



Synthesis and Swelling Behavior of Sodium Alginate/Poly(vinyl alcohol) Hydrogels

Sodyum Aljinat/Poli(vinil alkol) Hidrojellerinin Sentezi ve Şişme Davranışları

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ABSTRACT

Objectives: Hydrogels are macromolecular networks able to absorb and release water/biological fluids in a reverse-phase manner, in response to specific environmental stimuli. Such stimuli-sensitive behavior makes hydrogels interesting for the design of smart devices applicable to a variety of technological fields. They are able to absorb and retain 10-20% and up to 1000 times the water or biological fluids than their dry weight can. The aim of this study was to extend the work on drug delivery in the stomach at pH 2-2.2.

Materials and Methods: The authors synthesized sodium alginate (SA)/poly(vinyl alcohol) (PVA) hydrogels. These hydrogels were characterized by fourier transform infrared spectroscopy and scanning electron microscopy, and the swelling properties of the hydrogels were examined at different pH values, in different salts, at different temperatures, and in different acids and bases.

Results: The authors studied and reported the swelling effects or variations such as the effects of salts, acids, bases, temperature, and pH. The results for the crosslinking agent glutaraldehyde showed that 8 mL of glutaraldehyde had a higher swelling rate compared to that of 10 mL and 12 mL.

Conclusion: In this work the authors studied the swelling degree in different acids and bases. It is concluded that the degree of swelling decreases with increases in the concentration of glutaraldehyde and also depending on the concentrations of the acids. The swelling degrees of PVA/SA hydrogels gradually increase with increases in the concentrations of acids (low pH). The swelling of hydrogels decreases with increases in pH (>7) or at high alkaline. Based on the results for salt solutions the swelling behavior was found to be in the order: $K^+ > Na^+ > Ca^{2+} > Mg^{2+}$.

Key words: Swelling, pH, crosslinking agent, buffer solution, sodium alginate, PVA

ÖZ

Amaç: Hidrojeller, belirli çevresel uyaranlara yanıt olarak su/biyolojik sıvıları ters fazda emebilen ve serbest bırakabilen makromoleküler ağlardır. Bu tür uyaranlara duyarlı davranış, çeşitli teknolojik alanlara uygulanabilen akıllı cihazların tasarımı için hidrojelleri ilginç kılar. Kuru ağırlığından %10-20 ve 1000 veya daha fazla su veya biyolojik sıvıları emebilir ve tutabilirler. Bu çalışmanın amacı, midede ilaç dağıtım çalışmalarını pH 2-2.2'sinde genişletmektir.

Gereç ve Yöntemler: Yazarlar sentezlenmiş sodyum aljinat (SA)/poli(vinil alkol) (PVA) hidrojelleridir. Bu hidrojeller fourier dönüşümü kızılötesi spektroskopisi, taramalı elektron mikroskopu, farklı pH'larda hidrojellerin şişme özellikleri, tuzlar, farklı sıcaklık, farklı asitler ve bazlar ile karakterize edilir.

Bulgular: Yazarlar, tuzların, asitlerin, bazların, sıcaklığın ve pH'in etkisi gibi şişme etkilerini veya varyasyonlarını incelediler ve rapor ettiler. Çapraz bağlama maddesi glutaraldehitin etkisi, 8 mL glutaraldehidin, 10 mL ve 12 mL'nininkiyle karşılaştırıldığında en yüksek şişme oranına sahip olduğunu göstermektedir.

Sonuç: Bu çalışmada yazarlar farklı asit ve bazlarda şişme derecesini incelemişlerdir. Glutaraldehit konsantrasyonundaki artışla ve aynı zamanda asit konsantrasyonuna bağlı olarak şişlik derecesinin azaldığı sonucuna varılmıştır. PVA/SA hidrojellerinin şişme derecesi, asit konsantrasyonundaki artışla (düşük pH) kademeli olarak artmaktadır. Hidrojellerin şişmesi pH'in (>7) artmasıyla veya yüksek alkali ile azalır. Tuz çözeltilerinin etkisinde şişme davranışının sırasıyla: $K^+ > Na^+ > Ca^{2+} > Mg^{2+}$ olduğu bulunmuştur.

