



Synthesis of grafted polybutyl acrylate copolymer on fish collagen

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Abstract: Increasingly, scientists are turning to the study of marine, or fish, collagen, which is increasingly replacing collagen of terrestrial animals, due to the fact that it is hypoallergenic, since it is 96% identical to human protein. Materials based on fish collagen have a number of advantages over their analogue of animal origin: it is not a carrier of infectious diseases of animals transmitted to humans, it has a greater structural similarity to human collagen, which provides a higher level of biocompatibility. Materials based on collagen copolymers with synthetic monomers are promising. The use of hybrid materials also helps to reduce the consumption of non-renewable natural resources. Synthesis of grafted collagen copolymers with polybutyl acrylate was carried out at azobisisobutyronitrile initiation and triethyl borane – oxygen system initiation under comparable conditions under intensive stirring of aqueous solution dispersion of collagen and butyl acrylate. After the synthesis, the aqueous and organic phases of the reaction mixture were analyzed by composition and molecular weight parameters using infrared spectroscopy and size-exclusion chromatography. Changes indicating the formation of a copolymer are observed in the copolymer isolated from the aqueous phase, more pronounced in the triethyl borane – oxygen system. It is assumed that the formation of copolymer macromolecules for azobisisobutyronitrile and organoelement initiator takes place according to different schemes. Schemes for the formation of copolymer macromolecules for AIBN and an organoelement initiator are proposed. Only polybutyl acrylate is present in the organic phase. Biological studies were carried out for fungal resistance and bactericidal activity of the obtained copolymers.

Keywords: collagen, triethyl borane, butyl acrylate, bactericidal properties, grafted copolymerization

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Синтез привитого сополимера полибутилакрилата на рыбный коллаген

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Резюме: Сегодня ученые все чаще обращаются к исследованию морского, или рыбного, коллагена, который уверенно вытесняет коллаген наземных животных, ввиду того что он является гипоаллергенным, так как на 96% идентичен человеческому белку. Материалы на основе рыбного коллагена имеют целый ряд преимуществ по сравнению с аналогом животного происхождения: он не является переносчиком инфекционных заболеваний животных, передающихся человеку; имеет большее структурное сходство с коллагеном человека, обеспечивающее более высокий уровень биосовместимости. Перспективны материалы на основе сополимеров коллагена с синтетическими мономерами. Использование гибридных материалов, кроме того, позволяет снизить потребление невозобновляемых природных ресурсов. Синтез привитого сополимера полибутилакрилата на коллаген проводили при иницировании динитрилом азоизомасляной кислоты и иницирующей системы триэтилборан–кислород в сравнимых условиях при интенсивном перемешивании

дисперсии водного раствора рыбного коллагена и бутилакрилата. После проведения синтеза водную и органическую фазу реакционной смеси анализировали по составу и молекулярно-массовым параметрам методами инфракрасной спектроскопии и гель-проникающей хроматографии. В выделенном из водной фазы сополимере наблюдались изменения, свидетельствующие об образовании сополимера, в случае системы триэтилборан–кислород более ярко выраженные. Выдвинуто предположение, что формирование макромолекул сополимера для динитрила азоизомасляной кислоты и элементарного органического инициатора проходит по разным схемам. Предложены схемы формирования макромолекул сополимера для динитрила азоизомасляной кислоты и элементарного органического инициатора. В выделенной органической фазе присутствует только полибутилакрилат. Также были проведены биологические исследования полученных сополимеров на фунгицидные свойства и бактерицидную активность.

Ключевые слова: коллаген, триэтилборан, бутилакрилат, бактерицидный полимер, привитая сополимеризация

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INTRODUCTION

The use of secondary resources of the food industry is an important task. Waste from the fishing industry: skin, fins, tail contains collagen [1, 2]. Materials based on fish collagen have a number of advantages compared to the analogue of animal origin: first of all, it is a greater structural similarity with human collagen, providing a higher level of biocompatibility [1, 3–5].

Hybrid materials with the inclusion of collagen and polymers of another nature are widely used in medicine [6, 7], pharmacy [8], cosmetology [9, 10]. To obtain copolymers of collagen and its denaturant – gelatin with synthetic monomers, radical initiators of various nature are most often used [11–13], including trialkyl boranees [14–16]. Grafted copolymers [17] of polymethyl methacrylate and gelatin in aqueous dispersion were synthesized and characterized in the presence of tributyl borane and traces of oxygen. In terms of practical use, it is important that samples of the new material are biodecomposed, i.e. have the destruction prospect in the presence of microorganisms.

The aim of this work is the synthesis of grafted copolymer of polybutyl acrylate (PBA) with fish collagen in the presence of various initiators: azobisisobutyronitrile (AIBN) and the initiating triethyl borane (TEB) – oxygen system. The main task of the research is to determine the composition of grafted copolymers and molecular weight characteristics.

EXPERIMENTAL PART

Preparation of initial materials for the experiment. The initial collagen was isolated from cod skin in the form of acetic dispersion by the method [18].

Butyl acrylate (BA) for purification from the inhibitor was washed with 5% soda solution and then with distilled water to a neutral medium. The washed

butyl acrylate was dried with anhydrous sodium sulfate and further purified by vacuum distillation.

