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Research Article

Preparation, Characterization and Drug Release Properties Polyvinyl Alcohol and Polyvinyl Pyrolidone Blended Hydrogels

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Abstract: In this work, a new polyvinyl alcohol (PVA)/polyvinyl pyrrolidone (PVP) /Pumice composite has been synthesized by using gamma rays irradiation technique. The chemical characteristics of the hydrogels were determined by Fourier Transform Infrared Spectroscopy method. The properties of the hydrogels were investigated in terms of swelling, drug uptake and release behaviors. 5-Fluorouracil (5-FU) was used as a model drug for the study of drug uptake and release behaviour of hydrogels. The addition of pumice in the gel structure improved drug uptake and release capability of the new hydrogels.

Keywords: Drug, Hydrogel, Polyvinyl alcohol, Polyvinyl pyrrolidone, Pumice

Polivinil Alkol Ve Polivinil Pirolidon Hidrojellerinin Sentezi, Karakterizasyonu Ve İlaç Salım Davranışları

Özet: Bu çalışmada, yeni bir polivinil alkol (PVA) / polivinil pirolidon (PVP)/Pomza kompozit malzemesi gama ışınları ile radyasyon tekniği ile sentezlensi. Hidrojellerin kimyasal özellikleri Fourier Transform İnfrared Spektroskopi metotu ile belirlendi. Hidrojellerin şişme,, ilaç emilimi ve salım davranışları incelendi. 5-Fluorurasil (5-FU), hidrojellerin ilaç tutumu ve salım davranışlarının incelenmesinde model ilaç olarak kullanıldı. Pomzanın jel yapısına ilavesi hidrojellerin ilaç tutumu ve salım kapasitesini arttırdı.

Anahtar Kelimeler: İlaç, Hidrojel, Polivinil alkol, Polivinil pirolidon, Pomza

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1. Introduction

Since hydrogels are soft and wet, they can be used in various biomedical applications [1-3]. In our previous study, a novel class of hydrogels, namely, the copolymers of N-isopropylacrylamide (NIPAAm) and itaconic acid (IA) with the addition of pumice were recently introduced as intelligent hydrogels with the improved the adsorption capability of the water-soluble monovalent cationic dyes, methylene blue [4]. Pumice is a soft volcanic rock which can be used as adsorbents due to their porous structure, high specific surface area, chemical and mechanical stabilities, and a variety of surface and structural properties [5].

In our study, use of these low-cost minerals together with PVA/PVP hydrogels, inorganic–organic composite hydrogels can absorb and trap drug like 5-FU. However, no report is available in the literatures for combination of PVA/PVP and Pumice for uptake and controlled release of 5-Fluorouracil (5-FU). On the basis of the above background and our previous studies on superabsorbent polymers, this paper reports on the synthesis and characterization of the novel PVP/PVA/Pumice

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hydrogels with the improved the drug adsorption and release capabilities.

2. Experimental

2.1. Materials

Poly vinyl alcohol (PVA) with a molecular weight of 47000, poly vinyl pyrolidone (PVP); average molecular weight of 40000 and 5-FU (%99) were obtained from Sigma Aldrich Chemical Company. All the reagents mentioned above were used as received. Pumice was supplied from Soylu Group Industrial Mineral Company, Turkey. Prior to use in the experiments, Pumice samples were crushed and particle size of Pumice powder ranged from nano to micron (0-125 microns). All reagents were used without further purification.

2.2. Apparatus

The chemical characteristics of the hydrogels were determined by Fourier Transform Infrared Spectroscopy (Bruker VERTEX 70 ATR) methods. The concentration of 5-FU was measured by Shimadzu UV-Visible spectrophotometer (Shimadzu UV-2401Names of funding organizations should be written.

