

## Interaction of Chitosan with Hydrogel of Poly(Acrylic Acid) and Preparation of Encapsulated Drugs

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### Abstract

The complexation of linear chitosan with hydrogel of poly(acrylic acid) was studied in acetic acid solutions. It was found that the complexation is accompanied by contraction of hydrogel samples with formation of turbid layer on their surface. The dynamic changes of swelling ratio of poly(acrylic acid) hydrogel in course of the interaction with chitosan are interpreted from the diffusion theory point of view considering the properties of double electric layer on hydrogel-solution boundary. The FTIR spectroscopy method revealed the electrostatic mechanism of interaction between poly(acrylic acid) hydrogel and chitosan. The spectrum of polycomplex shows the bands, which are characteristic for both poly(acrylic acid) (1725, 1450, 1249  $\text{cm}^{-1}$ ) and chitosan (1648, 1536, 1165, 1091, 1023  $\text{cm}^{-1}$ ) confirming the sorption of the later polymer by hydrogel of poly(acrylic acid). The possibility of encapsulation of antibiotic levomycetin into polycomplex hydrogels as well as its release from the capsules has been studied. It was found that the maximal value of the drug released from the polycomplex capsule is achieved after the longer period in comparison with control experiment with its release from pure PAA hydrogel. It was shown that the interpolymer interactions between oppositely charged linear polymers and hydrogels could be successfully used for preparation of encapsulated forms of various physiologically active substances.

### Introduction

Chitosan is a cationic polymer that is produced by deacetylation of chitin, a naturally abundant mucopolysaccharide, and the supporting material of crustaceans, insects, etc. Chitosan is recommended as suitable functional material, because of its excellent properties such as biocompatibility, biodegradability, non-toxicity, absorption and chelation abilities, etc. [1]. These properties of chitosan attracted considerable attention of researchers for preparation of selective membranes, sorbents, flocculants, biomaterials and drug delivery systems [2].

A cationic nature of chitosan can be utilized for modification of its properties by interactions with various anionic polymers and preparation of polyelectrolyte complexes. A number of studies were done on the interaction between chitosan and different poly(carboxylic acids) in aqueous solutions [3-8].

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Some of the polyelectrolyte complexes (PEC) based on chitosan demonstrated good drug release properties [9-11]. However, to the best of our knowledge, only few reports are available in literature, which devoted to the combination of chitosan with poly(carboxylic acids), where at least one of the polymers is cross-linked [12].

In the present work we have studied the interaction of chitosan with hydrogel of poly(acrylic acid) and demonstrated the possibility of encapsulation of antibiotic drug levomycetin into PEC.

### Experimental

Chitosan was purchased from Aldrich and used without further purification. The solution of chitosan was prepared in 1 % acetic acid. Hydrogels of poly(acrylic acid) (PAA) were prepared by three-dimensional polymerization of acrylic acid in the presence of azoisobutyronitrile as initiator and N,N'-

methylene-bis-acrylamide as cross-linker. The synthesized hydrogels were washed by distilled water during 2 weeks and then by 1 % aqueous solution of acetic acid during 1 week. The levomycetin used in encapsulation and release experiments was of analytical grade.

The measurements of hydrogels linear size in course of the interaction with chitosan were done using the V-630 cathetometer at room temperature. The results are expressed as the swelling ratio  $V/V_0$ , where  $V$  is the volume of the gel in swollen state and  $V_0$  is the volume of the gel right after synthesis.

The equilibrium swelling degree of the hydrogels was determined by the formula  $\alpha = (m - m_0)/m_0$ , where  $m$  is the weight of the gel sample in equilibrium swollen state and  $m_0$  is the weight of dry sample.

The release of the drug was monitored by UV-spectroscopy using UV-Vis spectrophotometer (Shimadzu, Japan) at the wavelength  $\lambda = 279$  nm.