AIBN was purified from impurities by recrystallization of this initiator from alcohol solution. To do this, it was dissolved in ethyl alcohol at 40 °C in a water bath. The hot solution was filtered and then cooled to recrystallize AIBN. The laid-down crystals were dried in a vacuum at 25 °C.

To improve the safety of operation and storage, TEB was used in combination with hexamethylene diamine, which releases the initiator in the acidic reaction medium.

Fish collagen extraction method. Collagen was extracted from the cod skin, which was cleaned of scales, lumps of muscle tissue and fat, washed with distilled water, frozen. The raw cod skin was cleaned of scales, lumps of muscle tissue and fat, washed with water and frozen. Prepared and frozen raw material was crushed with scissors and placed in 3% acetic acid for a day at 25 °C, after which the resulting collagen dispersion was separated using a filter with a pore size of 1 µm from parts of the crushed fish skin and other impurities. We used the isolated aqueous solution of collagen in 3% acetic acid. The mass fraction of collagen in the resulting solution is 8%.

Method of butyl acrylate copolymer synthesis with collagen. Synthesis of collagen and butyl acrylate copolymers with both initiators was carried out, as follows. The mixture of aqueous 3% solution of collagen and butyl acrylate in a weight ratio of 1:1 was bubbled by argon for 15 minutes at room temperature and intensive stirring before synthesis. The initiator in amount of 1% from weight of collagen was added to mixture and quickly heated to 50 °C, without ceasing to stir intensively. The synthesis was carried out for 1 hour in an argon atmosphere. The organic phase was separated from the aqueous

layer by decantation. The copolymer is in the aqueous phase.

Method of composition determining of the aqueous phase of butyl acrylate copolymer with collagen. The composition of the obtained materials was studied using infrared (IR) spectroscopy. IR spectrophotometer "IRPrestige-21" manufactured by Shimadzu, Japan, was used to record IR spectra of absorption. Films on the KBr plate were prepared to record the IR spectrum. The spectra interpretation was carried out independently.

Method of composition determining of the organic phase of butyl acrylate copolymer with collagen. The organic layer of the synthesized copolymers was investigated in a chloroform solution by IR-Fourier-transform spectrophotometer Shimadzu FTIR-8400S in KBr cells with an optical path length of 0.26 mm in the wave number range 5500–550 cm^{-1} , the error in the determination did not exceed $\pm 0.05 \text{ cm}^{-1}$. The copolymer composition was determined using a calibration graph on the characteristic peak area of the analytical band at 1726 cm^{-1} , which corresponds to the presence of a carbonyl group. The proportion of butyl acrylate was calculated according to the intensity of this band.

The calibration curve was plotted in the absorption intensity (optical density) – concentration axes (Fig. 1) by absorption of poly methyl methacrylate (PMMA) solution. This method used MMA, not BA due to polybutyl acrylate is insoluble.

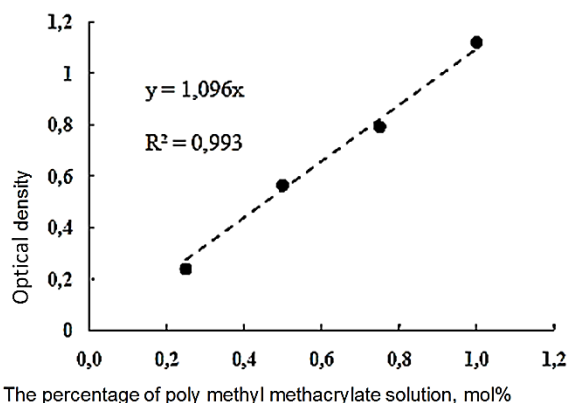


Fig. 1. Calibration curve for determining the copolymers composition

Рис. 1. Градуировочный график для определения состава сополимеров

Spectra of PMMA solutions in chloroform of precisely known concentration (0.2–1.0% PMMA) were integrated to plot the curve. Absorption intensity was determined by the "baseline" method [19]. The error in determining the concentration of fragments in the copolymer was $\pm 5\%$.

The calculation of PBA mass fraction in the copolymer organic layer was carried out according to the formula:

$$\omega(\text{BA}) = \frac{M(\text{BA})}{M(\text{MMA})} \times \frac{D}{1.095} \times \frac{m(\text{BA})}{m(\text{CHCl}_3)}, \text{ were.}$$

D is the optical density of polymethyl methacrylate, $M(\text{BA})$ is the molar mass of butyl acrylate, $m(\text{BA})$ is the mass of butyl acrylate, $M(\text{MMA})$ is the molar mass of methyl methacrylate, according to which the calibration graph was used, $m(\text{CHCl}_3)$ is the mass of chloroform in which the solution was prepared, 1.096 is the slope of the calibration curve.

The experiment showed that 100% PBA is formed in the organic layer when both initiators are used.

Analysis of molecular weight characteristics of the copolymer of butyl acrylate with collagen. The molecular weight characteristics of collagen and collagen-containing copolymers were studied by size-exclusion chromatography (SEC). This method is based on the molecule separation by volume sizes. Sample preparation was carried out by filtration using nozzle membranes Millipore Millex-LCR (PTFE 0.45 μm). To do this, a disposable syringe filled with a collagen aqueous solution was fitted with a nozzle membrane Millipore Millex-LCR and filtered at a rate of about 1.2 ml/min.

