VP in aqueous solution at 333 K and different ratio between reagents. In some cases N,N- methylenebisacrylamide (MBA) was used as cross-linking agent.

Copolymer films were prepared from Chi-PVP solutions. The solutions were spread into Petri dishes and left to dry for 72 h at 313 K.

The swelling behaviour of the films was measured by swelling the films in aqueous medium with different pH at room temperatures using Dogadkin’s devise .

The swelling ratio was calculated using the equation:

$$\alpha = (W_t - W_0) / W_0, \quad (4)$$

where W_0 – the weight of dry sample, g; W_t – the weight of the swollen sample for the moment of time t, g.

The equilibrium swelling ratio was calculated from the following equation:

$$\alpha = (W_e - W_0) / W_0, \quad (5)$$

where W_e – the weight of swollen state at the equilibrium.

2.9. Evaluation of antibacterial activity

The antibacterial properties of Chi, its derivatives Chi-VEP and modified polySt were determined against the bacterial culture *Sarcina flava* and bacillus culture *Bacillus cereus*. *S.flava* and *B.cereus* were selected and incubated as test cells because they are widely spread in the environmental medium.

3. Results and Discussion

3.1. Creating of peroxide containing chitosan with primary-tertiary peroxide groups by polymeranalogical interactions

Polymeranalogical interaction of Chi macromolecule is one of the perspective directions of

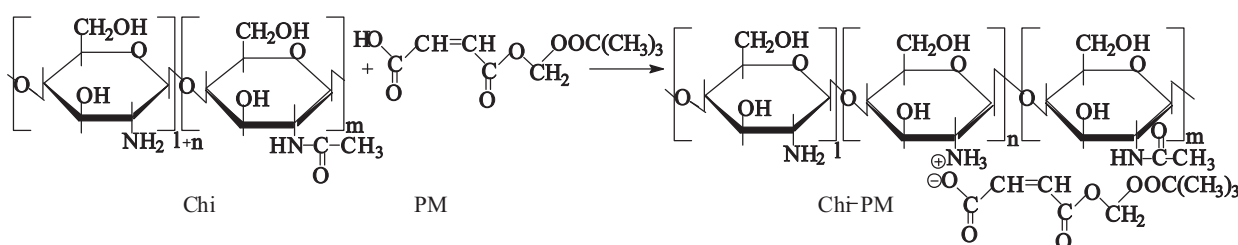
creating new biocompatible and biodegradable materials based on Chi. New Chi derivatives which contain primary-tertiary peroxide fragments were received by interaction between Chi and *tert*-butyl peroxide methyl ester of butane dicarboxylic acid (PM) according to scheme 1.

IR spectrum of Chi-PM in comparison with the spectrum of initial Chi (Fig. 1.) has a number of distinctive bands, which testifies to the formation of ionic bonds at the interaction of Chi and PM.

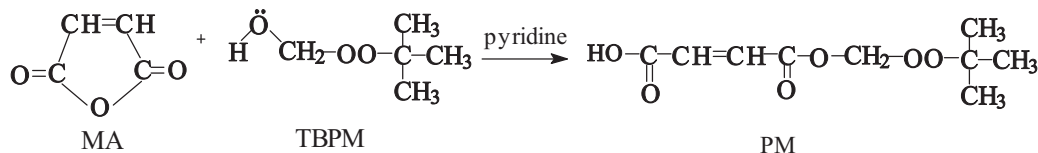
The bands in the Chi-PM spectrum at 1580 cm^{-1} and 1540 cm^{-1} are characteristic for COO^- carboxylated group. In the area of 3000 cm^{-1} one may observe the expansion which is characteristic for $-\text{NH}_3^+$ group in the

condensed state. It is noticeable that the expansion to the left and to the right is observed in the Chi-PM spectrum in the area of 3100 cm^{-1} , and a new absorption band at 3060 cm^{-1} testifies to the presence of the $\text{CH}=\text{CH}$ group with conjugated linkage. The band at 864 cm^{-1} , characteristic for *tert*-butoxyl substitute and the band at 888 cm^{-1} referred to $-\text{OO}-$ absorbing group, confirm the presence of a peroxide fragment.

The synthesis of PM, which was used as a reagent for peroxychitosan obtaining, was carried out by acylation of *tert*-butylperoxymethanol (TBPM) with maleic anhydride (MA) in the presence of pyridine according to the scheme 2.



Scheme 1. Obtaining of peroxide containing Chi by polymeranalogue interactions



Scheme 2. Acylation of TBPM by maleic anhydride

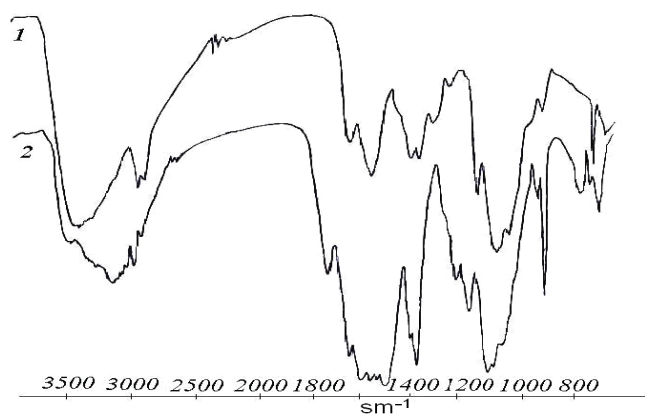


Fig. 1. IR-spectra of Chi (1), Chi-PM (2)