2.3. Preparation of hydrogels

An equal ratio of 10 wt% from PVA and PVP were prepared by dissolved in distilled water at temperatures 85°C, 45°C, respectively. The solutions were mixed at the ratio (50:50) of (PVA/PVP). A certain amount of pumice was added to the mixture with continuous stirring for 2 h. The reaction mixture was purged bubbling with N_2 gas. The solution was added to small glass tubes. The prepared solutions were put in glass tubes (5 mm inner diameter) and stoppered. Irradiations of all solutions were performed with a Nordion-Canada model JS 9600 model gamma irradiator in Gamma-Pak Ind &Trade Inc under air at 25°C. A total of 25 kGy dose was absorbed (at a dose rate of 3 kGy/h). The crude hydrogels were kept in water used as the extraction solvent at 25°C. When polymerization completed, cross-linked copolymers were taken out from tubes and the produced hydrogels were divided into pieces of 1 cm. Each gel pieces was put in water for approximately one week period and the water was replaced every other day until remaining no extractable polymer. This extraction process helps to remove residual monomers and uncross-linked polymers from the gel. Extracted gels were stored in vacuum oven (30°C) until reaching to a constant dry weight before calculating the gel fraction. The gel fraction was determined with this given formula from the results measured gravimetrically.

$$\text{Gelation \%} = W_g/W_o \times 100\% \quad (1)$$

W_g, represents the weight of sample after extraction.W_o represents the weight of sample before extraction.

The dried hydrogels were put into a certain amount of phosphate buffer at pH 7.4 at 37ºC. The dry gels were stayed in phosphate buffer at pH 7.4 at 37ºC for a certain time of the period until the equilibrium degree of swelling,

$$\text{Mass swelling (\%)} = [(m_t-m_o)/ m_0] \times 100 \quad (2)$$

$$\text{Equilibrium mass swelling (Seq\%)} =[(m_\infty-m_o)/m_o] \times 100 \quad (3)$$

where m_0 is the weight of the dry gel and m_t and m_∞ is the weight of swollen gel at a particular time t and at equilibrium, time, respectively.

The equilibrium water content (EWC) and the water absorption were (A_w) calculated as follows:

$$\text{EWC (\%)} = \frac{W_s-W_d}{W_s} \times 100\ \% \quad (4)$$

where W_s and W_d are the weights of swollen state and dried state respectively.

To study the adsorption of drug, namely, 5-FU, the hydrogels were placed in aqueous solutions of 5-FU adsorption isotherm and allowed to equilibrate for 24 hours. 5-FU uptake and release experiments were analyzed at 266 nm by ultraviolet spectrophotometer.

3. Results and Discussions

3.1. Effect of Pumice on Gelation Percent of PVA/PVP Blend

Irradiaton of PVA/PVP solution results in the synthesis of hydrogels [6]. Table 1 shows the effect of Pumice particles on the gelation percent of PVA/PVP hydrogels. The distribution of Pumice particles with the interchain hydrogen bonding between the hydroxyl group of the PVA chains and carbonyl groups of PVP chains would eventually facilitate exposure of additional sites to gamma irradiation leading high gelation percent. Gelation % values of PVA/PVP/Pumice hydrogels were found to be increase from 73 to 91 with increasing amount of Pumice content in the gel structure at the irradiation dose of 25 kGy.

Table 1. The effect of Pumice particles on the gelation percent of PVA/PVP hydrogels

Gel name	Gelation (%)
PVA/PVP	73
PVA/PVP/Pumice-1*	79
PVA/PVP/Pumice-2*	87
PVA/PVP/Pumice-3*	91

* added amounts of Pumice to 3 mL PVA/PVP solution are 10 mg (1), 20 mg (2) and 30 mg (3) respectively.

3.2. *Swelling*

Figure 1 shows that swelling of the hydrogels in phosphate buffer at pH 7.4 and 37ºC increases with time up to certain level, then levels off. Seq % of PVP/PVA is 1260, PVA/PVP/Pumice hydrogel is 5890 with the incorporation of Pumice particles into PVA/PVP chains. In Table 2, it is observed that the addition of Pumice content cause a decrease of the equilibrium swelling percentage, Seq (%). The decrease of the Seq (%) is directly related to the packing effect caused by the Pumice in the matrix, therefore reducing the available free volume for swelling. Moreover, Pumice acting as co-crosslinking points of the PVA/PVP chains causes decreased porosity in the network structure and decrease in Seq% of PVA/PVP/Pumice hydrogels. All EWC values of the hydrogels (0.73-0.99) were greater than the percent values of

body about 0.6. This confirms that the PVA/PVP/Pumice hydrogels showed fluid contents similar to those of living tissues [7].