The FTIR spectra of dried chitosan, PAA and polycomplex were recorded in KBr tablets with the help of FTIR Satellite (Mattson, USA).

## Results and discussion

### *Interaction of chitosan with hydrogels of poly(acrylic acid)*

The interaction of polyelectrolyte hydrogels with oppositely charged linear polymers usually are accompanied by contraction of the samples and formation of turbid PEC layer on their surface [13-15]. The hydrogels of PAA were immersed into solutions of chitosan with different concentrations. The changes in the volume of hydrogels registered by cathetometer are plotted in Fig. 1. It is clearly seen that the hydrogel of PAA in 0.001–0.01 M solution of chitosan undergoes contraction. However, the dependence of volume ratio on time for diluted solution of chitosan ( $C = 0.001$  M) is more complicated. During the first days of the interaction the hydrogels increase their volume additionally, then they began to shrink. Such a behavior can be explained from the viewpoint of diffusion theory for swelling of polyelectrolyte hydrogels [16]. According to the theory the swelling of polyelectrolyte hydrogels is considerably dependent on the charge density of their surface. The higher the charge density is, the more the swelling ability of the hydrogel is observed. One can suppose that in solutions of low chitosan concentration in the first stage the interaction is occurred mainly on the sur-

face of the hydrogel. The chitosan interacts with the surface of the network by electrostatic contacts but some segments of its macromolecules are remained free and contribute the positive charge. Then, after the penetration of chitosan into the hydrogel the charge density of the gel on the surface as well as in the internal area is decreased leading to the total contraction. In solutions of higher chitosan concentration the macromolecules of linear polymer penetrate into the gel already in the first stage of the interaction and only contraction is observed.

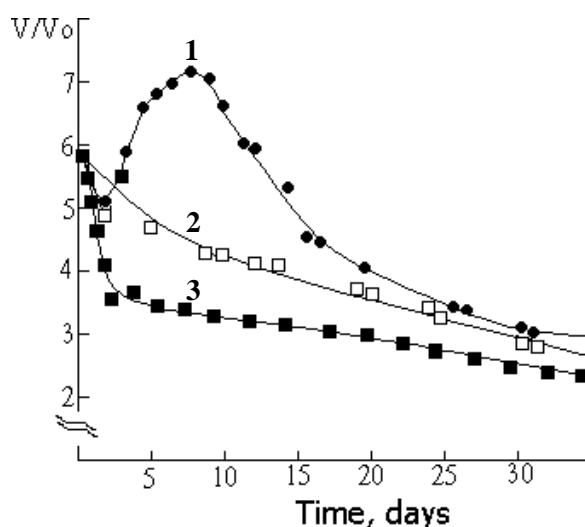


Fig. 1. Dependence of swelling ratio of PAA gels immersed into solutions of chitosan on time. [Chitosan] = 0.001 (1), 0.005 (2), 0.01 mol/L (3)

We have checked the influence of chitosan concentration on the equilibrium swelling degree of PAA hydrogels. For this purpose the PAA samples were immersed into chitosan solutions of various concentrations and were stored during 2 weeks. The dependence of equilibrium swelling degree of the obtained polycomplex hydrogels on the concentration of chitosan is plotted in Fig. 2. It is seen that the hydrogels undergo considerable contraction even in solutions of chitosan with very low concentration.

In order to clarify the mechanism of interaction between PAA hydrogels and chitosan we prepared the dry samples of polycomplexes in the vacuum drier. The FTIR spectra of the PAA, chitosan and polycomplex samples are shown in Fig. 3.