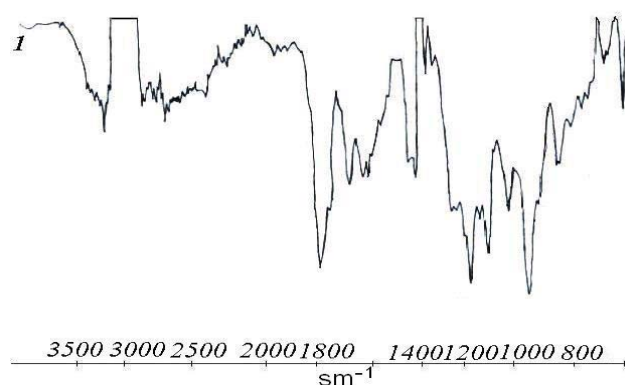


Fig. 2. IR-spectrum of PM

The PM structure was confirmed by IR-and PMR-spectroscopy, gas-liquid and thin-layer chromatography.

IR spectrum (compensated) of PM drip layers in vaseline oil (Fig. 2) shows the absorption bands of OH stretching vibrations ($\nu_{\text{OH bound}}$) in the range of 3200–2570 cm^{-1} , 1710 cm^{-1} ($\nu_{\text{C=O}}$), and 940 cm^{-1} ($\delta_{\text{OH nonplanar}}$), which are typical of carboxyl groups. Absorption bands of stretching vibrations of C=C ($\nu_{\text{C=C}}$) at 1665 cm^{-1} of feeble intensity and 976 cm^{-1} ($\delta_{\text{CH nonplanar}}$) of strong intensity are characteristic of R'HC=CHR'' fragment of *trans*-configuration. The absorption band of stretching vibrations of C=C ($\nu_{\text{C=C}}$) at 1636 cm^{-1} of medium intensity and 704 cm^{-1} (δ_{CH}) of medium intensity are characteristic for fragment R'HC=CHR'' of *cis*-configuration. Bands at 1740 cm^{-1} ($\nu_{\text{C=O}}$) and 1196 cm^{-1} ($\nu_{\text{C-O}}$) are characteristic of ester linkage. Absorption bands at 880 cm^{-1} are

characteristic of *tert*-butoxyl group, as well as that at 840 cm^{-1} (O–O) testify to the presence of peroxide fragment.

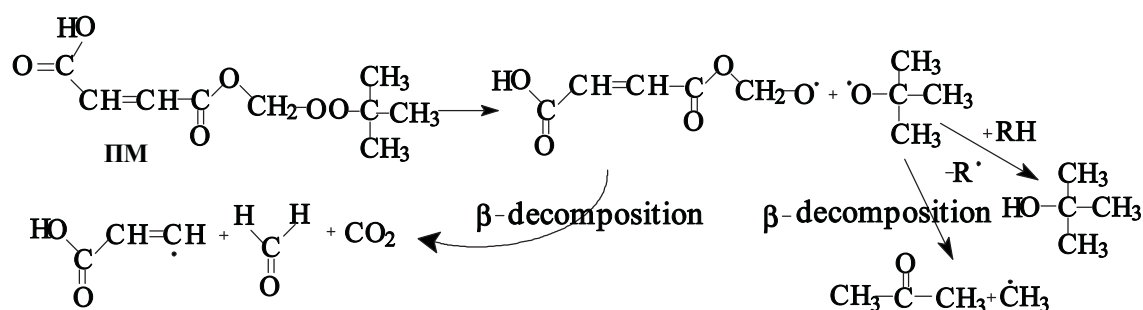
Characteristics of obtained peroxychitosans with primary-tertiary peroxide fragments are shown in Table 1. Thus, peroxychitosans with primary-tertiary peroxide groups which can be used as precursors of formation of hydrogels and modifiers of surface polymers have been created for the first time.

The chromatographic analysis, IR spectroscopy and functional analysis of PM thermal decomposition products allowed to introduce the scheme of PM decomposition according to scheme 3.

Firstly obtained peroxychitosans with primary-tertiary peroxide groups were used as precursors for creating hydrogels and as modifiers of polymer surfaces.

Table 1

Chi-PM peroxychitosan characteristics



Scheme 3. Scheme of PM thermal decomposition

3.2. Obtaining of peroxide containing chitosan with ditertiary groups by radical grafted copolymerization

Peroxide containing Chi with ditertiary peroxide groups is a chitosan-graft-poly-5-*tert*-butylperoxy 5-methyl-1-hexene -3-in (Chi-VEP) copolymer, which contains ditertiary peroxide groups in branches of polymer chains of VEP monomer. The synthesis of Chi-VEP was carried out via radical copolymerization of Chi and VEP at the initiation by APS.

The idea of Chi-VEP synthesis is the creation of a surface active macroinitiator which could contain

hydrophobic areas of grafted chains of polyVEP and hydrophobic areas of Chi in the macromolecule. Polymer of such structure may be used as a modifying surface-active macroinitiator for initiating the processes of aqueous polymerization of vinyl monomers with simultaneous modification of the surface of latex particles, other disperse system or polymer macrosurfaces by its grafting onto the surfaces.