Method for determining fungal resistance and bactericidal activity. Tests for fungal resistance were carried out in accordance with GOST 9.049-91 "Unified system of corrosion and ageing protection. Polymer materials and their components. Methods of laboratory tests for mould resistance". Microscopic fungi, active destructors of polymeric materials, were used as test cultures: *Aspergillus niger*, *Aspergillus terreus*, *Aspergillus oryzae*, *Chaetomium globosum*, *Paecilomyces variotium*, *Penicillium cyclospium*, *Penicillium funiculosum*, *Trichoderma viride*. Samples were placed in Petri dishes. Then the surface of the samples was inoculated with a suspension of micromycete spores and the Petri dishes with the samples were placed in a thermostat. The test duration is 28 days at a temperature of $29 \pm 2 \text{ }^\circ\text{C}$ and a humidity of more than 90%.

The bactericidal activity was determined in relation to the association of test cultures of bacteria: *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis*. The presence of bactericidal properties was assessed by the size of the zone of inhibition of bacterial growth around the test object placed on an agar MPA medium. Cultivation conditions – in a thermostat at $37 \text{ }^\circ\text{C}$. Exposure time – 24 hours.

RESULTS AND DISCUSSION

In connection with stated objective, the synthesis of grafted collagen copolymers with PBA was carried out at the AIBN initiation and the TEB-oxygen initiating system under comparable conditions. After the synthesis, the resulting copolymer was separated by decantation into an organic viscous layer and a liquid aqueous layer. 100% of homopolybutyl acrylate was found in the viscous organic phase.

The IR spectra of the samples isolated from the aqueous phase for the studied initiators are shown in Fig. 2 and Fig. 3 in comparison with the IR spectra of collagen and PBA. For the sample from the reaction mixture using the AIBN initiator, as in the case of the TEB initiator, a change is observed compared to the IR spectra of the original collagen and PBA.

Molecular weight (MW) characteristics of samples with different initiators isolated from the aqueous phase are presented in the form of molecular weight distribution MWD curves (Fig. 4, 5) and MW values in Table.

The MWD curves for samples obtained under different conditions are offset with respect to the collagen MWD curve. In the case of copolymerization initiation by the TEB – oxygen system, this offset is more noticeable. Presumably this indicates a

greater proportion of PBA grafting to collagen when initiated by an organometallic initiator. These data are confirmed by the values of MW of grafted copolymer, obtained using the TEB – oxygen system: they are higher than the original collagen by a greater amount than in the case of AIBN.

The obtained data testify that BA grafting to collagen in the presence of the TEB – oxygen system is more visible than for AIBN. This may be due to the fact that both upon initiation with a metal-containing initiator and AIBN, grafting is carried out (2) due to the abstraction of a hydrogen atom by an active radical ($R\bullet$, $RO\bullet$) from a collagen macromolecule (1) by active radicals formed in the case of AIBN due to thermal decomposition of the initiator, or due to the oxidation of thermopile according to the known scheme [20].

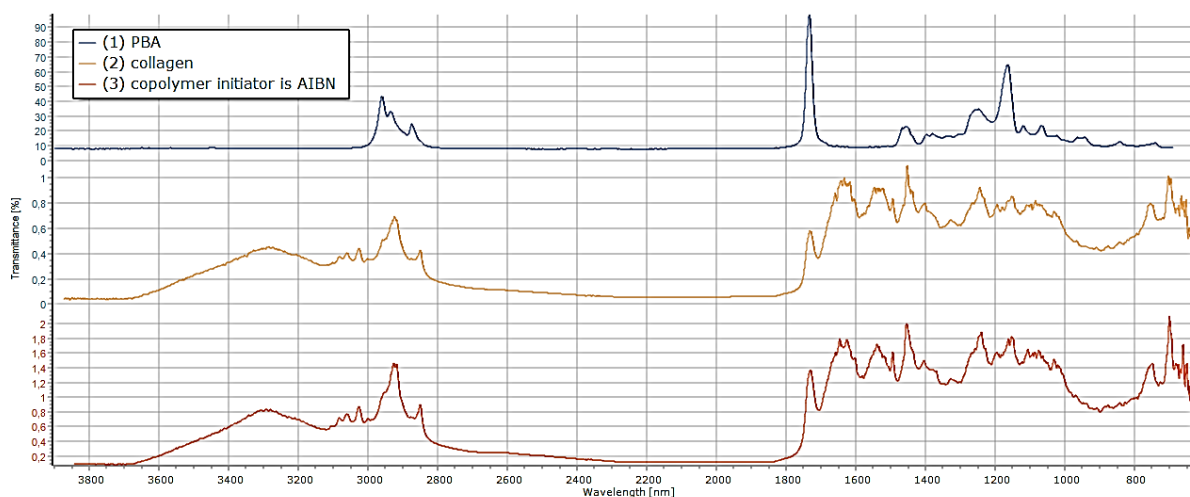


Fig. 2. Infrared spectra of collagen (1), collagen and BA copolymer initiated by azobisisobutyronitrile (2), and polybutyl acrylate (3)

