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[1]Kuanova A.O., [1*]Nurpeissova Zh.A., [1]Mangazbayeva R.A., [2]Park K.

[1]Al-Farabi Kazakh National University, Almaty, Kazakhstan
[2]Purdue University, Department of Pharmaceutics, West Lafayette, USA
[*]e-mail: zhansaya0406@mail.ru

The obtaining of composite materials based on carboxymethylcellulose and polyvinyl alcohol

Abstract. In this work, hydrogels based on carboxymethylcellulose (CMC) and polyvinyl alcohol (PVA) by the method of radiation crosslinking were obtained. The presence of absorption bands of hydroxyl, simple ether and carbonyl groups in the hydrogel compositions by FTIR spectroscopy method was revealed. Also, the presence of both components CMC and PVA in hydrogel composits was proved. The kinetics of swelling of composite materials based on CMC/PVA with different volumetric ratios was studied. The influence of absorbed dose on the degree of swelling and gel contents was determined. Also, in this work the morphology of hydrogels by scanning electron microscopy (SEM) were studied. Also, optimum conditions the possibility of use as a drug carrier have been defined. Technological scheme of the obtained composite materials based on CMC/PVA was development.

Key words: carboxymethylcellulose, polyvinyl alcohol, hydrogel, radiation crosslinking, composite material.

Introduction

Currently, polymeric materials based on the natural polysaccharides and synthetic polymers find more and more broad application in the most various areas of the industry, such as pharmaceutical industry, medicine, agriculture. In this regard, the increasing value is gained by development of new composite materials on the basis of natural polysaccharides and synthetic polymers.

Poly(vinyl alcohol) (PVA) has a wide commercial application due to its unique chemical and physical properties. It is a nontoxic, highly crystalline, and water-soluble polymer and has good film forming and high hydrophilic properties. Poly(vinyl alcohol) could be considered as a good host material due to good thermo-stability, chemical resistance and film forming ability. Due to their simple structure and unique properties , polymers based on PVA have found applications in different industries including textile, paper, adhesives, food, biomedical and pharmaceutical in particular [1].

Carboxymethyl cellulose (CMC) is a biopolymer derived from cellulose. It is a copolymer of β -D-glucose and β -D-glucopyranose 2-O-(carboxymethyl)-monosodium salt which are connected via β -1,4-glycosidic bonds. CMC is widely used in pharmaceutical, cosmetic, and food applications. It is a nontoxic, biocompatible polymer, which resistant to the surrounding environment [2].

Materials and methods

Materials

In our work, we used carboxymethylcellulose (CMC) powder, purchased from «Altey» (Russia) used without purification. PVA (number average molecular weight 70 $\times 10^4$ g/mol) was purchased from Merck KGaA (Germany) used without purification.

Preparation of solutions

PVA solutions with concentration of 10 wt% were prepared by dissolving dry polymer in the deionized water at 80°C with constant stirring for 5 h. Then these solutions were stirred at room temperature overnight. Aqueous CMC solutions (10wt%) was prepared by dissolving CMC powder in the deionized water and mixed at 60°C and stirred to obtain clear solution for 6 h.

Preparation of Radiation Crosslinked Carboxyethylcellulose/Polyvinyl alcohol Hydrogels

To obtain hydrogels 10 wt % of polyvinyl alcohol and 10 wt % carboxymethylcellulose solutions mixed in the following proportions $\varphi_{CMC:}\varphi_{PVA}$ =70:30, 50:50, 30:70. Then 20 ml of each prepared CMC/PVA solutions was poured into a Petri dish. Afterward, all samples were irradiated by Electron beam (E-beam) irradiation at the semi-industrial electron accelerator ELV-4 (1,3 MeV) at the Institute of Nuclear Physics (INP), (Almaty region, Alatau village).The absorption dose of radiation were 40, 80 and 120 kGy.

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Swelling Degree and Gel fraction of Carboxyethylcellulose/Polyvinyl alcohol Hydrogels

The swelling degree of CMC/PVA hydrogels was determined by gravimetric methods. Samples of composite materials (0,1 g.) was placed in 10 ml distilled water, then every 15 min was measured by the steady mass of the sample on an analytical weight. The degree of swelling was calculated using the following formula:

$$\alpha = \frac{m_t - m_0}{m_0}$$

where, m_0 – initial mass of sample, g; m_t is the mass of the swollen sample in t time, g.