It is known that the Chi chains are destructed under the action of persulphates of alkali metals [14, 15]. With the aim of conducting of purposeful synthesis of peroxychitosan with the defined length of chains, the degradation of initial Chi macromolecules, used during synthesis under APS action, was researched.

3.4. The research of peroxychitosan with ditertiary peroxide fragments

On the basis of reports in literature [16] on mechanisms of Chi chains destruction under the influence of peroxide sulphate and experimental data obtained, the formation of Chi-VEP copolymers may be presented in schemes 5 i 6.

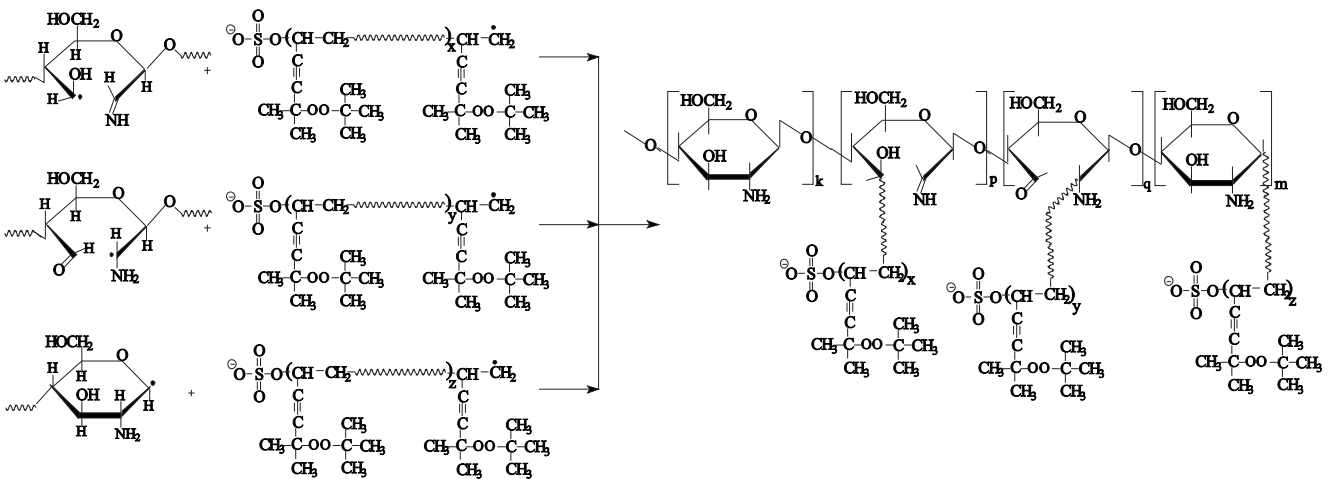
It is obvious that APS initiates the origination and growth of polyVEP chain (scheme 5), degradation of Chi chain and breaking of C₂-C₃ and C₁-O-C₄ links with the formation of radicals according to scheme 5, which participate in breaking of the chain and formation of Chi-VEP grafted copolymers.

The composition of Chi-VEP copolymers was confirmed by an element analysis, IR spectroscopy (Fig. 3), DTA and chromatographic researches.

In IR spectrum of Chi-VEP copolymers, unlike the spectrum of initial Chi, there are the following absorption bands: bands at 1360 cm⁻¹ and at 1380 cm⁻¹ referred to oscillation doublet of *tert*-butyl group, which testifies to the presence of *tert*-butoxyl fragments of polyVEP; the absorption bands at 880 cm⁻¹, which corresponds to the oscillations of C-O- in *tert*-butoxyl group; the absorption bands at 1248 cm⁻¹, 1195 cm⁻¹, 840 cm⁻¹, characteristic of the skeleton oscillations of *tert*-butyl group; the intense absorption band at 2940 cm⁻¹, referred to the oscillations of the -CH₂- group in grafted chains of polyVEP, formed as a result of polymerization of the vinyl fragment.



Scheme 5. Initiation and growth of the chain of poly-(5-*tert*-butyl-5-methyl-1-hexen-3-in)



Scheme 6. Formation of Chi-VEP grafted copolymers (break of the chain)

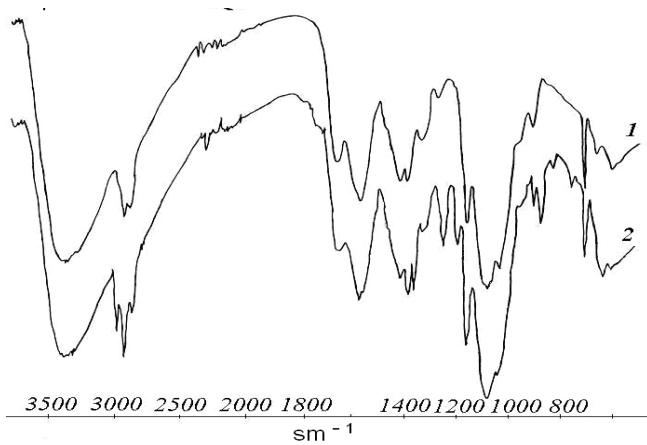


Fig. 3. IR spectra of Chi (1) and Chi-VEP (2)