The chitosan spectrum shows the characteristic absorption bands at  $\sim 3420$   $\text{cm}^{-1}$  (hydroxyl groups),  $1650$   $\text{cm}^{-1}$  and  $1550$   $\text{cm}^{-1}$  (amide I and amide II, respectively),  $1381$   $\text{cm}^{-1}$  ( $-\text{CH}_2$  bending). The absorption bands at  $1151$   $\text{cm}^{-1}$  (anti-symmetric stretching of

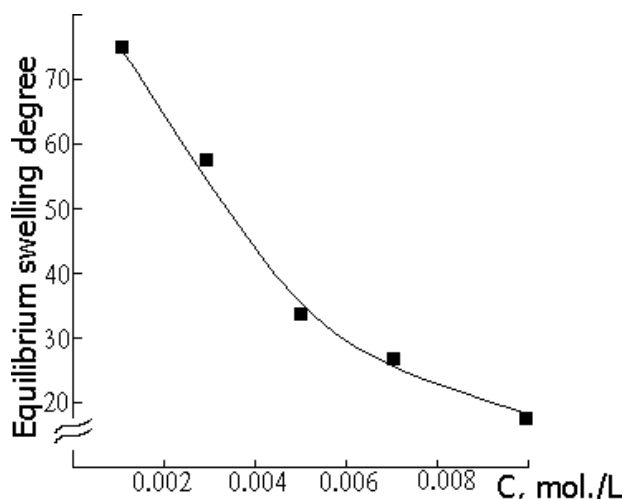


Fig. 2. Dependence of equilibrium swelling degree of PAA gel on the concentration of chitosan in solution.

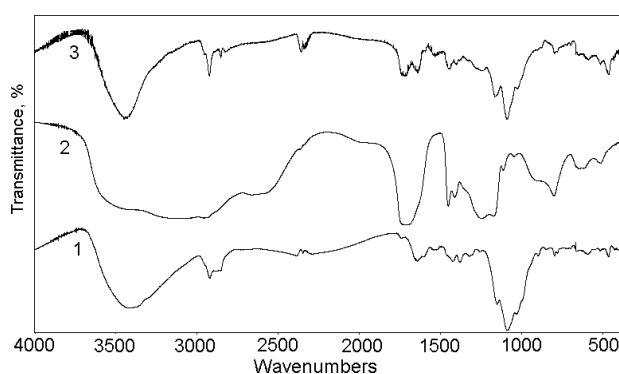


Fig. 3. FTIR spectra of chitosan (1), PAA (2) and poly-complex (3)

the C-O-C bridge),  $1090\text{ cm}^{-1}$  and  $1033\text{ cm}^{-1}$  (skeletal vibrations involving the C-O stretching) are characteristics of its polysaccharide structure [17, 18].

The characteristic absorption bands of PAA are located at frequencies  $3418$ ,  $2954$ ,  $1715$ ,  $1453$ ,  $1413$ ,  $1247$  and  $1173\text{ cm}^{-1}$ . In the region of  $2000$  to  $1500\text{ cm}^{-1}$  the PAA shows an intense and broad band ( $1715\text{ cm}^{-1}$ ) corresponding to the carbonyl stretching. The broadening of the carbonyl-stretching band of pure PAA is attributed to the presence of two carbonyl populations, one corresponding to the intra- and intermolecular hydrogen bonding ( $-\text{OH}\cdots\text{O}=\text{C}-$ ) and another due to a free carbonyl group [19].

The spectrum of polycomplex shows the bands, which are characteristic for both PAA ( $1725$ ,  $1450$ ,  $1249\text{ cm}^{-1}$ ) and chitosan ( $1648$ ,  $1536$ ,  $1165$ ,  $1091$ ,  $1023\text{ cm}^{-1}$ ) confirming the sorption of the later polymer by hydrogel of PAA. Besides, the appearance of new band at  $1401\text{ cm}^{-1}$  (symmetrical stretching of  $\text{COO}^-$  groups) and broadening of peak at  $1649\text{ cm}^{-1}$  (asym-

metrical stretching of  $\text{COO}^-$  groups) allows us to suggest the electrostatic mechanism of interaction between chitosan and PAA hydrogel according to the next scheme (Fig. 4). This result is in good agreement with the data obtained by the authors [3-5] for poly-complexes of chitosan with linear poly(acrylic acid).