Anahtar kelimeler: Şişme, pH, çapraz bağlama maddesi, tampon çözelti, sodyum aljinat, PVA

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INTRODUCTION

Hydrogels have been used in various chemical and biomedical applications in ophthalmology as contact lenses and surgical sutures, as well as in numerous other areas like agricultural applications.

Sodium alginate (SA) is an anionic copolymer composed of 1,4-linked β -D-mannuronic acid (M-blocks) and α -L-guluronic acid (G-blocks), interspersed with regions of alternating structure. Gel formation and three-dimensional network structures occur when divalent ions (Ca^{2+} , Ba^{2+} , Fe^{2+} , Si^{2+} , etc.) or trivalent ions (Al^{3+} , etc.) crosslink with G-blocks in the polymer chain. Such binding zones between G-blocks are often referred to as "egg boxes". These crosslinked ions stabilize alginate chains, forming a gel structure, with more freely movable chains that bind and entrap large quantities of water or biological fluids. The gel formation (gelification) process is characterized by the eviction of water.¹ The softer, more fragile, and lower porosity gels are made of M-rich alginate groups. This is due to the lower binding strength between the polymer chains and to the higher flexibilities of the molecules. The gel formation process is highly dependent on diffusion of gel formation ions into the polymer network. Visco-elasticity and transmittance of alginate structures are highly affected by the M/G ratio. Alginic acid and its salts of sodium and calcium are used in the medical, pharmaceutical, cosmetic, and food industries because of its nontoxicity and biocompatibility.² The main advantage of hydrogels is that they possess a degree of flexibility very similar to that of natural tissues, due to their significant water content. Their stimuli-sensitive behavior makes hydrogels interesting for the design of smart devices applicable to a variety of technological fields.

Hydrogels are, in general, materials composed of three-dimensional hydrophilic polymer networks and water that fills the free spaces inside this network. Hydrogels are able to absorb and retain 10-20% up to 1000 times the water or biological fluids than their dry weight can. Hydrogels respond reversibly to slight changes in the properties of surrounding media; hence they are called "intelligent materials". This ability means hydrogels have found many applications in industry and in pharmaceuticals, for example as controlled drug delivery systems.³ The swelling and dehydration behavior is one of the most important properties of hydrogels.⁴ Applications of hydrogels include drug delivery systems (slow drug release), wound dressings, dental applications, transdermal implants, injectable polymers, contact lenses, superabsorbents, and environmentally sensitive hydrogels.⁵⁻⁹ Hydrogels interact with aqueous solutions and swell to a certain equilibrium and retain a significant proportion of water within their structure.¹⁰ SA is a hydrophilic polysaccharide, a natural polymer, composed of a mannuronic acid unit. This compound has been used for a long time in various industries, such as agriculture, food, medicine, textile, cosmetics, and printing. SA is also used as a thickener, stabilizer, and emulsifier and for microencapsulation, as well as in slow release drug delivery systems and fertilizers.¹¹ SA has a molecular structure similar to collagen; therefore it can make the skin smooth and elastic and can accelerate wound healing, and it can be used as a natural alternative product for health

care and cosmetics.¹²⁻¹⁴ SA is of biological origin and has good characteristics, such as biocompatibility, biodegradability, and gel-forming ability. Poly(vinyl alcohol) (PVA) is a hydrophilic polymer and is of great interest for use as a biomaterial because of its good biocompatible properties. It has chemical stability, high durability, and a high degree of swelling in water or biological fluids. PVA is nontoxic to viable cells, noncarcinogenic, has high biocompatibility, and has a consistency similar to soft tissue, film forming with high mechanical strength, and long-term temperature stability. Its three-dimensional network enables diffusional exchange of nutrients and waste products with the surrounding environment, and it is used in various biomedical, pharmaceutical, biotechnological, and other industrial fields.¹⁵⁻²⁰ However, even though PVA is a biomaterial it is brittle in nature; therefore, it needs to be blended with other polymers or by copolymerization, e.g., with SA, to obtain a better property that can be used to encapsulate or entrap or to immobilize an enzyme or drug in micron or submicron (nano) size, to keep the constancy of its activity, or to prevent activity decreases drastically. Hence it works more effectively and efficiently compared to when it is in free condition.^{6,21,22} The crosslinked alginate hydrogels have been used as a controlled release medium for drugs,²³⁻²⁷ pesticides,²⁸ superabsorbent filament fibers,²⁹ and flocculants.³⁰