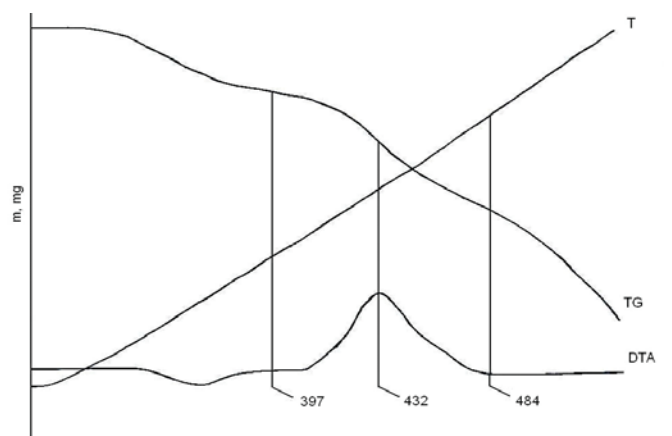


Fig. 4. DTA of Chi-VEP peroxide containing copolymer

As it is seen from Fig. 4, in the temperature interval 398–458 K a significant loss of the weight of the sample is observed, which makes 26 % according to the data of the TG-curve. The maximum rate of decomposition of the substance in this temperature interval according to the DTG curve corresponds to 428 K. The weight loss of the sample in the mentioned temperature interval is accompanied by brightly expressed exothermal effect on DTA curve which is stipulated by the decomposition of ditertiary peroxide groups with following fragmentation of radicals and formation of volatile products [17].

The quantitative content of peroxide links in Chi-VEP is defined by the summary quantity of products of full decomposition of ditertiary peroxide fragments in grafted chains of polyVEP, which are propanone and 2-methyl-2-propanol using gas-liquid chromatograph Selmichrom-1.

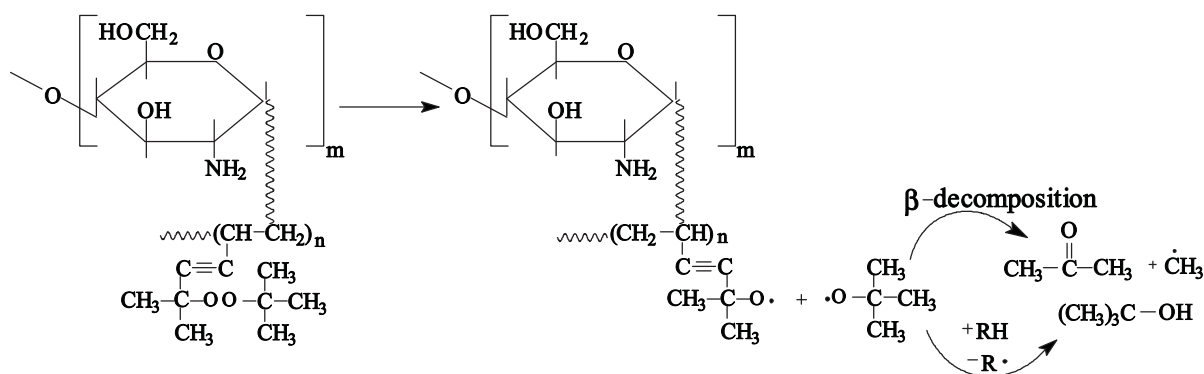
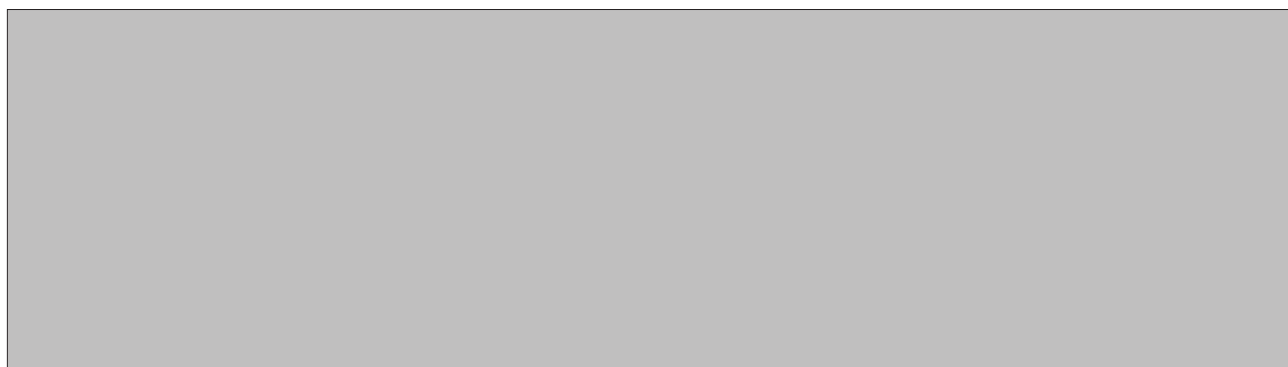
The results of DTA and chromatographic analysis of Chi-VEP are shown in Table 3. These results are confirmed by an element analysis of nitrogen, which was used for the calculating of Chi chains content.

According to the data of IR spectroscopic research, chromatographic analysis and literature data on thermal decomposition of VEP polymer chains, the following scheme of thermal decomposition of peroxide fragments in Chi-VEP composition is suggested (scheme 7).