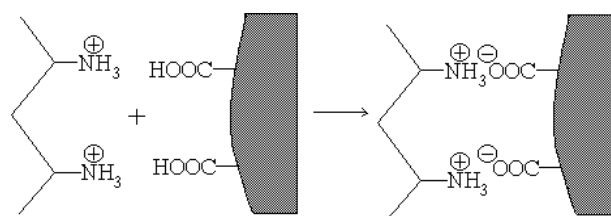


Fig. 4. Scheme of interaction between PAA gel and chitosan

### Encapsulation and release of levomycetin from polycomplexes

Levomycetin was selected as the model drug, which has no charged groups and is not able to interact with chitosan or PAA via ionic contacts. Before the experiment the hydrogels of PAA were immersed into  $0.0005\text{ M}$  solution of levomycetin in  $1\%$  acetic acid during 7 days. Then the samples of PAA loaded by levomycetin were placed into  $0.01\text{ M}$  solution of chitosan to form the polycomplex capsule for 10 minutes. In parallel experiment the PAA sample was immersed into  $1\%$  acetic acid. Then the gel samples were removed and placed into the beakers with  $50\text{ ml } 1\%$  acetic acid and the release of the drug was monitored by UV-spectrophotometric measurements. The sequences of the procedures for preparation of capsules and monitoring the release are shown in the Fig. 5.

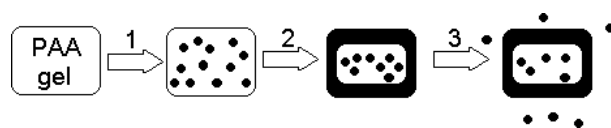


Fig. 5. Loading of PAA by the drug (1), covering the gel by PEC layer (2) and release of the drug from capsule (3)

The release profiles of levomycetin from poly-complex capsule and from pure PAA hydrogel are plotted in Fig. 6. It is seen that the maximal value of the drug released from the polycomplex capsule is achieved after the longer period in comparison with control experiment with the release from pure PAA hydrogel. Besides the amount of the drug released in the case of capsule is higher because in course of its

formation (Fig. 5, stage 2) the less amount of levomycetin is lost.

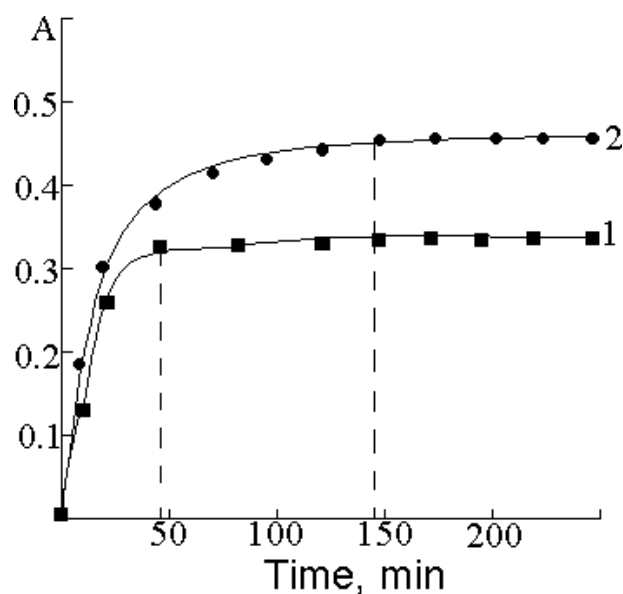


Fig. 6. Release of levomycetin from hydrogel of PAA (1) and polymeric capsule (2)

## Conclusion

The complexation between weakly cross-linked poly(acrylic acid) and linear chitosan is accompanied by contraction of hydrogel samples with formation of turbid polycomplex layer on their surface. The formation of polyelectrolyte complexes on the hydrogel-solution boundary represents the promising methodology for encapsulation of drug substances.

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