Immobilization of Alchidine on Polyvinyl Alcohol Gels

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The regularities of immobilization of natural medicinal substances - alchidine on gels of poly(vinyl alcohol) - are investigated. It is shown that the polymer components of alchidine interact with nonionic polymer with formation of interpolymer complexes. The influence of the different factors on the properties of complexes is considered and the constants of alchidine distribution in the system gel - water are calculated.

Keywords : Polyvinyl alcohol, Polymers, Alchidine, Nonionic polymer, Interpolymer complexes

1. INTRODUCTION

Polyvinyl alcohol (PVA) is one of the attractive nonionic polymers for medical application that is connected with its water-solubility and fine complexation ability by means of intermolecular hydrogen bounds, due to the proton-donating secondary OH-groups [1]. Another advantage of PVA is its gelation ability in some conditions: polymer concentration, temperature, time, solvent nature and etc., that allows to introduce desirable quantity of medicinal matter into the gel before gelation [2]. In this connection in the present work the immobilisation conditions of alchidine on poly(vinyl alcohol) gels have been studied.

The biological active complex - alchidine extracted from «Alhagi Kirgisorum Schrenk» shows anti-inflammation, anti-septic, blood-coagulation and astringent effects. It was obtained by scientists of Department of Organic Chemistry and Chemistry of Natural Compounds(al-Farabi Kazakh State National University). The main component that provides alchidine's activity is polymeric proantocyanidine.

2. EXPERIMENTAL

The concentration of drug (alchidine) was determined by UV - spectroscopy method. UV - spectra were recorded on «SF-26» in quarts cuvetes with thickness 1 cm. Initially, UV - spectra of solutions of drug were recorded for establishment of calibration curve. The measurements were conducted at the wavelength $\lambda = 272$ nm which is characteristic for proantocyanidines. In order to determine the quantity of drug released from gel, the sample of gel was placed into 50 ml of the distilled water and aqueous part of alchidine content was analyzed during 3 days with the help spectrophotometer «SF-26». The swelling degree of gels was determined by method of equilibrium swelling and calculated as a ratio of weight of swollen sample to the weight of dry sample according to the formula [3]:

$$\alpha = (m-m_0)/m_0$$

where m_0 - weight of dry sample, m - weight of swollen sample. The reduced viscosity of solutions was measured with the help of Ubbelohde viscometer with the flow time $\approx$ 100 sec. The temperature of experiments was kept

out with accuracy ± 0.1 °C. The accuracy of viscosity determination was η ± 1%.

3. RESULTS AND DISCUSSION

In order to get the information about the character of interaction of PVA with alchidine the viscometric titration of 0.01 M PVA solution by alchidine solution with concentration 0.1 g/dL was carried out. Upon addition of alchidine solution to the polymer a sharp decrease of reduced viscosity of the system was observed indicating the compaction of PVA macromolecules as a result of complexation with alchidine (Fig. 1).

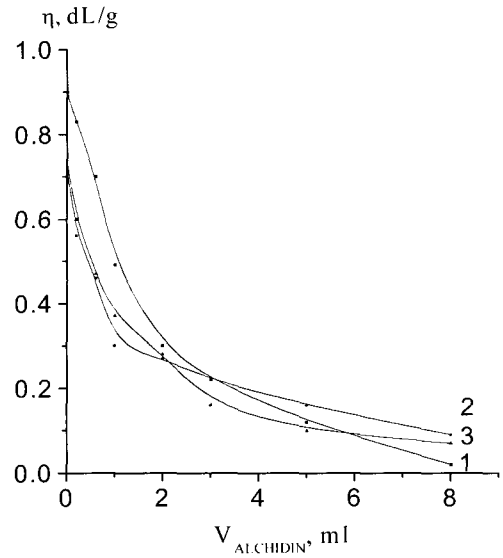

Fig. 1. Viscometric titration of 0.01 M solution PVA by alchidine solution at 25 °C (1, 3), 37 °C (2) into water and physiologic solution (3). [Alchidine] = 0.1 g/dL.

Taking into consideration that constitute components of alchidine are proantocyanidines and polysaccharides one can suppose that the interaction of PVA and alchidine results in the formation of interpolymer complexes (IPC), as it take place between complementary macromolecules in aqueous solutions [4,5].

