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The effect of drying and shelf life on the biological properties of chitosan composites containing enzymes and various therapeutic agents

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Abstract

One of the ways of development of pharmaceutical science is the design and introduction into medical practice new highly effective drugs for the treatment and prevention of wound healing. Selective accumulation of drugs in the lesion allows to solve several problems at the same time: increase the effectiveness of the drug, reduce its consumption, eliminate the undesirable effects of the drug on healthy organs and tissues. One of the problems in the modification of the therapeutic agent polymer is the loss of biological activity immediately after modification or during storage (during storage of chitosan films in the air can occur keratinization (acylation), or during operation (liquid medium, pH and temperature 37 °C).

The effect of different concentrations of chitosan on the preservation of enzymatic activity of a number of proteases (trypsin, chymopsin, bromelain, proteolytic complex of crab hepatopancreas) both in the process of obtaining composites and after drying and storage was studied. The multidirectional action of different polymers on the only one enzyme and on the single polymer on different enzymes was established.

The decrease of enzymatic activity in the process of drying immobilized (stabilized) enzymes during storage (at room temperature) and thermal inactivation in solution under physiological conditions was established. The multidirectional action of inactivation factors on the enzymes and their immobilized (stabilized) forms was shown. During the storage of immobilized materials based on chitosan solid-phase modification of chitosan-containing derivatives occurs. It has been established that neither chitosan nor the enzymes used affect the biocidal properties of Miramistin.

References

[1] A method for producing a medical film based on chitosan (variants). *RF Patent RU 2 429 022 C1*
[2] S.G. Shapovalov. Modern wound coverings in kombustiologii. *FAR Mindeks-Praktik.* **2008**. No.8. P.38-46. (russian)
[3] A.A. Belov. Development of industrial technologies for the production of new medical materials based on modified fiber-forming polymers containing biologically active protein substances. *Diss. on sos. the scientific step. doct. technical. Moscow: RHTU.* **2009**. P.385. (russian)
[4] E. Dosadina, L.L. Brkich, N.V. Pyatigorskaya, M.A. Bikineeva, A.Y. Evdokimenko, E.E. Savelyeva, E.O. Medusheva, A.S. Kulagina, L.A. Pavlova, and A.A. Belov. Use of chitosan as a carrier for proteinases and Miramistin for obtaining of enzyme-containing gel. *Butlerov Communications.* **2016**. Vol.48. No.10. P.49-59. DOI: 10.37952/ROI-jbc-01/16-48-10-49
[5] M.V. Pogorelov, O.V. Kalinkevich, T.V. Ivakhnyuk et al. Experimental substantiation of the use of a gel based on chitosan acetate for the treatment of burns. *Russian Medical Biological Herald. acad. I.P. Pavlova.* **2012**. No.4. P.34-44. (russian)
[6] K.G. Skryabin, G.A.Vikhorevaya, V.P. Varlamov. Chitin and chitosan. Reception, properties and application. *Moscow: Science.* **2002**. 368p. (russian)
[7] S.P. Miranda Castro, E.G. Lizarraga. Paulin Is Chitosan a New Panacea? Areas of Application. *Desiree Nedra Karunaratne "The Complex World of Polysaccharides" (Chapter 1)– InTech.* **2012**. P.3-46.

[8] A.A. Grishin, N.V. Zorina, V.I. Lutsky. Chitin and chitosan: chemistry, biological activity, application. *Izvestiya VUZov. Applied Chemistry and Biotechnology.* **2014**. No.1(6). P.29-34. (russian)
[9] M. Sato, H. Onishi, J. Takahara, et al. In vivo drug release and antitimor characteristics of water-soluble conjugates of mitomycin C with glycol-chitosan and *N*-succinil-chitosan *Biol. Pharm. Bull*. **1996**. Vol.19. No.9. P.1170 -1177.
[10] Bychuk M.A. Acquisition and properties of polymer films based on poly-3-hydroxybutyrate and poly-ε-caprolactone Diss. on sos. the scientific step. doctor tech. *Moscow: MSUDT.* **2016**. P.169.
[11] A.A. Belov, A.I. Korotaeva, E.E. Dosadina, O.E. Malenko, and M.A. Kulemetieva. Medical materials based on modified cellulose, chitosan and multienzyme complex. *Butlerov Communications.* **2014**. Vol.38. No.4. P.42-47. ROI: jbc-02/14-38-4-42
[12] E.E. Dosadina, M.A. Bikineeva, A.Y. Evdokimenko, E.E. Savelyeva, E.O. Medusheva, and A.A. Belov. Immobilization of proteinases of proteolytic complex of hepatopancreas of crab on some polysaccharides: production, properties, application. *Butlerov Communications.* **2016**. Vol.48. No.12. P.83-93. DOI: 10.37952/ROI-jbc-01/16-48-12-83
[13] L.A. Nudga, V.A. Petrova, I.V. Gofman et al. Chemical and structural transformations in chitosan films during storage of *LPG*. **2008**. Vol.81. Iss.11. P.1877-1881. (russian)
[14] Methods of optical spectroscopy Ed. Kulakova I.I., Fedorova O.A., Horoshutina A.V. *MSU.* **2015**. P.117. (russian)
[15] E.E. Dosadina, A.A. Belov. Interaction between chitosan solutions, cellulose carriers and some of the multi-enzyme complexes. *International Journal of Bioorganic Chemistry.* **2017**. Vol.2. No.2. P.51-60. doi: 10.11648/j.ijbc.20170202.12
[16] E.E. Dosadina, M.A. Kulmetyeva, A.A. Belov. The changing of enzymatic activity of hydrolases immobilized on natural polysaccharide matrix for purulent and burn wounds treatment during storing and exploitation. *Biointerface research in applied chemistry.* **2016**. Vol.6. Iss.3. P.1291-1298.
[17] Barbara Krajewska. Application of chitin- and chitosan-based materials for enzyme immobilizations: a review. *Enzyme and Microbial Technology.* **2004**. Vol.35. P.126-139.
[18] G.N. Rudenskaya, V.A. Isaev, A.M. Shmoylov et al. Preparation of proteolytic enzymes from kamchatka crab paralithodes camchatica hepatopancreas and their application. *App.Biochem.Biotech.* **2000**. Vol.22. P.175-184.
[19] V.V. Mosolov. Proteolytic enzymes. *Moscow: Nauka.* **1971**. 414p. (russian)
[20] A.V. Blednov. Immobilized enzymes and antiseptics in complex treatment of purulent wounds (Clinical and experimental research) The dissertation author's abstract on competition of a scientific degree of the candidate of medical sciences. *Minsk.* **2007**. P.23.
[21] Marguerite Rinaudo. Chitin and chitosan: Properties and applications. *Prog. Polym. Sci.* **2006**. Vol.31. P.603-632.
[22] A.B. Shipovskaya, I.V. Zudina, V.I. Fomina, and O.N. Malinkina. Novel antimicrobial drugs based on complex chitosan salts with chiral organic ligands. *Butlerov Communications.* **2015**. Vol.41. No.3. P.82-94. DOI: 10.37952/ROI-jbc-01/15-41-3-82
[23] Tamer M. Tamer, Mohamed A. Hassan, Ahmed M. Omer et al. Synthesis, characterization and antimicrobial evaluation of two aromatic chitosan Schiff base derivatives. *Process Biochemistry.* **2016**. Vol.51. Iss.10. P.1721-1730.