Рис. 2. Инфракрасные спектры коллагена (1); сополимера, иницированного динитрилом азоизомасляной кислоты (2); полибутилакрилат (3)

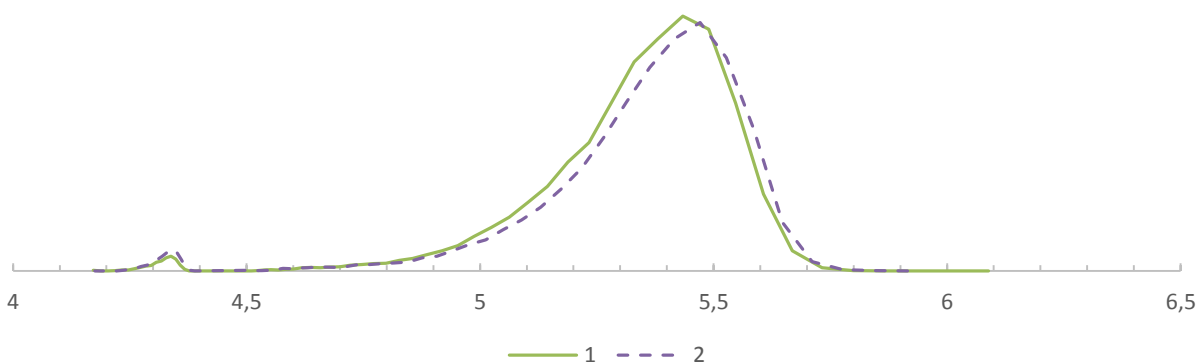


Fig. 3. Infrared spectra of collagen (1), collagen and BA copolymer initiated by the system triethyl borane – oxygen (2), and poly butyl acrylate (3)

Рис. 3. Инфракрасные спектры коллагена (1), сополимера, иницированного системой триэтилборан – кислород (2), и полибутилакрилат(3)

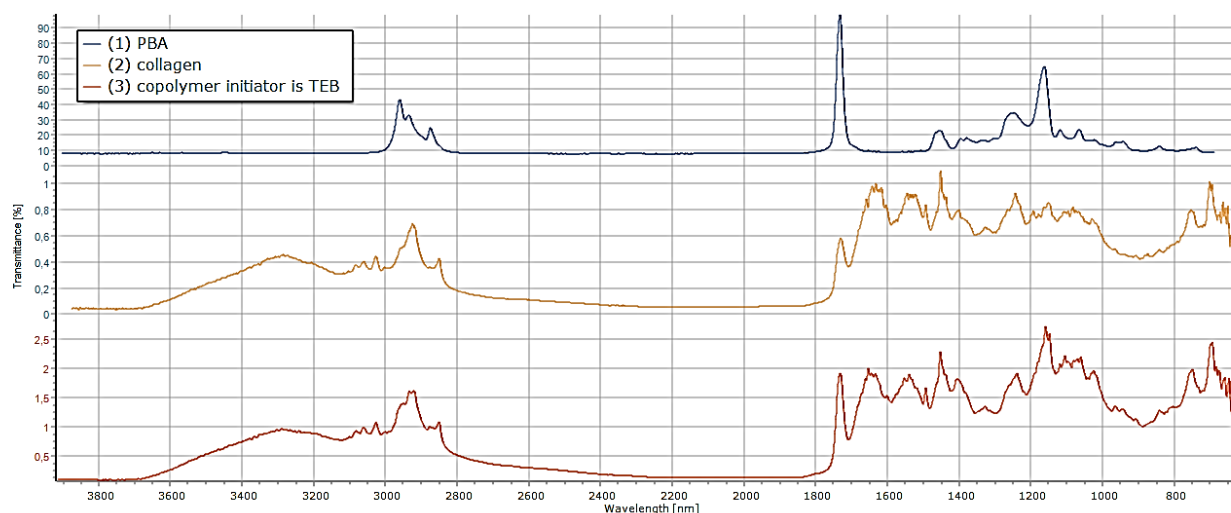


Fig. 4. Collagen (1) weight distribution and copolymer of collagen and butyl acrylate in the presence of azobisisobutyronitrile (2)

Рис. 4. Молекулярно-массовое распределение коллагена (1) и сополимера коллагена и бутилакрилата в присутствии динитрила азоизомасляной кислоты (2)

