ANNOTATION

of the dissertation for the degree of Doctor of Philosophy (PhD) in the specialty 6D072100 - «Chemical Technology of Organic Substances»

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On the topic: «Development of hydrogel forms of antiseptic and antibacterial disinfectants».

The relevance of the problem. An analysis of the consequences of the outbreak of the mutagenic coronavirus infection Covid-19 shows that they turned out to be so serious and severe that we should talk about a global epidemiological crisis that has engulfed almost the entire planet, which has rapidly acquired global proportions and posed numerous challenges to the world community. At the same time, according to the world's leading virologists and epidemiologists, most likely the epidemiological crisis "Covid-19", which the world faced in 2020, was far from the last, moreover, such outbreaks of viral infection can acquire a seasonal character. The current reality shows the correctness of such assumptions.

In this regard, the issue of developing adequate protection measures is of particular relevance. This circumstance highlights the need to expand the range of preventive means to protect the population from new threats, including including a set of sanitary and hygienic and anti-epidemic measures aimed at preventing infectious diseases in general.

To date, the leading disinfection method is chemical, based on the use of DS, which are based on active active substances - biocides or disinfectants, which actually determine the antimicrobial activity of DS.

The purpose of the thesis research

The purpose of the dissertation research is to create hydrogel forms of the broad-acting antiseptic chlorhexidine bigluconate and the antibiotic gentamicin using poly-N-vinylpyrrolidone, gellan as gel-forming polymers, as well as hybrid thermosensitive pH-dependent copolymers based on N,N-dimethylacrylamide and acrylic acid.

Research objectives:

- investigation of the basic laws of the synthesis of polymer hydrogels in the process of radiation three-dimensional polymerization of N-vinylpyrrolidone in the presence of a crosslinking agent and the physico-chemical properties of the crosslinking polymers formed in this case;
- development of laboratory technology for the production of hydrogel ointments and dressings based on poly-N-vinylpyrrolidone containing the antiseptic chlorhexidine bigluconate;
- the study of phase transitions in aqueous solutions of gellan under the action of additives of low molecular weight salts, the study of the physico-chemical properties of the hydrogels formed at the same time, the development of antiseptic ointments based on them
- synthesis and investigation of physico-chemical properties of hybrid thermosensitive pH-dependent copolymers based on N,N-dimethylacrylamide (DMA) and acrylic acid (AK);

- biomedical investigation of the obtained hydrogel forms of chlorhexidine bigluconate and gentamicin

Research methods: Fourier transform infrared spectroscopy, UV and visible spectroscopy, elemental analysis, turbidimetry, gravimetry, deformation and mechanical testing of hydrogels, scanning electron microscopy, rotational viscometry, rheology.

Objects of research: hydrogels based on poly-N-vinylpyrrolidone, gellan and copolymers N,N-dimethylacrylamide and acrylic acid;

Subject of research: radiation three-dimensional polymerization of VP; physico-chemical properties and structural parameters of hydrogels formed in the processes of three-dimensional polymerization of VP and radiation crosslinking of PVP; gelation in aqueous solutions of gellan under the action of additives of low molecular weight salts; stimulus-sensitive behavior of water-soluble and water-swelling copolymers DMA-AK; biomedical properties of hydrogel ointments and dressings based on PVP, gellan and DMA-AK copolymer containing HCG or gentamicin.

The main provisions submitted for protection:

- antiseptic hydrogel ointments and bandages containing chlorhexidine bigluconate (HCG) with anti-inflammatory and wound healing activity can be obtained using three-dimensional radiation polymerization of N-vinylpyrrolidone monomer or radiation crosslinking of poly-N-vinylpyrrolidone macromolecules
- antiseptic hydrogel ointments with pronounced antifungal and antibacterial activity can be obtained on the basis of chlorhexidine bigluconati and gellan hydrogel formed during the phase transition in its aqueous solution under the influence of additives HCG and sodium thiosulfate
- the presence of ionic and hydrophobic components in the structure of water-soluble and water-swelling copolymers DMA-AK determines their sensitivity to the effects of both temperature and pH of the medium, manifested in the ability to phase transitions when exposed to these two parameters

The main results of the study:

1. The formation of polymer hydrogels in the process of radiation three dimensional radical polymerization of N-vinylpyrrolidone (VP) using N,N'-methylene bis-acrylamide as a crosslinking agent (CA) was studied. It is shown that an increase in the radiation dose and the concentration of the crosslinking agent in the initial monomer mixture (IMS) is accompanied by an increase in the yield of the gel fraction and the modulus of elasticity of the formed gels, the equilibrium degree of swelling in the water of which decreases. It was also found that when diluting IC with water, an abnormal effect of increasing the yield of the gel fraction is observed, due to an increase in the rate of three-dimensional polymerization due to an increase in the activity of VP molecules in radical polymerization.
2. On the basis of PVP hydrogels formed during radiation three-dimensional polymerization, a laboratory technology for the production of hydrogel ointments

containing the antiseptic chlorhexidine bigluconate has been developed, for which biomedical animal tests have been conducted. It has been established that the developed hydrogel ointments containing HCG, due to their antibacterial and fungicidal properties in combination with high drainage ability, have pronounced anti-inflammatory and wound healing activities

3. A laboratory technology for the production of hydrogel dressings based on PVP containing the antiseptic chlorhexidine bigluconate has been developed. The technology includes radiation crosslinking of PVP macromolecules with a high molecular weight, which makes it possible to combine two operations in one technological stage: the formation of a finished product (hydrogel dressing) and its sterilization. As a result of bio-medical studies conducted in "in vivo" conditions, it was found that the obtained hydrogel dressings, due to their antibacterial and fungicidal properties, combined with high drainage ability, have pronounced anti-inflammatory and anti-burn activities
4. A laboratory technology has been developed for the production of a hydrogel ointment based on gellan containing a broad-acting antiseptic HCG. In this case, gellan hydrogel was used, formed during the phase separation of its aqueous solution under the action of additives of HCG and sodium thiosulfate. For antiseptic hydrogel ointments containing HCG, as a result of the conducted biomedical studies, their pronounced antifungal and antibacterial activity has been established
5. In order to obtain new hybrid thermosensitive pH-dependent polymers, linear and three-dimensional radical copolymerization of N,N-dimethylacrylamide (DMA) and acrylic acid (AC) was carried out. It was found that the obtained copolymers (CPL) are simultaneously sensitive to changes in pH and temperature of the surrounding solution. Thermally induced continuous coldup is observed for DMA-AK mesh SPL, the parameters of which are regulated by changes in the composition of the SPL and the pH of the medium. It is shown that the temperature dependence curves of SPL DMA-AK hydrogels can have a complex form, including the stages of swelling and contraction, due to the presence of ionic and hydrophobic components in the structure of the obtained hydrogels.

6. Biomedical studies of the antibacterial activity of SPL DMA-AK hydrogels containing the antibiotic gentamicin were conducted using the test bacteria. It was found that the antibiotic diffuses well into the environment from hydrogel carriers, suppressing the growth of test microorganisms and creating a lysis zone around the carrier with antibiotics, which indicates a well-expressed ability of hydrogels to deliver drugs.

Tests of hydrogel ointments based on PVP and gellan for antiseptic and disinfection treatment have been carried out in medical institutions. It has been shown that hydrogel ointments, creating a protective film on the surface of equipment or rigid furniture for a long time (at least three days), are active in infections of bacterial, viral, fungal etiology. When used for antiseptic treatment of the hands of medical personnel, unlike other antiseptic agents, hydrogel ointments based on gellan with chlorhexidine biglucanate and sodium thiosulfate do not cause dry skin of the hands and any allergic reactions. The obtained test results indicate

the high efficiency and prospects of practical use of hydrogel ointments containing HCG in medical institutions as antiseptic and disinfectants.

Substantiation of the novelty and importance of the results obtained.

Results 1-6 are characterized by novelty and significance, since they were obtained for the first time and are aimed at realizing the main goal of the dissertation work on the creation of hydrogel forms of the broad-acting antiseptic chlorhexidine bigluconate and the antibiotic gentamicin using polymers of various nature.

Theoretical significance of the results. The results of the study of the physico-chemical behavior of DMA-AK copolymers of linear and mesh structure and phase transitions with their participation induced by the influence of temperature and pH of the medium make a significant contribution to the development of theoretical ideas about the features of macromolecular design and functioning of stimulus-sensitive polymers.

Practical significance of the results.

The hydrogel ointments and dressings based on PVP and gellan obtained in the work can be recommended as effective antiseptic, antibacterial, disinfectants and wound healing agents.