The gel fraction of hydrogels was measured by extraction in hot distilled water at 100°C for 48 h and dried at 70°C for 48 h until they reached constant weight. The gel content was defined by equation below:

$$Gel = \frac{W_d}{W_0} x100$$

where, W_d is the dried gel weight after extraction, and W_0 is the initial weight of polymer.

The structure of the obtained composite materials was carried out by IR spectrometric analysis**.** FTIR spectroscopy of pure PVA, pure CMC and CMC/PVA hydrogels were recorded using Carry 660FTIR spectrophotometer (Agilent, USA). The samples were finaly with potassium bromide (KBr) to make pellets under hydraulic pressure of 600kg/cm^2 and scanned between 4000 and 400cm^{-1}.

The morphology of the freeze dried samples of the CMC/PVA hydrogels were examined with Tabletop Scanning Electron Microscope (Hitachi, Japan) at acceleration voltage of 10 kV. All samples were freeze dried (Thermo LL300) and the dried hydrogels were gold sputter coated before analyzed by SEM.

*The study of the kinetics of drug release from hydrogel.*was estimated by UV spectrophotometry instrument «Shimadzu UV / VIS-2401 PC» (Japan). To study the kinetics of drug sorption by hydrogel 1g of sample were placed to 1 hour in Lidocaine solution. Every hour sorption of drug by measuring of changes of the optical density of lidocaine solution at a wavelength λ=266 nm determined. Measurement was performed on quartz cell with a 1 mm thick. The calibration curve was constructed for Lidocaine f (c) = D – dependence of the optical density of the solutions D concentration c (%).

To study the release of lidocaine hydrochloride from hydrogel adsorbed hydrogels for 24 hours were placed in a isotonic solution and measured the optical density every hour. Concentration of absorbed and desorbed lidocaine by a calibration curve was determined.

The amount of drug released after time t was determined by the calibration line according to the (3) formula:

$$W = \frac{C}{C_0} \cdot 100\% \qquad (3)$$

where, W is the amount of released drug, C is an Lidocaine concentration in the surrounding solution at time t, C_0 is a concentration of drug in the feed solution.