It is defined that Chi-VEP synthesized peroxychitosans as well as initial Chi and samples of degraded Chi show antibacterial activity. During researches the content of cells of bacterial culture *Sarcina flava* in the initial bacterial suspension was $408 \cdot 10^3$ cel/ml. It was found out that these samples fully inhibit the growth of cells of the bacterial culture *Sarcina flava*.

Table 3

Results of Chi-VEP derivatographic and chromatographic analyses



Scheme 7. Scheme of decomposition of Chi-VEP

3.5. Peroxychitosans with ditertiary peroxide groups as macroinitiators for emulsion polymerization

Chi-VEP peroxidated chitosans as well as low molecular Chi (mol. weight 32000 Da) show feeble surface activity. Isotherms of surface tension have a view typical of SAA polymer without defined CMC.

While carrying out the emulsion polymerization of styrene for the formation of aqueous dispersions of

polystyrene (polySt) simultaneously with emulsifier-macroinitiator Chi-VEP, cation-active trimethylcetylammuniumbromide (MCAB) was used as a coemulsifier. Chi-VEP and MCAB coemulsifiers were used simultaneously taking into consideration that the emulsion polymerization of styrene (St) practically did not occur only in the presence of non-modified Chi as an emulsifier (at initiation by APS). At the same time the modification of the surface of the latex particles of Chi does not occur.

In the presence of alone Chi-VEP copolymer as an emulsifier and an initiator the emulsion polymerization of St under the similar condition occur only to the conversion of 10–15 %. It was also defined, that in the emulsion polymerization of St with MCAB as a single emulsifier and APS as an initiator under the similar conditions, the conversion is no more than 40 %, and the obtained latexes are not stable.

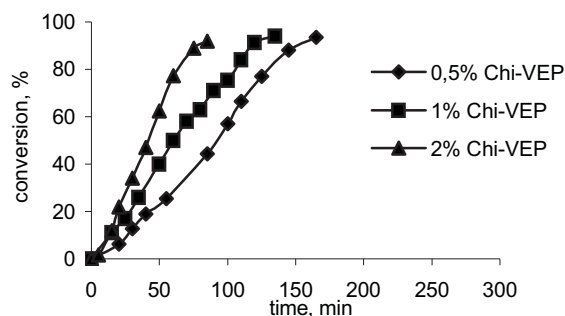


Fig. 5. Typical kinetic curves of the emulsion polymerization of St at different concentration of Chi-VEP at 2 % MCAB and 343 K

The emulsion polymerization of St with Chi-VEP and MCAB proceeds with high rates during 1–3 hours to the conversions of 96–98 %.

The aggregative stability of the disperse particles is provided by electrostatic stabilization owing to MCAB and by steric stabilization owing to Chi-VEP. The initiation of water-dispersed polymerization of St is carried out owing to peroxide fragments of Chi-VEP.

One may observe the synergism of stabilizing action of Chi-VEP and MCAB at their simultaneous application which can be explained by the formation of macromolecular complexes by MCAB molecules and Chi-VEP macromolecules which contain sulphate end groups (scheme 5). At the same time, each of these substances

taken separately at given concentrations does not provide stabilization of aqueous dispersion.

Kinetic researches allowed to obtain equations of the rate of the emulsion polymerization of styrene in the presence of Chi-VEP and MCAB, which coordinates with Medvedev's theory for the case of emulsion polymerization, when the generation of initiating radicals occurs in absorbing layers of PMP:

$$W \sim k [\text{Chi-VEP}]^{0.5} [\text{MCAB}]^{0.5} [\text{styrene}]^1$$

It is defined that the diameter of the particle grows with the increase of Chi-VEP concentration (Table 4), and the temperature and concentration of MCAB emulsifier do not have a significant influence on the size of the particles (Table 5).

The growth of the particle diameters of latexes at the growth of concentration of Chi-VEP initiator is explained in the following way. As the result of the transfer of the chain and recombination of macroradicals which occur on the surface of PMP, chains of Chi-VEP macromolecules chemically graft to the fragments of polySt latex particles. Chemical grafting Chi-VEP to PMP is accompanied by the displacement of physically absorbed low molecular surface active coemulsifier MCAB from the surface to the disperse medium. As the result, the stability of PMP decreases owing to electrostatic component. It is proved by the reduction of surface tension of end latexes at the growth of concentration of Chi-VEP and the diameter of the particles (Table 4).

DTA researches and an element analysis of nitrogen helped to define that the samples of latex polySt, separated from the latex by means of freezing-out and washed from MCAB and non-grafted Chi-VEP, contain covalently grafted Chi-VEP chains onto polySt.