The complexes are stabilized by intermolecular hydrogen bounds between OH - groups of PVA, proantocyanidines, and polysaccharides and also by hydrophobic interactions of hydrocarbon radicals. Actually, the interaction of PVA with alchidine is accompanied by a noticeable contraction of macromolecules and formation of insoluble precipitate of the complex. The analogic data were obtained at 37 °C and in physiological solution (Fig. 1, curves 2, 3), however, in this experiment the lower values of intrinsic viscosity are observed. This is probably connected with deterioration of the solvent thermodynamic quality [6,7], stabilizing the IPC, and strengthening the hydrophobic interactions.

One of the most important physico-chemical properties of polymeric gels is their swelling ability [8].

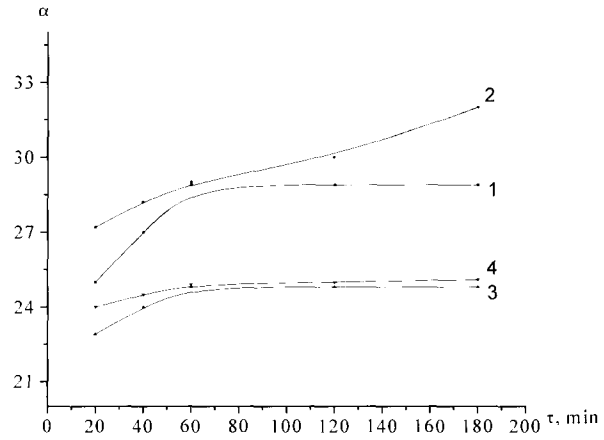

Fig. 2. Kinetics of 5 % PVA gel swelling with alchidine content 1 % in water (1, 2); in physiologic solution (3, 4); at 25 °C (1, 3), 37 °C (2, 4).

The experimental results on the swelling kinetics of PVA gels with alchidine (Fig. 2) confirm the above mentioned statement. The increase of alchidine content leads to some decrease of equilibrium swelling degrees of the gel indicating the complex formation and decrease of gel flexibility.

The information about the release of drugs from medicinal forms is of great importance for practical application. Alchidine release from PVA gels was evaluated controlling the proantocyanidines desorption - active component of alchidine. The data of quantitative investigations carried out by spectrophotometic method are shown in the Fig. 3.

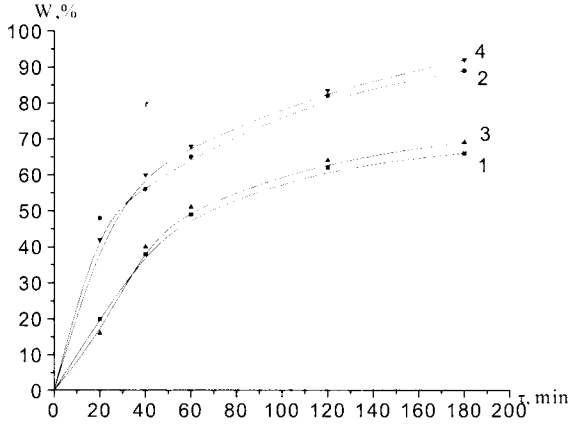

Fig. 3. Kinetics of alchidine release from PVA gel into water at 25 °C (1), 37 °C (2); into physiologic solution at 25 °C (3), 37 °C (4). c_{alch} = 2 %, c_{PVA} = 5 %.

As it is seen from the figure that the main amount of the drug is released at first 60 minutes and then the small monotonous decrease of desorption rate is observed. The significant increase of drug release is occurred with temperature decrease from 25 to 37 °C that is probably connected with destruction of intermolecular hydrogen bonds of the complex. As it is seen from the presented in the Fig. 3 the presence of low molecular electrolyte (in physiological solution) practically does not influence the rate of the drug release. This is probably connected with nonionic nature of polymers forming IPC.

The evaluation of swelling kinetics shows that the quantity of alchidine release from PVA gels during one day was 60 - 80 % that indicates the effectiveness of the studied system as prolonged medicinal form. The analogic data was obtained for gels consisting 1 and 3 % of alchidine. The Figure 4 shows the dependence of alchidine desorption kinetics for gels with different PVA concentrations. It is seen from the figure that an increase of PVA content in alchidine gels increases the amount of the drug release. One can expect that an increase of PVA content in gels would increase the hydrogen bonds density between polymer and drug and the strengths the stability of IPC. It would decrease the alchidine release from the gel phase. This seeming discrepancy probably can be explained by the fact that the intramolecular hydrogen bonds are predominated in comparison with intermolecular from more affinity of PVA functional groups with each other.