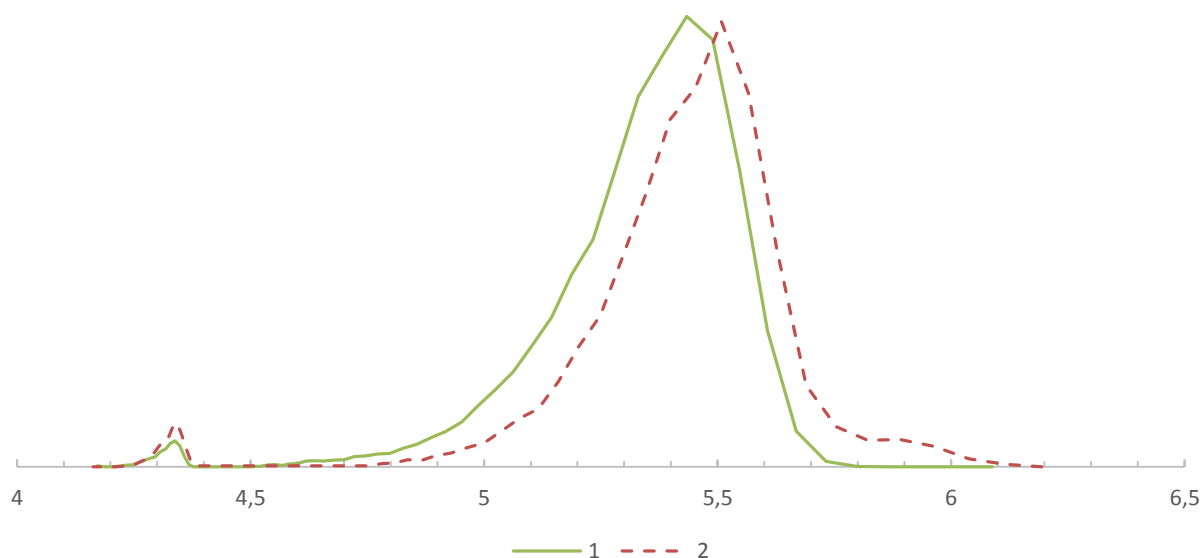


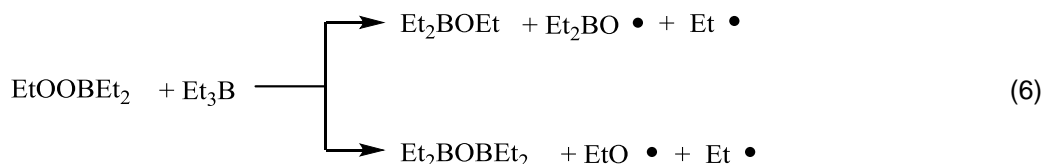
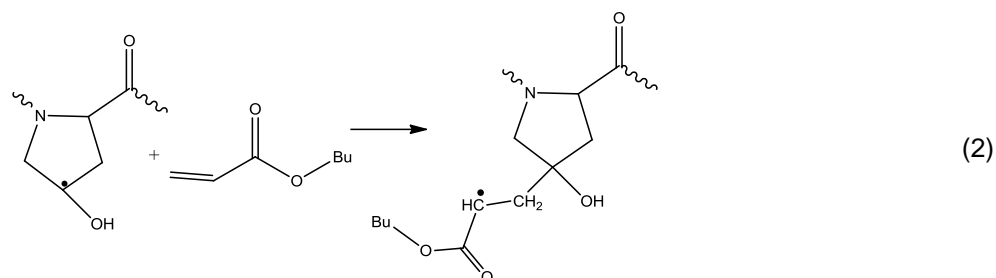
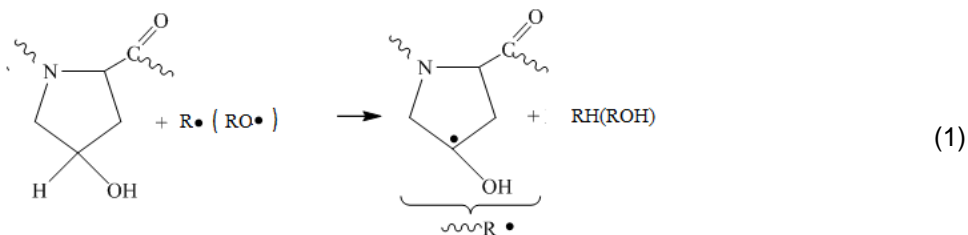
Fig. 5. Collagen (1) weight distribution and copolymer of collagen and BA in the presence of the system triethyl borane – oxygen (2)

Рис. 5. Молекулярно-массовое распределение коллагена (1) и сополимера коллагена и БА в присутствии системы триэтилборан – кислород (2)

Collagen molecular weight characteristics and copolymers of collagen and butyl acrylate in the presence of azobisisobutyronitrile and the system triethyl borane – oxygen

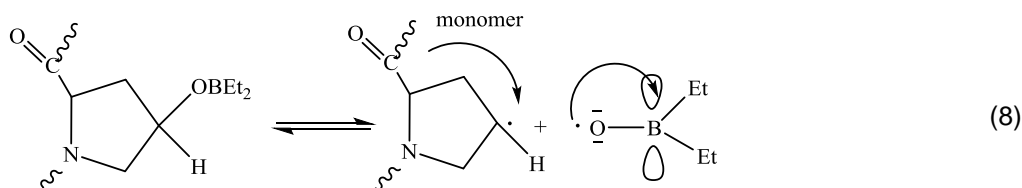
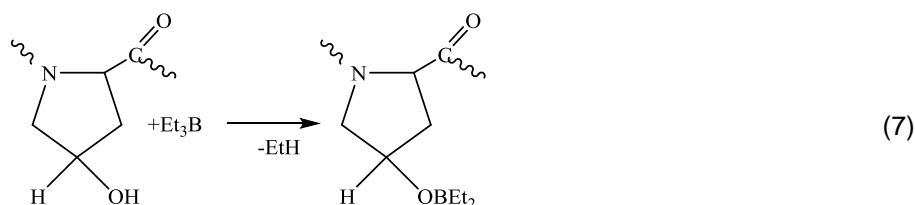
Молекулярно-массовые характеристики коллагена и сополимеров коллагена и бутилакрилата в присутствии динитрила азоизомасляной кислоты и системы триэтилборан – кислород