The microbiological research of antibacterial activity of polySt and polybutylacrylate, modified by Chi-VEP, which were separated from the latex in a way described

Table 4

The influence of Chi-VEP concentration on the particle sizes of polySt of latexes*

--

*emulsion polymerization was carried out in the presence of 2 % MCAB from the weight of St

Table 5

The influence of MCAB concentration on the particle diameters of latexes polySt*

--

*emulsion polymerization was carried out in 1 % solution of Chi-VEP with oleo: aqueous phases ratio 1:9.

above, has shown that they fully inhibit the growth of the cells of *Sarcina flava* bacterial culture and *Bacillus cereus* bacillary culture. The amount of the cells of *Sarcina flava* in initial researched bacterial suspensions was $1.961 \cdot 10^7$ cel/ml and *Bacillus cereus* – $2.872 \cdot 10^7$ cel/ml. An antimicrobial action of polySt and polybutylacrylate modified by Chi exhibits at 2.8–8 % grafting of Chi-VEP onto polymer, when non-modified analogues do not show antimicrobial action, which also testifies to covalent grafting of Chi-VEP onto the surface of PMP.

Thus, it is shown that latex polymerization of vinyl monomers in the presence of Chi-VEP as a coemulsifier and a macroinitiator helps to obtain polymers, chemically modified by Chi, with pronounced antimicrobial properties.

3.6. Peroxychitosans with primary-tertiary peroxide groups as macroinitiators for δI -sensitive hydrogels obtaining

In the last few years the chemistry of medical-biological polymer has developed rapidly. Polymer biomaterials are used for drugs delivery, implants, and for the tissue design [18, 19]. Hydrogels which can change volume according to the environment – pH, temperature, chemical composition, radiation, so called smart hydrogels, are extremely important. Such hydrogels can adsorb medical and other bioactive substances and be not only biodegradable biocompatible matrixes-carriers, but also regulate the process of drug release depending on the environment [20-22].

Grafted copolymerization of vinylpyrrolidone (VP) and Chi-PM was used to create pH- sensitive hydrogels. The network of hydrogels is formed during radical grafting of the polyvinylpyrrolidone (PVP) chains to peroxychitosans with Chi-PM primary-tertiary peroxide group and the following formation of three-dimensional matrix.

Copolymers of Chi-PVP were obtained by copolymerization of VP and Chi-PM salt, in aqueous solutions at 333 K and different ratio between reagents. The initiation of radical process occurred due to radicals which are formed at the thermolysis of primary-tertiary peroxide group in Chi-PM structure.

Chi-PVP copolymers, formed in the film by means of exsiccation of the final reacting blends, form hydrogels at swelling in aqueous solutions. It seems obvious that the content of basic aminogroup in Chi chains and the number of grafted PVP chains will define the conformation of copolymer macrochains in the solution and its capacity for ionization. The number of initiating fragments of PM will influence the structure of polymer network, the degree of grafting of PVP chains, which defines its capacity for swelling. Therefore, the influence of correlation of VP, Chi and PM on the capacity for swelling of the obtained copolymers Chi-PVP was researched.

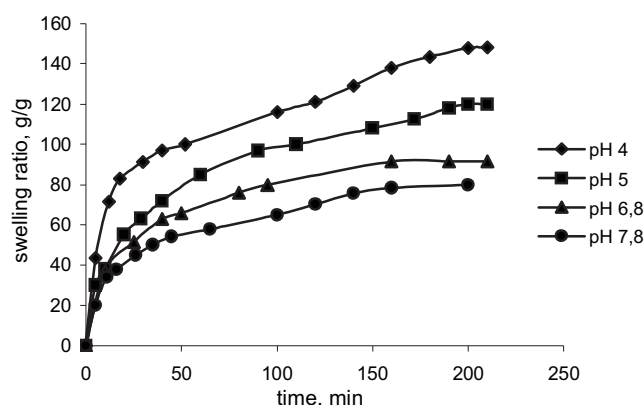


Fig. 6. Typical kinetic curves of the swelling of Chi-PVP copolymer with PVP content 91 %, obtained by copolymerization of Chi ($6.2 \cdot 10^{-2}$ kmol/mi) and VP ($11.9 \cdot 10^{-1}$ kmol/mi) at the initiation by PM ($30.0 \cdot 10^{-4}$ kmol/mi) in aqueous solution with different pH

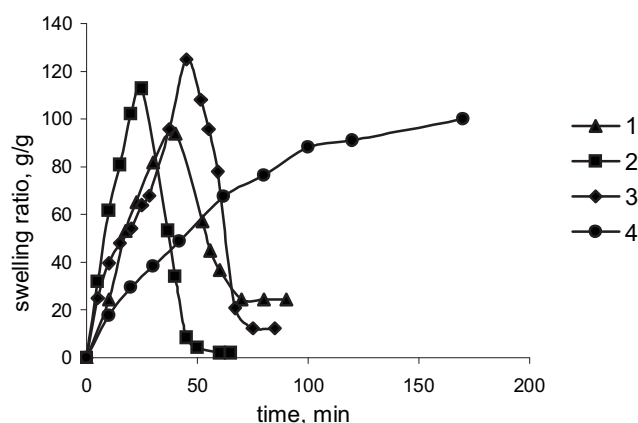


Fig. 7. Kinetic curves of Chi-PVP copolymer swelling at pH= 4.0, obtained by copolymerization of Chi = $6.2 \cdot 10^{-2}$ kmol/mi, VP = $11.9 \cdot 10^{-1}$ kmol/mi (1, 2, 3) and $2.5 \cdot 10^{-1}$ kmol/mi (4) at initiation by APS = $10.0 \cdot 10^{-4}$ kmol/mi (1), $30.0 \cdot 10^{-4}$ kmol/mi (2), $60.0 \cdot 10^{-4}$ kmol/mi (3) and $30.0 \cdot 10^{-4}$ kmol/mi (4)