In the presence of an aqueous solution, the polymer chains absorb water and the association, dissociation, and binding of various ions to polymer chains cause the hydrogel to swell. The shrinking and swelling properties of hydrogels are currently being exploited in a number of applications including the control of microfluidic flow,³¹ muscle-like actuators,^{32,33} filtration/separation,³⁴ and drug delivery.^{35,36} The structure and properties of hydrogels are similar to those of many biological tissues such as cartilage and the corneal stroma in the eye.^{37,38} Hydrogels are accomplished through large reversible deformation in response to changes in several environmental factors.³⁹ For example, hydrogel size is sensitive to pH, temperature, concentration of salts, and electric fields.

EXPERIMENT

MATERIALS AND METHODS

Materials

SA, PVA molecular weight 125,000, and glutaraldehyde (25%) were purchased from S.D. Fine Chem Limited, Mumbai, India. Hydrochloric acid, perchloric acid, sodium hydroxide, and acetic acid were purchased from Reachem Laboratory Chemicals Private Ltd, Chennai, India. Calcium chloride, magnesium chloride, sodium chloride, and potassium chloride were purchased from E-Merck Limited, Mumbai, India, and double distilled water was used throughout the experiment.

Methods

Preparation of SA/PVA hydrogels

First 7 g of SA was dissolved in 100 mL of water with constant stirring. Then 9 g of PVA was dissolved in the same solution with stirring for about 3 h at 80°C to 85°C, 12 mL of glutaraldehyde

(25%) was added to the same solution, and this solution was kept at 80°C for 3 h. After 3 h the obtained hydrogel was washed with distilled water and ethanol to remove the excess monomer and crosslinking agent. After washing 2-3 times the hydrogel was dried at 40°C in an oven. Likewise the different SA/PVA hydrogels synthesized with varying volume of glutaraldehyde (10 and 8 mL) were used for swelling studies.

CHARACTERIZATION

Fourier-transform infrared spectroscopy

The FTIR spectra of the SA, PVA, and the crosslinked hydrogel samples were recorded in the range of 4000 to 500 cm^{-1} to provide the proof of hydrogels (Figure 1).

Surface morphology of hydrogels

The surface morphology of the SA, PVA, and glutaraldehyde crosslinking hydrogels were investigated using scanning electron microscopy (SEM) (SEM Zeiss, LS15) (Figure 2).

Swelling behavior of hydrogels

For the swelling behavior of hydrogels, the swelling ratio of the hydrogel samples was measured at different temperatures in different solvents by gravimetric method. Pre-weighed dry hydrogel samples were immersed in excessive different solutions and left undisturbed for 24 h, 48 h, and 72 h at different temperatures like room temperature, 30°C, 37°C, and 40°C until constant values were obtained. Degree of swelling rate can be calculated by the following equation:

$$\% \text{ DS} = (W_2 - W_1) / W_1 \times 100 \dots \dots \dots \text{(Equation 1)}$$

% DS is the degree of swelling expressed in a percentage and W_1 and W_2 are the masses of sample before and after swelling, respectively (Figures 3 to 5) (Table 1).