Polymer	MWD		
	$M_n \cdot 10^{-3}$	$M_w \cdot 10^{-3}$	M_w/M_n
Collagen	182	228	1.3
Copolymer with azobisisobutyronitrile initiator	189	238	1.3
Copolymer with the system triethyl borane – oxygen initiator	239	291	1.2



However, when the TEB – oxygen system initiates the interaction of TEB with collagen (7) or a boroxyl radical formed according to the scheme: (6)

with a growing radical, a labile bond is formed, along which the growth of the chain can pass through the mechanism of reversible inhibition (8) [21, 22].



Chain breakage by quadratic breakage of growing radicals leads to breakage of the polymer chain.

CONCLUSION

Grafted collagen copolymers with polybutyl acrylate were obtained in the aqueous phase of dispersion of aqueous collagen solution and butyl acrylate at initiation of AIBN and TEB – oxygen initiation system. The copolymers were characterized on the

composition and molecular weight parameters using IR spectroscopy and SEC. In case of the TEB – oxygen system, butylacrylate grafting is more pronounced. The scheme for the formation of copolymer macromolecules to organoelement and AIBN initiator were proposed.

These compositions can be used as mushroom resistant and bactericidal materials.

REFERENCES

1. Radhika Rajasree SR, Gobalakrishnan M, Aranganathan L, Karthih MG. Fabrication and characterization of chitosan based collagen gelatin composite scaffolds from big eye snapper *Priacanthus hamrur* skin for antimicrobial and anti oxidant applications. *Materials Science and Engineering: C*. 2020;107:110270. <https://doi.org/10.1016/j.msec.2019.110270>
2. Pattanaik SS, Sawant PB, Xavier KAM, Dube K, Srivastava PP, Dhanabalan V, et al. Characterization of carotenoprotein from different shrimp shell waste for possible use as supplementary nutritive feed ingredient in animal diets. *Aquaculture*. 2020;515: 734594. <https://doi.org/10.1016/j.aquaculture.2019.734594>
3. Dale HF, Madsen L, Lied GA. Fish-derived proteins and their potential to improve human health. *Nutrition Reviews*. 2019;77(8):572–583. <https://doi.org/10.1093/nutrit/nuz016>
4. Eshar D, Wyre NR, Schoster JV. Use of collagen shields for treatment of chronic bilateral corneal ulcers in a pet rabbit. *Journal of Small Animal Practice*. 2011;52(7):380–383. <https://doi.org/10.1111/j.1748-5827.2011.01077.x>
5. Greenwald Y, Kleinmann G. Use of collagen shields for ocular-surface drug delivery. *Expert Review of Ophthalmology*. 2008;3(6):627–633. <https://doi.org/10.1586/17469899.3.6.627>
6. Fitzpatrick SD, Mazumber MAJ, Lasowski F, Fitzpatrick LE, Sheardown H. PNIPAAm-grafted-collagen as an injectable, in situ gelling cell delivery scaffold. *Biomacromolecules*. 2010;11(9):2261–2267. <https://doi.org/10.1021/bm100299j>
7. Ma Z, Gao C, Gong Y, Shen J. Cartilage tissue engineering PLLA scaffold with surface immobilized collagen and basic fibroblast growth factor. *Biomaterials*. 2005;26(11):1253–1259. <https://doi.org/10.1016/j.biomaterials.2004.04.031>
8. Muthukumar T, Sreekumar G, Sastry TP, Chamundeeswari M. Collagen as a potential biomaterial in biomedical applications. *Reviews on Advanced Materials Science*. 2018;53(1):29–39. <https://doi.org/10.1515/rams-2018-0002>