It is defined that the radicals which are formed during PM thermolysis do not destruct Chi chain, unlike known initiation by water-soluble initiators – persulphates of alkali metals. If we compare kinetic curves of hydrogels swelling, obtained by copolymerization of VP and Chi-PM and hydrogels, obtained under similar conditions, but at initiation by APS (Fig. 7), we can see that the destruction of Chi chains, at the action of persulphate, leads to the unlimited swelling of the samples of grafted copolymers and finally to their dissolution, when the hydrogel obtained at the initiation by PM fragment is accompanied by the formation of Chi-PM cross-linked polymer network. It is shown that the ratio and equilibrium swelling ratio of Chi-PVP copolymers α_p depend on pH of aqueous medium. It is defined that the equilibrium swelling ratio of Chi-PVP

grows symbotically to the concentration of an initiator (fragment PM) in the reaction mixture, which is explained by the increase of the grafting degree of hydrophilic PVP chains (Table 6).

The density of crosslinking of hydrogel polymer network was regulated by N,N-methylenebisacrylamide crosslinking agent. The increase of MBA favours three-dimensional crosslinking and growth of crosslinking density, accompanied by the decrease of equilibrium swelling ratio (Fig. 8).

The degree of ionization of main aminogroups in the composition of Chi links depends on pH medium. Under non-ionized conditions or at low degree of ionization Chi-PVP copolymer is in the collapse state. At the increase

of ionization ($\text{pH} > 5.5\text{--}6$) there is a swelling due to the electrostatic repulsion of equal charged links and "pushing" osmotic pressure of counterions. At the increase of pH aqueous medium, close to the values 5.5–6, the equilibrium swelling rapidly decreases, and the hydrogels are close to the collapse state. Collapse pH depends on copolymer composition. Increase of Chi content accents pH collapse to the lower values, what is stipulated by a higher content of main aminogroups in the copolymers.

The research of antibacterial properties of hydrogels based on Chi-PVP has shown that they inhibit the growth of cells of *Sarcina flava* bacterial culture and *Bacillus cereus* bacillary culture.

Table 6

Dependence of equilibrium swelling ratio on pH medium and composition of Chi-PVP copolymer, obtained by grafted copolymerization Chi (0.062 kmol/m^3) and VP at initiation by PM

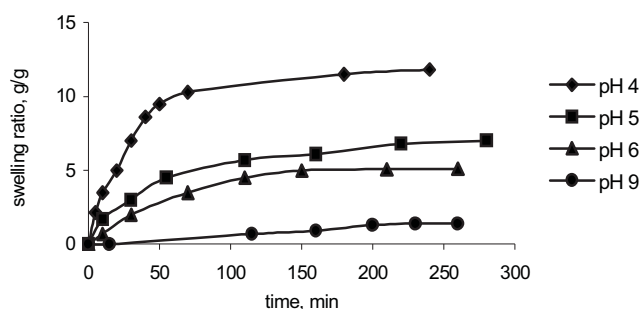


Fig. 8. Kinetic dependence of Chi-PVP copolymer swelling containing 84 % of PVP, obtained by copolymerization of Chi ($6.2 \cdot 10^{-2} \text{ kmol/mi}$) and VP ($11.9 \cdot 10^{-1} \text{ kmol/mi}$) at the initiation by PM ($20.0 \cdot 10^{-4} \text{ kmol/mi}$) in the presence of MBA (2 % from Chi)

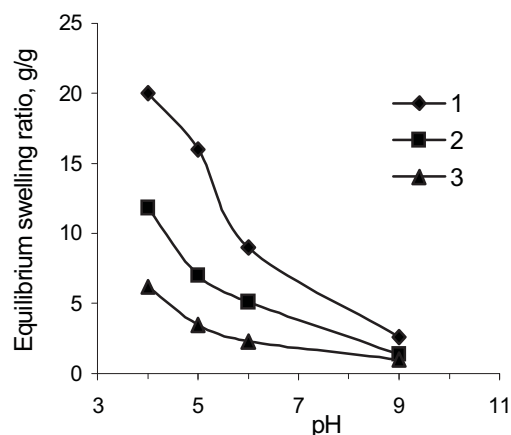


Fig. 9. Dependence of equilibrium swelling ratio of Chi-PVP copolymers on pH medium: PVP = 91 %, Chi = 9 %, [PM] during the synthesis = $30.0 \cdot 10^{-4} \text{ kmol/mi}$ (1); PVP = 89 %, Chi = 11 %, [PM] during the synthesis = $20.0 \cdot 10^{-4} \text{ kmol/mi}$ (2), PVP = 85 %, Chi = 15 %, [PM] during the synthesis = $10.0 \cdot 10^{-4} \text{ kmol/mi}$ (3)

4. Conclusions

Thus, the obtaining methods of new reactive biopolymers based on Chi with primary-tertiary or ditertiary peroxide fragments have been elaborated. The

usage of grafted copolymers with hydrophobic grafted to Chi chains poly-VEP, containing ditertiary peroxide groups in the processes of aqueous emulsion polymerization of styrene (and butylacrylate) allows to obtain latexes with macromolecules of peroxychitosan which are covalently

attached to latex polymer. Such macromolecules impart antibacterial properties to emulsion polymers.