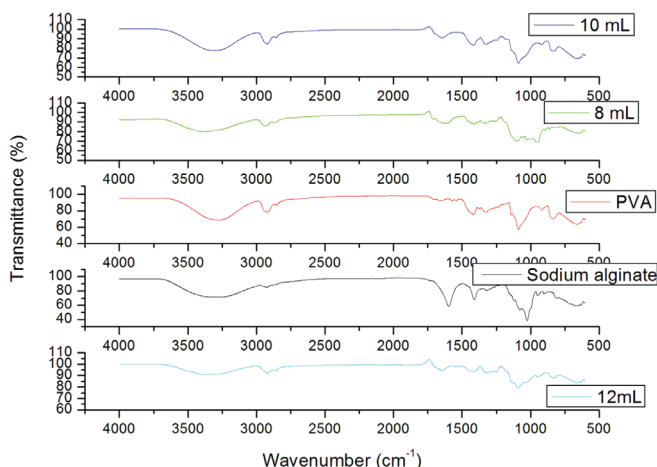


Figure 1. FTIR spectra of pure SA, PVA, 12% glutaraldehyde crosslinked, 10% glutaraldehyde crosslinked, and 8% glutaraldehyde crosslinked hydrogels

FTIR: Fourier transform infrared spectroscopy, SA: Sodium alginate, PVA: Poly(vinyl alcohol)

Swelling at various pHs

The solution was adjusted to acidic, basic, and neutral pH by diluting with phosphate buffer (pH 3.2, pH 7, pH 2, and pH 10) solutions at room temperature, 30°C, 37°C, and 40°C. The pH values were checked by pH meter. The dried hydrogel samples were used for the swelling measurement according to Equation (1) (Figure 6).

Swelling in salt solutions

The swelling capacity of hydrogels was determined in different salt solutions (KCl, NaCl, CaCl_2 , and MgCl_2) and also with various concentrations like 0.4, 0.6, 0.8, 1, and 1.2 N according to the above method (Figure 7).

RESULTS

The authors reported the swelling effects on hydrogels of different salts, acids, bases, temperatures, and pH values. A higher swelling rate was shown by 8 mL of glutaraldehyde compared to 10 mL and 12 mL. Figure 1 shows the FTIR spectra of the molecular interaction between SA and PVA. The surface morphology of the hydrogels was studied using SEM (SEM Zeiss, LS15) as shown in Figure 2; Figures 3 to 5 and Table 1 represent the swelling behavior of the hydrogels at different temperatures, i.e. 30°C, 37°C, 40°C, and room temperature, with different salts. Figure 6 shows the behavior of the hydrogels at different pH values.

DISCUSSION

Fourier transformed infrared spectral analysis

Figure 1 represents the FTIR spectra, characterizing the molecular interaction of SA and PVA hydrogels. The FTIR spectra of SA show the characteristic absorption peak at 3270.47 cm^{-1} is for the hydroxyl (-OH) group. The asymmetric and symmetric stretching vibration of the carboxylic (COO^-) group is found to be at 1597.36 and 1412 cm^{-1} , respectively.^{40,41} The peak at 2925.38 cm^{-1} represents the C-H alkyl stretching bond.⁴² An absorption peak around 2919.05 cm^{-1} shows the characteristic spectra of PVA. This peak arises from the C-H stretching at 1570 to 1420 cm^{-1} is assigned for CH_2 (vinyl group), while the sharp absorption peak at 1150-1050 cm^{-1} is used for indication of PVA.⁴³ In addition, it was found that the peak at 1549-1453 cm^{-1} is a stretching band for the CH_2 group. This band is also found in pure PVA and crosslinked SA/PVA hydrogels. The decrease in wave number of the carbonyl peak from 1652.14 to 1635.24 cm^{-1} is for the crosslinking of SA/PVA hydrogels. Crosslinking of glutaraldehyde takes place at 2863 to 2750 cm^{-1} .

SEM images

SEM describes the surface morphology of SA/PVA hydrogels in Figure 2. According to the SEM images (Figure 2a), the pure SA shows a very smooth surface nearly devoid of any surface feature.⁴³ In Figure 2b the SEM images of pure PVA show a very smooth, uniform, and nonporous surface structure, which may be attributed to the crystallization of PVA.⁴⁴ However, the addition of SA to PVA hydrogel in different portions provides very tiny pores at the surface and these pores decrease with an increase in glutaraldehyde concentration (Figures 2c to 2e).