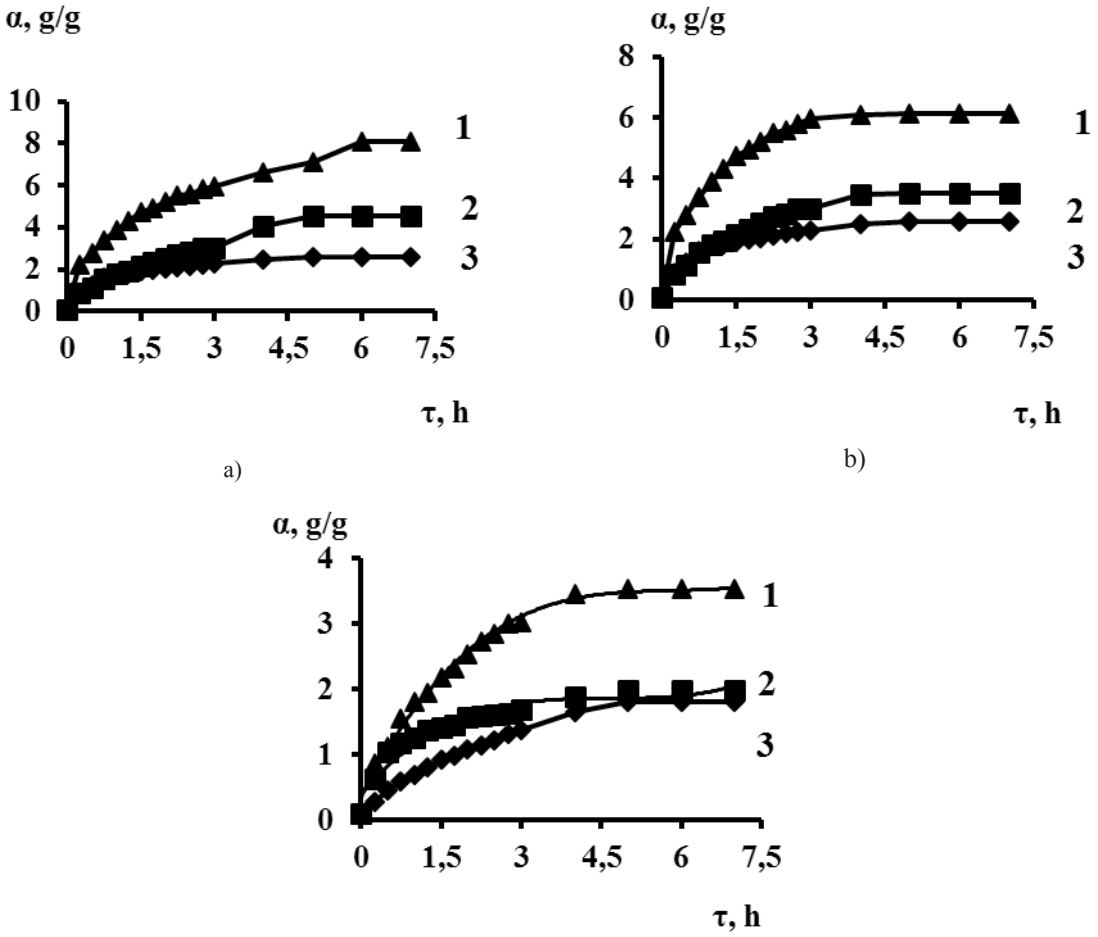
Results and Discussion

Swelling Behaviour of Polyvinyl alcohol/Carboxymethylcellulose Hydrogels

To learn the ability to swell and to prove that the carboxymethylcellulose and polyvinyl alcohol were crosslinked, at different doses of irradiation (40 kGy, 80 kGy, 120 kGy) kinetics of swelling of hydrogels based on PVA-CMC was investigated. It can be seen that at lower doses of irradiation the degree of swelling increases (Figure 1). The maximum equilibrium degree of swelling of $\varphi_{CMC:}\varphi_{PVA}$= 30:70 hydrogels at 40 kGy was 8,1 g/g and at 120 kGy was 2,6 g/g. Additionally, as can be seen from figure 1 swelling capabilities of hydrogel compositions are increased by increasing the PVA content. This proves that the hydrophilicity of PVA in comparison with cellulose ether is higher and can be explained by the fact, that increasing content of PVA in the hydrogel will result to enhancing the crosslinking by intramolecular hydrogen bonding between the PVA chains in the hydrogel network structure, which resulting to increase swelling.

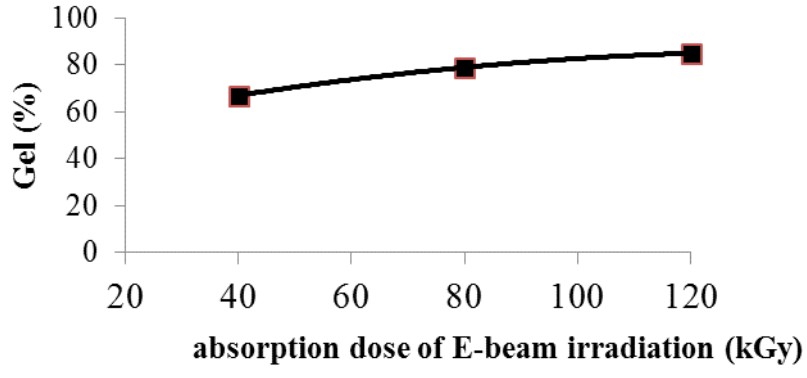
Gel Fraction of Crosslinked PVA/CMC hydrogels

Gel fraction is defined as the amount of insoluble polymer in any solvent. Gel contents of PVA/CMC hydrogels at various absorption dose of radiation (kGy) is presented in figure 2. In this figure, it was clearly seen that the gel contents of the crosslinked CMC/PVA hydrogels with volume ratio $\varphi_{CMC:}\varphi_{PVA}$= 30:70 increased with an increase of absorption dose of radiation.