9. Khanna ND, Kaur I, Bhalla TC, Gautam N. Effect of biogradation on thermal and crystalline behavior of polypropylene-gelatin based copolymers. *Journal of Applied Polymer Science*. 2010;118(3): 1476–1488. <https://doi.org/10.1002/app.32434>
10. Bas O, de Juan-Pardo EM, Chhaya MP, Wunner FM, Jeon JE, Klein TJ, et al. Enhancing structural integrity of hydrogels by using highly organised melt electrospun fibre constructs. *European Polymer Journal*. 2015;72:451–463. <https://doi.org/10.1016/j.eurpolymj.2015.07.034>
11. Ohya S, Matsuda T. Poly(N-iso-propylacrylamide) (PNIPAM)-grafted gelatin as thermoresponsive three-dimensional artificial extracellular matrix: Molecular and formulation parameters vs. cell proliferation potential. *Journal of Biomaterials Science, Polymer Edition*. 2005;16(7):809–827. <https://doi.org/10.1163/1568562054255736>
12. Kojima K, Iguchi S, Kajima Y, Yoshikuni M. Grafting of methyl methacrylate onto collagen initiated by tributylborane. *Journal of Applied Polymer Science*. 1983;28(1):87–95. <https://doi.org/10.1002/app.1983.070280108>
13. Ollivier C, Renaud P. Organoboranes as a source of radicals. *Chemical Reviews*. 2001;101(11): 3415–3434. <https://doi.org/10.1021/cr010001p>
14. Fujisawa S, Yoshinori K. Tri-n-butylborane/watercomplex-mediated copolymerization of methyl methacrylate with proteinaceous materials and proteins: A review. *Polymers*. 2010;2(4):575–595. <https://doi.org/10.3390/polym2040575>
15. Mirviss SB. The air oxidation of trialkylboranes. *Journal of the American Chemical Society*. 1961;83(14):3051–3056. <https://doi.org/10.1021/ja01475a020>
16. Kuznetsova YuL, Abramova NA, Ludin DV. Synthesis of copolymers of methyl methacrylate and butyl vinyl ether in the presence of the system tributylboron – 2,5-di-tert-butyl-p-benzoquinone. *Bulletin of the South Ural State University. Ser. Chemistry*. 2016;8(1):26–33. <https://doi.org/10.14529/chem160104>
17. Kuznetsova YuL, Morozova EA, Vavilova AS, Markin AV, Smirnova ON, Zakharycheva NS, et al. Synthesis of biodegradable grafted copolymers of gelatin and polymethyl methacrylate. *Polymer Science. Series D*. 2020;13:453–459. <https://doi.org/10.1134/s1995421220040115>
18. Semenycheva LL, Astanina MV, Kuznetsova YuL, Valetova NB, Geraskina EV, Tarankova OA. A method for obtaining a vinegar dispersion of high molecular weight fish collagen. Patent RF, no. 2567171; 2014. (In Russian)
19. Zimmermann B, Baranović G. Thermal analysis of paracetamol polymorphs by FT-IR spectroscopies. *Journal of Pharmaceutical and Biomedical Analysis*. 2011;54(2):295–302. <https://doi.org/10.1016/j.jpba.2010.08.023>
20. Okamura H, Sudo A, Endo T. Generation of radical species on polypropylene by alkylborane-oxygen system and its application to graft polymerization. *Journal of Polymer Science: Part A: Polymer Chemistry*. 2009;48(22):6163–6167. <https://doi.org/10.1002/pola.23659>
21. Semenycheva LL, Matkivskaia YO, Valetova NB, Chasova YO, Peguev NL, Eloyan AL, et al. Specific features of “compensating” copolymerization of butyl acrylate with vinyl butyl ether in the presence of triethylboron. *Russian Chemical Bulletin*. 2017;66(9): 1660–1664. <https://doi.org/10.1007/s11172-017-1938-x>
22. Chung T-C, Janvikul W, Lu HL. A novel “stable” radical initiator based on the oxidation adducts of alkyl-9-BBN. *Journal of the American Chemical Society*. 1996;118(3):705–706. <https://doi.org/10.1021/ja9527737>