Effect of pH on the swelling of hydrogels

The sensitivity of the hydrogels was measured from pH 2 to pH 10. No additional ions (through buffer solutions) were added to the medium for setting pH because the absorbency of an absorbent is strongly affected by ionic strength. Therefore, stock HCl (pH 1.0) and NaOH (pH 10.0) solutions were diluted with distilled water to achieve the preferred acidic or basic pH values, respectively. In Table 2 and Figure 6, the swelling

capacity of hydrogel at pH 2 can be accredited to the high repulsion of anion-anion COO⁻ groups. At basic conditions (pH ≥ 7), most of the carboxylate groups are protonated and the low swelling values of hydrogels can be attributed to the presence of nonionic hydrophilic -OH and -COOH groups in the PVA and alginate backbones, respectively. The swelling capacity is decreased with further increase in pH (pH 10 or pH >7). Again

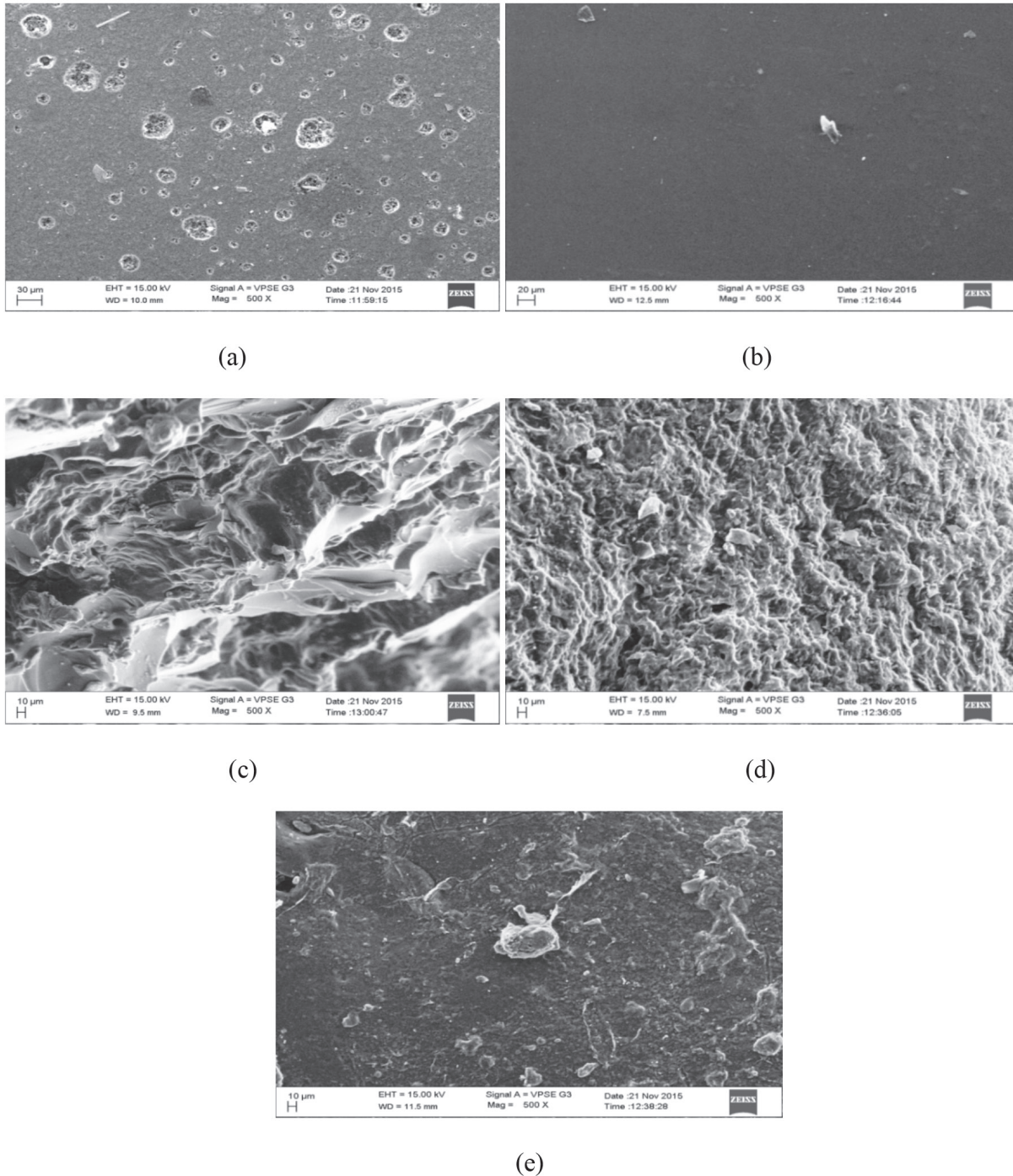


Figure 2. SEM images of (a) pure sodium alginate, (b) pure PVA, (c) 8 mL glutaraldehyde crosslinked SA/PVA hydrogel, (d) 10 mL glutaraldehyde crosslinked SA/PVA hydrogels, (e) 12 mL glutaraldehyde crosslinked SA/PVA hydrogels

SEM: Scanning electron microscopy, SA: Sodium alginate, PVA: Poly(vinyl alcohol)

the swelling loss is due to the counter ions, i.e. Na^+ , that shield the charge of the carboxylate anions and prevent efficient anion-anion repulsion. As a result, a remarkable decrease in equilibrium swelling is observed.