φ_{CMC}:φ_{PVA}= 30:70 (a); φ_{CMC}:φ_{PVA} = 50:50(b); φ_{CMC}:φ_{PVA} = 70:30 (c)
absorption dose of E-beam irradiation = 40 (1); 80 (2); 120 (3) kGy.

Figure 1 – The kinetics of swelling of hydrogels based on CMC/PVA by radiation crosslinking



φ_{CMC}:φ_{PVA}= 30:70

Figure 2 – Gel fraction of crosslinked CMC/PVA hydrogels
at various absorption dose of E-beam irradiation (kGy) .

The high gel fraction of hydrogels; caused by enhanced irradiation dose as a result of higher degree of crosslinking onto polymer network which cause higher gel content. The gel fraction of PVA/CMC samples at radiation dose of 40 kGy was 78% and at radiation dose of 120 kGy was 87%.

Fourier Transform Infrared Spectroscopy Studies

The IR spectra of pure PVA, CMC and crosslinked CMC/PVA hydrogel are shown in Figure 3. The PVA spectra shows characteristic broad band at 3284cm^{-1} corresponding to the O–H stretching vibration of the hydroxyl group of the PVA. The sharp band at 1715cm^{-1} corresponds to the C= O stretching of the acetate group of PVA.

The backbone aliphatic C–H stretching vibrations give sharp bands at 2942cm^{-1}. The IR spectrum of CMC shows the absorption bands due to C–H stretching (2894cm^{-1}) and that due to C–O stretching of the ether group of the carboxymethylation of cellulose or the ether linkage [1,4-β-d-glucoside] of cellulose at 1051cm^{-1}. The absorption bands in the spectrum *correspond* with the *data given* in the [3] literature.