It has been defined that the usage of peroxychitosan with primary-tertiary peroxide fragment for constructing and synthesis of hydrogel polymer network allows to obtain biocompatible, biodegradable, antibacterial and pH-sensitive hydrogels with regulated water absorption and collapse pH, possible for transportation of medicaments.

References

- [1] Skryabin K.G. (ed.): Chitin i chitosan. Poluchenie, svoistva i primenenie. Nauka, Moskva 2002.
- [2] Shantha K. and Harding D.: Int. J. Pharm., 2000, **207**, 65.
- [3] Bergera J., Reista M., Mayera J.M., Felth O., Peppasc N.A. and Gurnyb R.: European J. of Pharmaceutics and Biopharmaceutics, 2004, **57**, 19.
- [4] Chih-Chang Hsu, Trong-Ming Don and Wen-Yen Chin: J. Appl. Polym. Sci., 2002, **86**, 3047.
- [5] Chern C., Lee C. and Ho C.: Colloid & Polym. Sci., 1999, **277**, 507.
- [6] Yang S.C., Ge H.X., Hu Y., Jiang X.Q. and Yang C.Z.: Colloid & Polym. Sci., 2000, **278**, 285.
- [7] Artemenko S., Root L., Chechulin D., Ustinov M., Ovchinnikova G. and Ustinova T.: [in:] Materialy Pyatoj konferencyi "Novye perspektivy v isledovanii chitina i chitosana", 1999, 9.
- [8] Voronov S., Tokarev V., Datsyuk V., Seredyuk V., Bednarska O., Oduola K., Adler H., Puschke C., Pich A. and Wagenknecht U.: J. Appl. Polym. Sci., 2000, **76**, 1228.
- [9] Rojter Yu.V.: PhD thesis, Lviv 2002.
- [10] Nosova N., Roiter Yu., Samaryk V., Varvarenko S., Stetsyshyn Yu., Minko S., Stamm M. and Voronov S.: Macromolecular Symposia, 2004, **210**, 339.
- [11] Samaruk V.Ya., Rojter Yu.V., Nosova N.G., Stecysyn Yu.B., Varvarenko S.M. and Voronov S.A.: Dopovidi Nats.Akad.Nauk Ukrainy, 2004, **4**, 136.
- [12] Antonovskij V.L. and Hursan S.L.: Fizicheskaya himiya organicheskikh peroksidov, Academkniga, Moskva 2003.
- [13] Dickey F.H., Rust F.F. and Vanghan N.E.: J. Am. Chem. Soc., 1949, **71**, 1432.
- [14] Wang W., Bo S., Li S. and Qin W.: Int. J. Biol. Macromol., 1991, **13**, 281.
- [15] Chih-Chang Hsu, Trong-Ming Don and Wen-Yen Chin: J. Appl. Polym. Sci., 2002, **86**, 3047.
- [16] Sangamesh G. Kumbar, Kumaresh S. Soppimath and Tejjaj M. Aminabhavi: J. Appl. Polym. Sci., 2003, **87**, 1525.
- [17] Uolling Ch.: Svobodnye radikalny v rastvore. Izd. Inostr. lit., Moskva 1960.
- [18] Bolshakov I.N., Gorbunov N.S. and Shamova E.S: Pat. (19)RU(11)2254145(13)C1 (RU): GOU VPO KRASGMA MIZGRAVA ROSSII. – № 2003130390/15; Publ. 20.06.2005.
- [19] Pisarenko L.V., Ignatov G.G. and Alfalov V.V.: [in:] Materialy Sedmoj Megdunarodnoj konferencyi "Sovremennye perspektivy v ispolzovanii chitina i chitosana", 2003, 187.
- [20] Filippova O.E.: Priroda, 2005, **8**, 84.
- [21] Mincheva R., Manolova N., Sabov R., Kjurchiev G. and Rashkov I.: e-Polymers, 2004, **058**, 1.
- [22] Lopatin V.V. and Askadskij A.A.: Poliakrilamidnye gidrogeli v medicyne. Nauchnyj Mir, Moskva 2004.

ПЕРОКСИДНІ ПОХІДНІ ХІТОЗАНУ ТА ЇХНЄ ЗАСТОСУВАННЯ

Анотація. Радикальними реакціями хітозану з 5-трет-бутилперокси-5-метил-1-гексен-3-іном одержано перокси-хітозани з дитретинними пероксидними фрагментами, які можуть застосовуватися разом з низькомолекулярним катіонактивним емульгатором як коемульгатори і макроініціатори у водно-емульсійній полімеризації вінільних мономерів. Показано, що пероксихітозани прищеплюються до поверхні латексних частинок і надають емульсійному полімеру антибактеріальних властивостей. Полімераналогічними перетвореннями хітозану взаємодією з трет-бутилпероксиметилловим естером бутендикарбонової кислоти одержано пероксихітозани з регульованою кількістю первинно-третинних пероксидних фрагментів. На їхній основі одержано гідрогелі.

Ключові слова: хітозан, пероксихітозан, емульсійна полімеризація, макроініціатор-коемульгатор, модифікація поверхні, pH-залежні гідрогелі.