pH Dependence of the swelling rate of water

The swelling rate decreased with increasing pH from 2 to 10; it was evident from the data given. The negatively charged ionic backbones of PVA and SA are more expanded because the protonation of COO^- groups is negatively charged. This expanded form makes for easy diffusion of water molecules into the hydrogel network. On the other hand, the $-\text{OH}$ groups are mostly in the protonated form and show less polar character at $\text{pH} \geq 7$. Therefore, this results in a polymer with lower affinity to water. Thus, hydrogels are less expanded at $\text{pH} \geq 7$. The increases in swelling ratio are responsible for the theory of electrostatic repulsion between COO^- ions in the polymer chains and ionic present in the pH solution and the ionic osmotic pressure generated from mobile counter ions to charged ions in the network. Thus, the charge density of the hydrogel is diluted, because PVA is not ionic in character (Table 2). Figure 6 shows the swelling studies of phosphate buffered pH solutions. The glutaraldehyde crosslinked PVA/SA samples show a gradual increase (in swelling degree at pH 2 and 3.2) followed by a decrease in swelling degree at pH 7 and 10 at different temperatures (25°C , 30°C , 37°C). In these studies the 8% glutaraldehyde crosslinked hydrogel has a high swelling degree compared to the 10% and 12% glutaraldehyde crosslinked hydrogels.