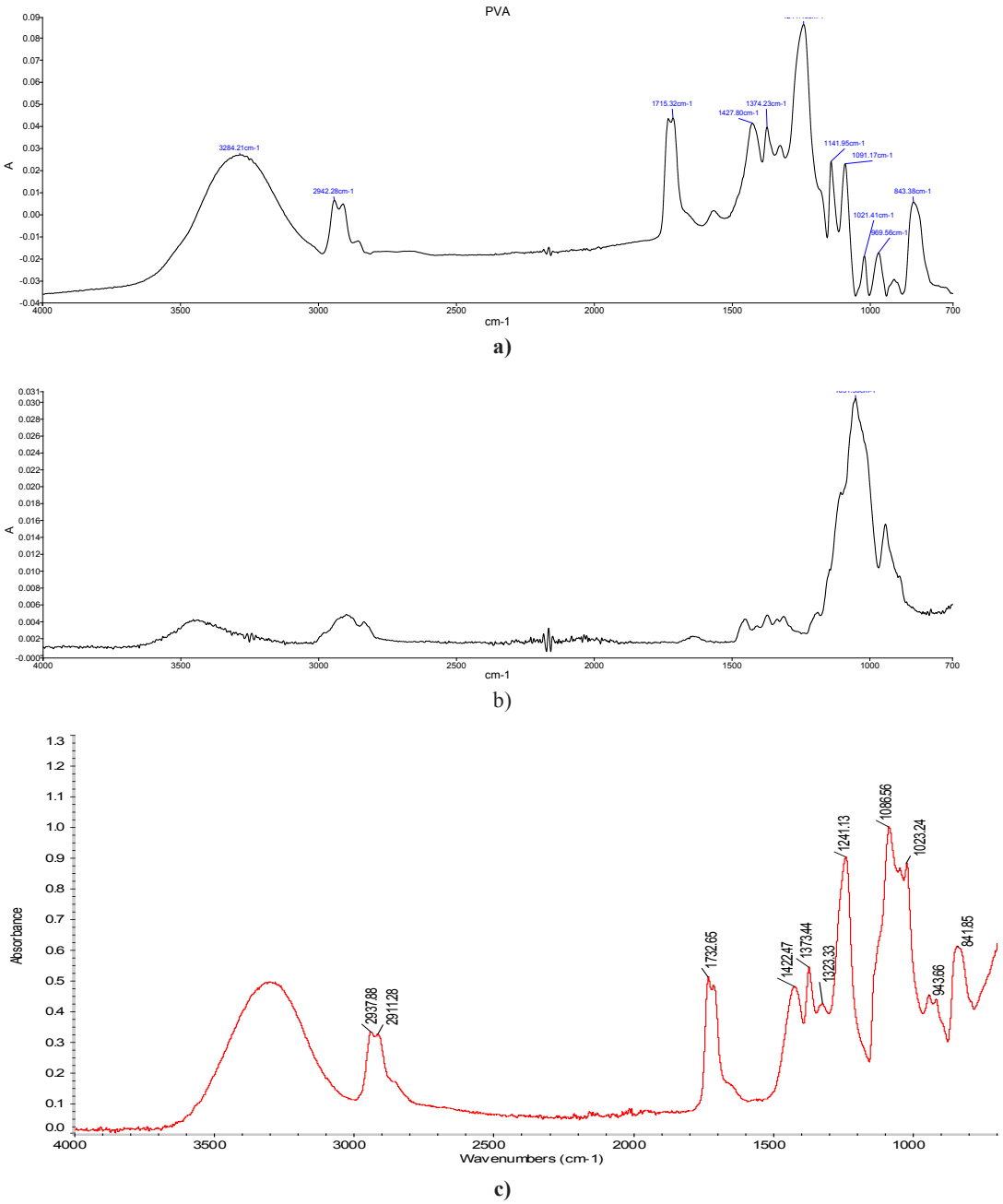


Figure 3 – FTIR spectra of PVA (a); CMC (b) and composite material based on CMC/PVA (c)

SEM studies

In general, the scanning electron microscopy (SEM) shows microstructure morphologies of hydrogels. The pore morphology of hydrogels can be related to their water uptake capacity. The hydrogels with denser and tighter structure will have a smaller pore size. The surface morphology of CMC/PVA hydrogels was detected by SEM. In the Figure 4 presents photomicrographs of hydrogels based on CMC/PVA. A homogenous structure with smooth surface can be observed in the PVA/CMC hydrogel. This picture confirmed that the CMC/PVA hydrogel has a porous structure

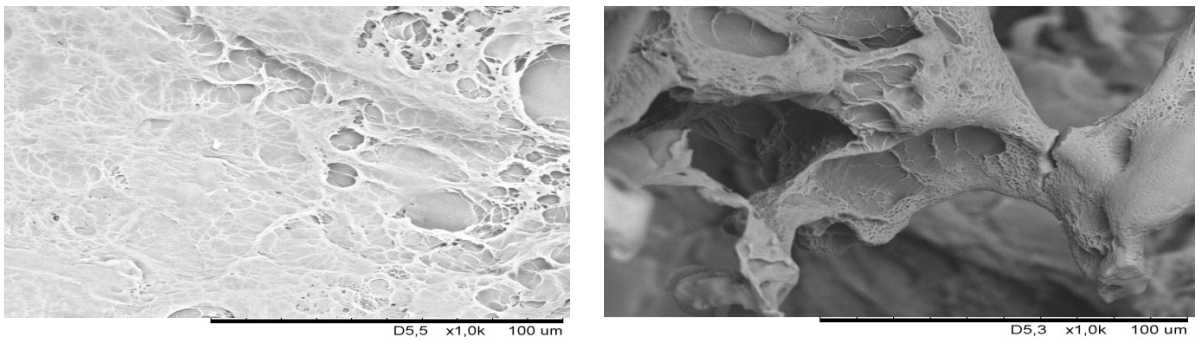


Figure 4 – SEM micrographs of hydrogel based on CMC/PVA

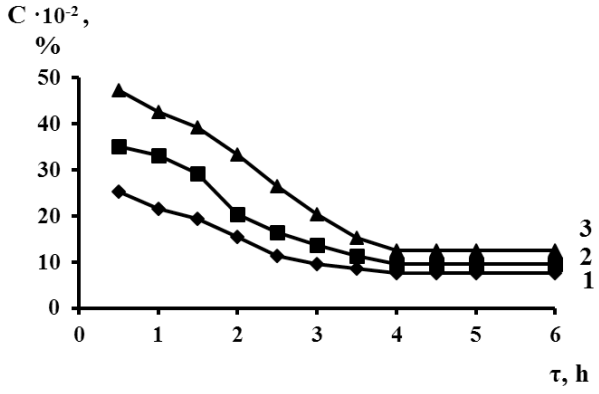
Studies of interactions of hydrogels based on CMC-PVA with medical substance