СПИСОК ЛИТЕРАТУРЫ

1. Rajasree S.R.R., Gobalakrishnan M., Aranganathan L., Karthih M.G. Fabrication and characterization of chitosan based collagen gelatin composite scaffolds from big eye snapper *Priacanthus hamrur* skin for antimicrobial and anti oxidant applications // *Materials Science and Engineering: C*. 2020. Vol. 107. 110270. <https://doi.org/10.1016/j.msec.2019.110270>
2. Pattanaik S.S., Sawant P.B., Xavier K.A.M., Dube K., Srivastava P.P., Dhanabalan V., et al. Characterization of carotenoprotein from different shrimp shell waste for possible use as supplementary nutritive feed ingredient in animal diets // *Aquaculture*. 2020. Vol. 515. 734594. <https://doi.org/10.1016/j.aquaculture.2019.734594>
3. Dale H.F., Madsen L., Lied G.A. Fish-derived proteins and their potential to improve human health // *Nutrition Reviews*. 2019. Vol. 77. Issue 8. P. 572–583. <https://doi.org/10.1093/nutrit/nuz016>
4. Eshar D., Wyre N.R., Schoster J.V. Use of collagen shields for treatment of chronic bilateral corneal ulcers in a pet rabbit // *Journal of Small Animal Practice*. 2011. Vol. 52. Issue 7. P. 380–383. <https://doi.org/10.1111/j.1748-5827.2011.01077.x>
5. Greenwald Y., Kleinmann G. Use of collagen shields for ocular-surface drug delivery // *Expert Review of Ophthalmology*. 2008. Vol. 3. Issue 6. P. 627–633. <https://doi.org/10.1586/17469899.3.6.627>
6. Fitzpatrick S.D., Mazumber M.A.J., Lasowski F., Fitzpatrick L.E., Sheardown H. PNIPAAm-grafted-collagen as an injectable, in situ gelling cell delivery scaffold // *Biomacromolecules*. 2010. Vol. 11. Issue 9. P. 2261–2267. <https://doi.org/10.1021/bm100299j>
7. Ma Z., Gao C., Gong Y., Shen J. Cartilage tissue engineering PLLA scaffold with surface immobilized collagen and basic fibroblast growth factor // *Biomaterials*. 2005. Vol. 26. Issue 11. P. 1253–1259. <https://doi.org/10.1016/j.biomaterials.2004.04.031>
8. Muthukumar T., Sreekumar G., Sastry T.P., Chamundeeswari M. Collagen as a potential biomaterial in biomedical applications // *Reviews on Advanced Materials Science*. 2018. Vol. 53. Issue 1. P. 29–39. <https://doi.org/10.1515/rams-2018-0002>
9. Khanna N.D., Kaur I., Bhalla T.C., Gautam N. Effect of biogradation on thermal and crystalline behavior of polypropylene-gelatin based copolymers // *Journal of Applied Polymer Science*. 2010. Vol. 118. Issue 3. P. 1476–1488. <https://doi.org/10.1002/app.32434>
10. Bas O., de Juan-Pardo E.M., Chhaya M.P., Wunner F.M., Jeon J.E., Klein T.J., et al. Enhancing structural integrity of hydrogels by using highly organised melt electrospun fibre constructs // *European Polymer Journal*. 2015. Vol. 72. P. 451–463. <https://doi.org/10.1016/j.eurpolymj.2015.07.034>
11. Ohya S., Matsuda T. Poly(N-isopropylacrylamide) (PNIPAM)-grafted gelatin as thermorespon-
sive three-dimensional artificial extracellular matrix: Molecular and formulation parameters vs. cell proliferation potential // *Journal of Biomaterials Science, Polymer Edition*. 2005. Vol. 16. Issue 7. P. 809–827. <https://doi.org/10.1163/1568562054255736>
12. Kojima K., Iguchi S., Kajima Y., Yoshikuni M. Grafting of methyl methacrylate onto collagen initiated by tributylborane // *Journal of Applied Polymer Science*. 1983. Vol. 28. Issue 1. P. 87–95. <https://doi.org/10.1002/app.1983.070280108>
13. Ollivier C., Renaud P. Organoboranes as a source of radicals // *Chemical Reviews*. 2001. Vol. 101. Issue 11. P. 3415–3434. <https://doi.org/10.1021/cr010001p>
14. Fujisawa S., Yoshinori K. Tri-n-butylborane/watercomplex-mediated copolymerization of methyl methacrylate with proteinaceous materials and proteins: A review // *Polymers*. 2010. Vol. 2. Issue 4. P. 575–595. <https://doi.org/10.3390/polym2040575>
15. Mirviss S.B. The air oxidation of trialkylboranes // *Journal of the American Chemical Society*. 1961. Vol. 83. Issue 14. P. 3051–3056. <https://doi.org/10.1021/ja01475a020>
16. Kuznetsova Yu.L., Abramova N.A., Ludin D.V. Synthesis of copolymers of methyl methacrylate and butyl vinyl ether in the presence of the system tributylboron – 2,5-di-tert-butyl-p-benzoquinone // *Bulletin of the South Ural State University. Ser. Chemistry*. 2016. Vol. 8. Issue 1. P. 26–33. <https://doi.org/10.14529/chem160104>
17. Kuznetsova Yu.L., Morozova E.A., Vavilova A.S., Markin A.V., Smirnova O.N., Zakharycheva N.S., et al. Synthesis of biodegradable grafted copolymers of gelatin and polymethyl methacrylate // *Polymer Science. Series D*. 2020. Vol. 13. P. 453–459. <https://doi.org/10.1134/s1995421220040115>
18. Пат. № 2567171, Российская Федерация. Способ получения уксусной дисперсии высокомолекулярного рыбьего коллагена / Л.Л. Семеньева, М.В. Астанина, Ю.Л. Кузнецова, Н.Б. Валетова, Е.В. Гераскина, Таранкова О.А.; патентообладатель ООО «Системы качества жизни»; заявл. 06.10.2014; опубл. 10.11.2015. Бюл. 31.
19. Zimmermann B., Baranović G. Thermal analysis of paracetamol polymorphs by FT-IR spectroscopies // *Journal of Pharmaceutical and Biomedical Analysis*. 2011. Vol. 54. Issue 2. P. 295–302. <https://doi.org/10.1016/j.jpba.2010.08.023>
20. Okamura H., Sudo A., Endo T. Generation of radical species on polypropylene by alkylborane-oxygen system and its application to graft polymerization // *Journal of Polymer Science: Part A: Polymer Chemistry*. 2009. Vol. 48. Issue 22. P. 6163–6167. <https://doi.org/10.1002/pola.23659>
21. Semenycheva L.L., Matkivskaia Y.O., Valetova N.B., Chasova Y.O., Pegeev N.L., Eloyan A.L., et al. Specific features of “compensating” copolymerization of butyl acrylate with vinyl butyl ether in the presence of triethylboron // *Russian Chemical*

Bulletin. 2017. Vol. 66. Issue 9. P. 1660–1664.
<https://doi.org/10.1007/s11172-017-1938-x>

22. Chung T.-C., Janvikul W., Lu H.L. A novel “stable” radical initiator based on the oxidation ad-

ducts of alkyl-9-BBN // Journal of the American Chemical Society. 1996. Vol. 118. Issue 3. P. 705–706. <https://doi.org/10.1021/ja9527737>

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