Approbation of the work. The main results of the dissertation were reported and discussed at the III International Scientific and Practical Conference "Research and Development in promising scientific fields" (Novosibirsk, Russia, 2018), at the International Scientific Conference of Students and Young Scientists "FARABI ALEMI" (Almaty, Kazakhstan, 2018), at the Uzbek-Kazakh Symposium "Modern Problems Polymer Sciences", (Tashkent, Uzbekistan, 2020), at the International Symposium "Science, Education, Innovation: Global Trends and Regional Aspects", dedicated to the 80th anniversary of the birth of Academician E.E. Ergozhin (G. Almaty, Kazakhstan, 2021), at the 22nd International Conference on Science and Technology Russia-Korea-CIS (Moscow, Russia, 2022).

The personal contribution of the author

The author's personal contribution consists in the direct execution of the experimental part of the work, participation in the analysis, discussion and interpretation of the experimental data obtained.

Publications. 1 Myltykbaeva Zh.K., Kairbekov Zh., Asanov M.K., Kovaleva G.G. Studies of the effectiveness of the disinfectant "Zhusan Formin" // KBTU Khabarshysy. - 2018, Vol. 15, Issue 1., pp. 53-59.

2 Myltykbaeva Zh.K., Asanov M.K., Kovaleva G.G. Evaluation of the effectiveness and safety of the disinfectant “Zhusan Mega" // Bulletin of KazNITU. 2019 No3 pp.53-58.

3 Kovaleva G.G., Myltykbaeva Zh.K., Asanov M.K. Smile M, Turegeldieva G., Smile M// Effectiveness of a disinfectant containing amines and chlorine on spore-forming microorganisms // Bulletin of PSU, Chemical and Biological series, - 2019. - No. 2. - pp. 19-27.

4 U. Nakan, SH. Bieerkehazhi, B. Tolkyn, Grigoriy A. Mun, Assanov M., Merey E. Nursultanov, Raikhan K. Rakhmetullayeva, K.Toshtay, El-Sayed Negim and A. Ydyrys. Synthesis, Characterization and Antibacterial Application of

Copolymers Based on N,N-Dimethyl Acrylamide and Acrylic Acid. Materials 2021, 14, 6191, P 1-12. , Q2 (Wos and Scopus), IF=3,748 (WoS); Percentile 55 (Scopus), https://doi.org/10.3390/ma14206191.

5 Kim K.I., Mangazbaeva R.A., Asanov M.K., Ermukhambetova B.B., Alikulov A.J., Balabaeva A.M., Zezin A.A. Creation of antiseptic ointments based on gellan hydrogels and chlorhexidine bigluconate // Proceedings of the scientific and technical society "KAHAK". - 2023. - No. 2 (80). – pp. 48-73.

6 Myltykbaeva Zh.K., Asanov M.K., Kovaleva G.G. Production of disinfectants as a component of infectious safety // Materials of the III International Conference "Research and Development in promising scientific fields". - Novosibirsk, January 23, February 21, 2018 From-13-17 5 .

7 Asanov M.K. Myltykbayeva Zh.K., Evaluation of the effectiveness of the disinfectant "Zhusan Formin" // Collection of abstracts of the International scientific Conference of students and young scientists "Farabi alemi", Almaty, 2018. p. 274.

The structure and scope of the thesis. The dissertation is presented on 127 pages of typewritten text and includes an introduction, 3 sections, conclusion, 25 tables, 63 figures and a list of used sources from the titles.

Compliance of the work with priority areas of science development or state programs. The work was carried out in the priority area "Rational use of natural resources, including water resources, geology, processing, new materials and technologies, safe products and structures" within the framework of the Target scientific and technical Program BR05236419 "Creation of functionalized organic substances and materials with a wide range of possible highly effective practical applications (2018-2020).

Description of the doctoral student's contribution to the preparation of each publication.

The main materials of the dissertation work are published in scientific publications in the form of 5 scientific articles. When preparing each publication, M.K. Asanov carried out a large amount of work personally on the analysis of scientific and patent literature on the topic of publications, the synthesis and development of necessary polymers and polymer hydrogels was carried out, direct participation in all experiments and research, processing, analysis and interpretation of the results obtained, writing and preparing the initial version of the article, preparing responses to reviewers' comments, further revision and editing until the article is fully accepted for publication.