Nowadays, at designing and modification of new and well-known drugs, the improvement of their therapeutic effects is an important and actual problem. The immobilization of the drug into a biocompatible and biodegradable polymer matrix is the one way of solving this problem, because it has advantages over usual dosage forms, including reformed efficacy, diminished toxicity, cost effective therapeutic treatment. Hydrogels can transport drugs in a controlled manner due to the open porous structure [4].

Polyvinyl alcohol and cellulose ethers are widely used in controlled release studies because of its hydrophilic and nontoxicity.

In this study the possibility of using the hydrogel based on carboxymethylcellulose and polyvinyl alcohol as a drug carrier was considered. For this purpose, the kinetics of absorption and release of drug from hydrogel were studied. As a drug the local anesthetic – lidocaine hydrochloride was used. The absorption of lidocaine to the hydrogel was investigated by UV spectroscopy at a wavelength of 266 nm. It can be seen that the rate of the drug absorption by hydrogel increases with enhanced PVA content. As a result, the hydrogel with volume ratio $\varphi_{CMC:}\varphi_{PVA}$= 30:70 showed a high absorption ability of the drug substance. It can be concluded that the composite material with volume ratio $\varphi_{CMC:}\varphi_{PVA}$= 30:70 shows good absorption ability.

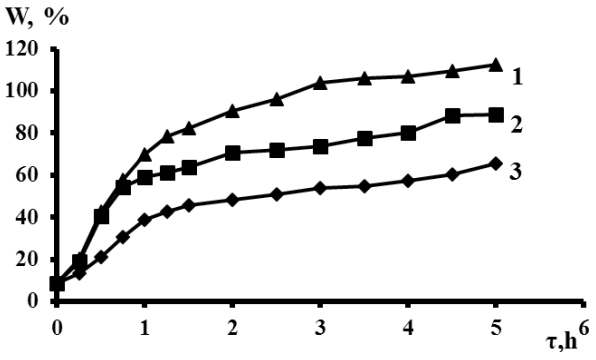
Besides this, to provide the prolonged effect the release of drug from the hydrogel should be slow. Thus, the kinetics of drug release from the hydrogel to an isotonic solution (0.9% NaCl) was studied to determine the release time. It has been noticed that the drug release during the process is intensive due to the influence of low-molecular ions. As a result, it was found that from the hydrogel with the volume ratio $\varphi_{CMC:}\varphi_{PVA}$= 70:30 the drug release goes quickly, while at volume ratio $\varphi_{CMC:}\varphi_{PVA}$= 30:70 release of the drug is slow.



$\varphi_{CMC:}\varphi_{PVA}$= 30:70 (1); $\varphi_{CMC:}\varphi_{PVA}$= 50:50(2); $\varphi_{CMC:}\varphi_{PVA}$= 70:30 (3)

Figure 5 – The kinetics of sorption of Lidocaine by hydrogel based on CMC/PVA at 40 kGy

As a conclusion, basing on the obtained results of adsorption-desorption process, the composite materials at volume ratio $\varphi_{CMC:}\varphi_{PVA}$= 70:30 are perspective in use as the matrix of lidocaine carrier.



$\varphi_{CMC:}\varphi_{PVA}$= 30:70(1); $\varphi_{CMC:}\varphi_{PVA}$= 50:50(2); $\varphi_{CMC:}\varphi_{PVA}$= 70:30 (3).

Figure 6 – The kinetics of desorption of Lidocaine from hydrogel based on CMC/PVA at 40 kGy in isotonic solution

Technological part

To obtaining the hydrogel based on carboxymethylcellulose and polyvinyl alcohol technological schemes at figure 7 can be used.