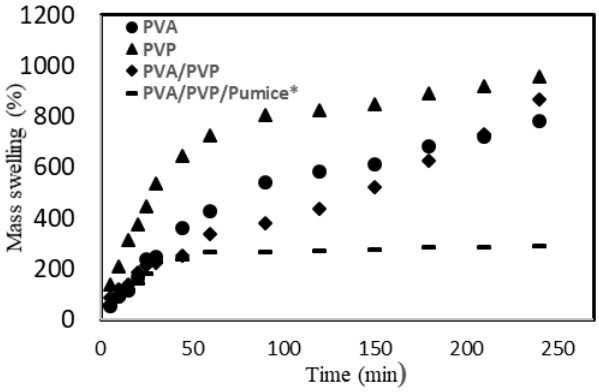

Figure 1. Swelling of the hydrogels prepared at an irradiation dose of 25 kGy in phosphate buffer at pH 7.4 at 37ºC * contains 30 mg Pumice

Table 2. Seq (%) and EWC values of the hydrogels prepared at an irradiation dose of 25 kGy.

Gel name	Seq(%) (water)	Seq(%) (5-FU)	EWC (water)	EWC (5-FU)
PVA	976.2	959.7	0.9058	0.9056
PVP	961.6	941.8	0.9070	0.9040
PVA/PVP	1095.4	963.7	0.9163	0.9919
PVA/PVP/Pumice*	496.9	273.4	0.8467	0.7322

* contains 30 mg Pumice.

3.3. FTIR analysis

FT-IR spectra of the hydrogels were taken as seen in Fig. 2 and 3, respectively. Fig. 2 represents the FT-IR spectra of Pumice and PVA/PVP/Pumice hydrogel. In Fig. 2 (a), the peak at ~460 and ~780 cm^{-1} can be assigned to the bending vibration of Si-O-Si bond. The band at the Si–O stretching vibration 1009 cm^{-1} is shown in the spectrum of the Pumice In Fig. 2 (b), the characteristics adsorption peaks of –OH (3283.05 cm^{-1}) belonging to PVA.; the characteristics adsorption peaks of –C=O (1643.67 cm^{-1}), –C-N– (1286.71 cm^{-1}) and water (3000-3500 $cm^{-1)}$ belonging to PVP and the characteristics adsorption peaks of Si–O stretching vibration 1009 cm^{-1} can be found in the FTIR spectrum of the synthesized hydrogel confirming the formation of PVA/PVP/Pumice hydroge [8]. Fig. 3 represents the FT-IR spectrum for PVA/PVP and PVA/PVP/Pumice hydrogels. The addition of Pumice content results in a decrease on the intensity of the 3000-3600 cm^{-1} band. This fact proves the presence of hydrogen bonding between PVA/PVP hydrogels and Pumice, since the interactions between –OH groups are strongest in the bulk PVA/PVP hydrogels than PVA/PVP/Pumice hydrogels.

3.3 Drug loading and drug release

For the investigation of drug uptake behavior of PVA/PVP/Pumice hydrogels, we measured the amount of adsorbate per unit mass of adsorbent (qe) and thus determined the drug uptake capacities of hydrogels. qe values (mg/g) were calculated according to the formula given below [9].