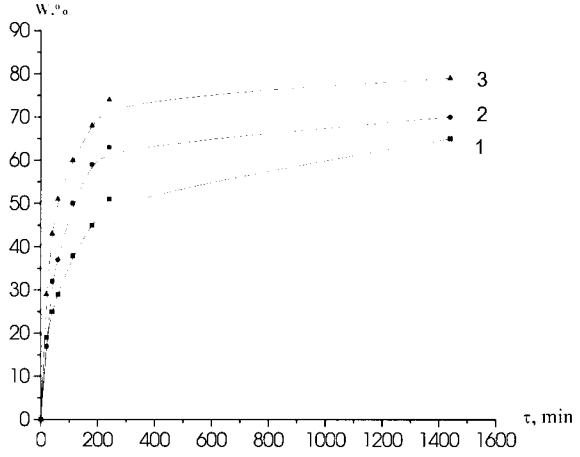

Fig. 4. Kinetics of alchidine release from PVA gel into water at 25 °C. c_{alch} = 3 %, c_{PVA} = 5 % (1), 6 % (2), 7 % (3).

Constants of alchidine distribution between PVA-gels phases and external solution were calculated from data of desorption kinetics and swelling [9] and summarized in the Table 1. They complete the information about the drug release from polymer matrix. Thus our investigations show the possibility of development the gel medicinal alchidine forms with regulated release.

Table 1. Constants of alchidine distribution in PVA gel and external solution in course of desorption. T= 25 °C, c_{arxh}=3 %, c_{PVA} = 6 %.

External solution	t, min							
	20	40	60	120	180	240	300	1440
Water	4,7692	2,125	1,678	0,973	0,685	0,674	0,666	0,407
Phys. solution	3,166	2	1,777	1,027	0,744	0,595	0,53	0,25

4. CONCLUSION

Polyvinyl alcohol (PVA) is the attractive nonionic polymers for medical application. The information about the release of drugs from medicinal forms is of great importance for practical application. As alchidine solution added to the polymer a sharp decrease of viscosity of the system was observed and it meant the compaction of PVA macromolecules as a result of complexation with alchidine. Alchidine release from PVA gels was evaluated controlling the proantocyanidines desorption - active component of alchidine. As a results, the main amount of the drug was released at first 60 minutes and then the desorption rate decreased with the small monotonousness. And the presence of low molecular electrolyte (in physiological solution) practically did not influence the rate of the drug release.

REFERENCES

[1] V. I. Lozynskiy, "Criotropic gelation of poly(vinyl alcohol) solutions", Uspehi himii, Vol. 67, No. 7, p. 641, 1998.

[2] Soh Deawha, Fan Zhanguo, and Gao Weiying "Zone-melting process of NdBaCuO under low oxygen pressure", Transaction on EEM, Vol. 3, No. 2, p. 24, 2000.

[3] E. V. Kuznetsov, S. M. Divgun, A. A. Budarina, N. I. Avvakumova, and V. F. Kurenkov, "Practical guide on chemistry and physics of polymers", M: Himiya, p. 256, 1977.

[4] V. Yu. Baranovskiy, L. A. Kazarin, A. A. Litmanovich, I. M. Papisov, and V. A. Kabanov, "Complex of poly(methacrylic acid) with polyacrylamide", Vysokomol. soed., Vol. 36, No. 7, p. 1480, 1994.

[5] E. A. Bekturov and L. A. Bimendina, "Interpolymer Complexes", Alma-Ata: Nauka, p. 270, 1977.

[6] S. S. Voyutskiy, "Course of colloid chemistry", M: Himiya, p. 512, 1976.

[7] V. V. Khutoryanskiy, G. A. Mun, Z. S. Nurkeeva, and S. E. Kudaibergenov, "Vestnik KazSU, Seriya himicheskaya", No. 10, p. 64, 1998.

[8] E. A. Bekturov, and I. E. Suleimenov, "Polymeric hydrogels", Gylym, Almaty, p. 240, 2000.

[9] G. A Bektenova "Immobilization of enzymes on inorganic and organic polymeric carriers", Gylym, Almaty, p. 287, 2000.