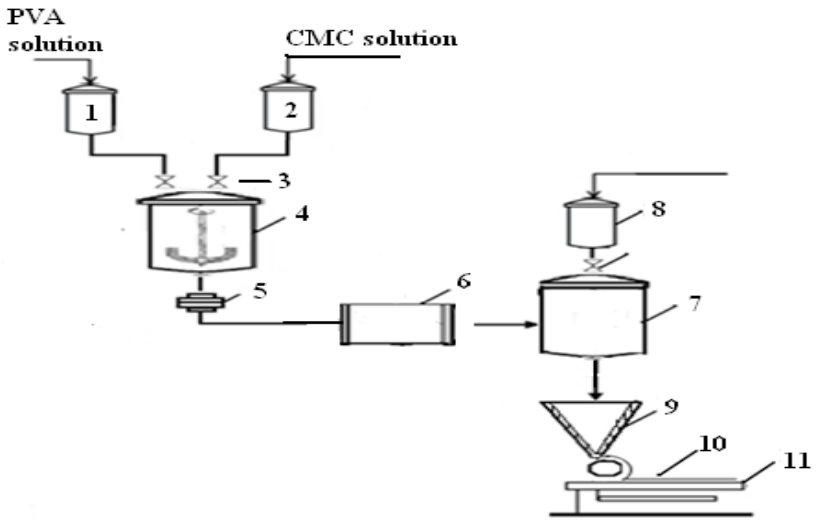
Process of hydrogel dressing receiving consists from the following stages:

1. Preparation of initial polymer solutions (polyvinyl alcohol and carboxymethylcellulose);
2. Mixing
3. Radiation exposure
4. Impregnation of hydrogel by medicinal substance
5. Molding of hydrogel
6. Reception of finished products

For production of hydrogel 10 wt.% of carboxymethylcellulose and polyvinyl alcohol solution are used. Substances are used without preliminary cleaning.

According to this scheme solutions of PVA and solutions of CMC through dosing devices mixing in the reactor (4) until homogenous blend. Further, blends of CMC/PVA are supplied to the ELV-4 electron accelerator for radiation at absorption dose of 40 kGy for obtaining hydrogels. After the completion of radiation hydrogel is supplied to the mixer (7) for mixing it with the drug flowing from storage bunker of drug (8). Then the hydrogel with the drug substance is delivered for cutting and packaging.

For this method the smaller dose of radiation is used that promotes more economic production of hydrogel bandages.



1 – bunker of PVA solution; 2 – bunker of CMC solution; 3 – dosing devices; 4 – reactor for the mixing of initial components;5 – filter; 6 – electron accelerator ELV-4; 7 – mixer for introducing of the drug into the hydrogel; 8 – storage tank of drug; 9 – фильера; 10 – cutting; 11 – packaging.

Figure 7 – Principal technological scheme of obtaining hydrogel films based on carboxymethylcellulose (CMC) and polyvinyl alcohol (PVA) containing drug

Conclusion

CMC/PVA solutions were irradiated by E-beam irradiation in the following proportions $\varphi_{CMC:}\varphi_{PVA}$ =70:30, 50:50, 30:70 at various doses of 40, 80 and 120 kGy. Presence of absorption bands of hydroxyl, simple ether and carbonyl groups in the hydrogel compositions by IR spectroscopy method was revealed. The kinetics of swelling of composite materials based on CMC/PVA with different volumetric ratios was studied. The gel fraction increases with increasing irradiation dose, while the swelling of CMC/PVA hydrogel increase with decreasing irradiation doses and increase with increasing CMC content. The maximum degree of swelling hydrogel was 8,1 g/g at the sample $\varphi_{CMC:}\varphi_{PVA}$= 30:70 hydrogels. The morphology of the hydrogels has a porous structure by the method of scanning electron microscopy was determined. Basing on the obtained results of adsorption-desorption process, the composite materials at volume ratio $\varphi_{CMC:}\varphi_{PVA}$= 70:30 are perspective in use as the matrix of lidocaine carrier. Principal technological scheme of obtaining of composite material based on CMC/PVA was developed.

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