$$q_e = [(Ci - C) * V_t] / m \quad (5)$$

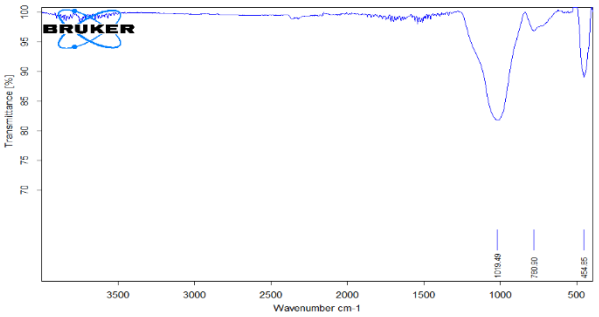

Figure 2a. FT-IR spectrum for pumice

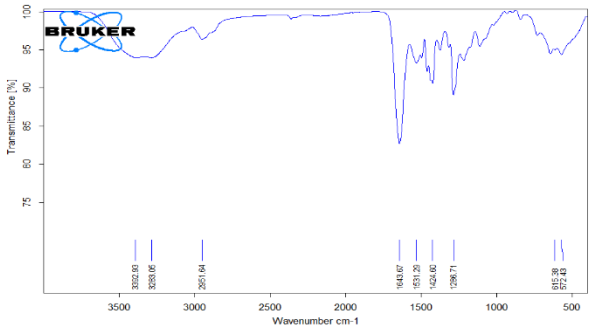

Figure 2b. FT-IR spectrum for PVA/PVP/Pumice hydrogels

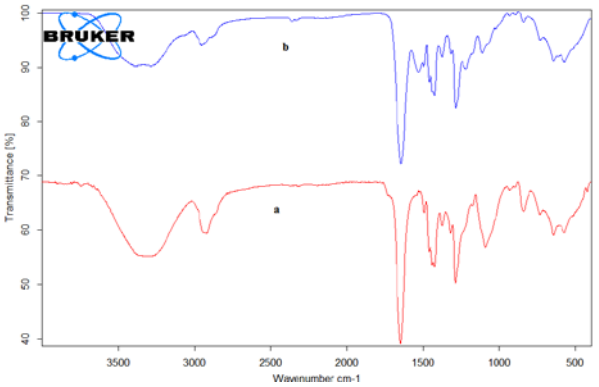

Figure 3. FT-IR spectrum for PVA/PVP (a) and PVA/PVP/Pumice *(b) hydrogels

In this equation, Ci represents the initial concentration of solution of adsorbate, C represents the equilibrium concentration of solution of adsorbate, Vt represents the volume of solution treated, and M represents the mass of dry adsorbent.

In this study, when adding Pumice into the PVA/PVP hydrogel, adsorption capacity increased from 8.95 to 22.62 mg 5-FU/g dry gel. Since Pumice contains anionic charges on its surface and, the addition of Pumice into PVA/PVP hydrogel leads to an increase in the number of anionic groups in the hydrogel [10].

On the contrary, Fig. 4 shows that the removal percent for adsorbed 5-FU was higher for pure PVA/PVP hydrogel than those for PVA/PVP/Pumice hydrogels. This can be explained by the increase in the diffusional path due to the high swelling of PVA/PVP hydrogels. It was found that 5-FU removal efficiencies were 70.8 and 30% for PVA/PVP and PVA/PVP/Pumice hydrogels.

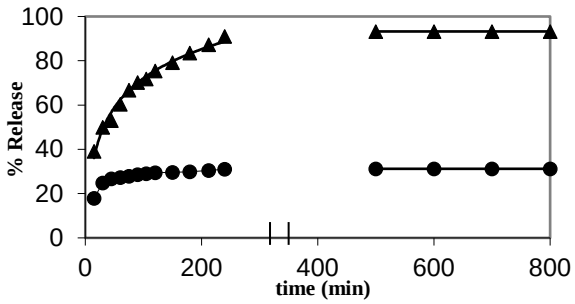

Figure 4. The release profiles of 5 FU in PVA/PVP (▲) and PVA/PVP/Pumice* (●) gels in phosphate buffer at pH 7.4 at 37°C, * contains 30 mg Pumice.

4. Conclusion

In this work, a new type of PVA/PVP/Pumice composite hydrogels using Pumice as physical crosslinker were synthesized by radiation induced polymerization. Further, the effect of the Pumice contents of synthesized hydrogels were tested in experiments on the swelling, diffusion, drug adsorption and release behaviors. The addition of Pumice in the gel formulation resulted in an increase in cross-linked percentage in the hydrogels and thus decreased the swelling ratios of the hydrogels. The improvement in the drug adsorption capability of the new hydrogels with the addition of Pumice in the gel structure was achieved. Adsorption capacities of 5-FU were found to be increasing from 8.95 to 22.62 mg/g with the addition of Pumice in the gel structure. The results showed that the PVA/PVP/Pumice hydrogel may be an appropriate alternative for drug release processes in human body.

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