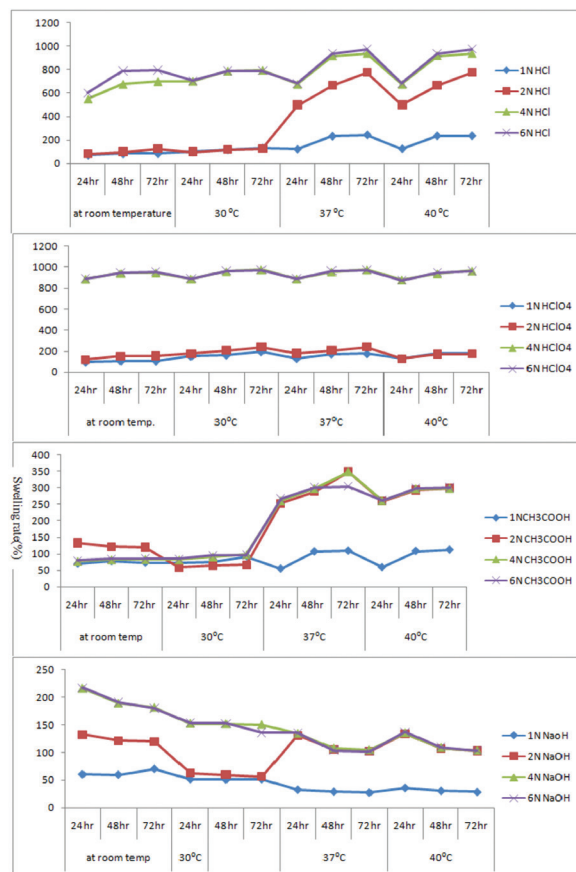


Figure 3. Swelling rate of 8 mL glutaraldehyde crosslinked hydrogels

Table 1. Data of swelling rate of 8 mL glutaraldehyde, 10 mL glutaraldehyde, and 12 mL glutaraldehyde crosslinked hydrogels at 37°C

Conc.	8 mL glutaraldehyde			10 mL glutaraldehyde			12 mL glutaraldehyde		
	24 h	48 h	72 h	24 h	48 h	72 h	24 h	48 h	72 h
1N CH_3COOH	54.46	107.56	109.85	45.78	63.39	66.32	14.02	32.15	33.85
2N CH_3COOH	252.3	288.74	348.05	51.23	69.34	70.15	14.71	32.79	34.21
4N CH_3COOH	260.74	297.36	348.05	60.19	72.43	74.12	14.97	33.56	34.69
6N CH_3COOH	266.08	300.42	303.35	63.48	74.12	77.06	15.09	33.81	34.8
1N HCl	70.16	229.4	240.17	61.19	67.93	71.72	12.43	23.79	25.77
2N HCl	495.5	662.89	771.3	88.49	112.83	115.98	19.19	28.07	32.08
4N HCl	673.93	918.08	938.37	126.25	133.29	137.58	28.18	35.93	40.34
6N HCl	679.83	937.44	973.77	129.18	133.7	139.0	55.44	69.88	71.86
1N HClO_4	124.47	169.92	173.65	132.12	133.5	137.56	11.09	10.69	11.79
2N HClO_4	179.23	209.78	239.01	166.09	207.7	209.05	17.74	22.18	27.19
4N HClO_4	890.19	957.01	976.08	260.01	268.59	277.18	19.21	23.29	31.07
6N HClO_4	892.27	968.14	973.0	263.72	268.72	278.29	23.41	32.17	34.02
1N NaOH	47.26	47.02	46.24	32.87	29 April	27.64	34.97	22.83	19.31
2N NaOH	50.75	50.13	49.08	130.31	105.43	101.92	35.21	29.01	29.09
4N NaOH	53.24	53.02	52.86	134.04	107.47	104.36	39.93	38.14	36.69
6N NaOH	55.23	54.71	53.01	135.6	104.25	102.1	41.74	37.25	36.07

Effect of temperature on the swelling of hydrogels

It is obvious from Figure 6 that the temperature leading to hydrogels with the highest absorbency is around 37°C. The swelling capacity of hydrogels decreased with increasing temperature above 37°C. The increase in swelling rates is dependent on the kinetic energy of the polysaccharide chains, which led to lower soluble content of the hydrogel as well as increasing concentration of glutaraldehyde diffusion rate of SA and PVA backbones. The higher reaction temperature proves the results from higher reactant movement and effective collision. At temperatures about 37°C, the possible “thermal

crosslinking” reaction to polysaccharide backbones may play a major role in the creation of low-swelling hydrogels. In addition, the swelling loss may be related to the increase in crosslinked bond formation of completion of the ester and ether formations by further reaction to the possible mono-ester species with another polysaccharides chain (Scheme 1).

Effect of salt solution on hydrogels

Hydrogels are considered polyelectrolytes, suggesting that their porosity should decrease as ionic strength increases. SA/PVA hydrogels with various chloride salt solutions are appreciably

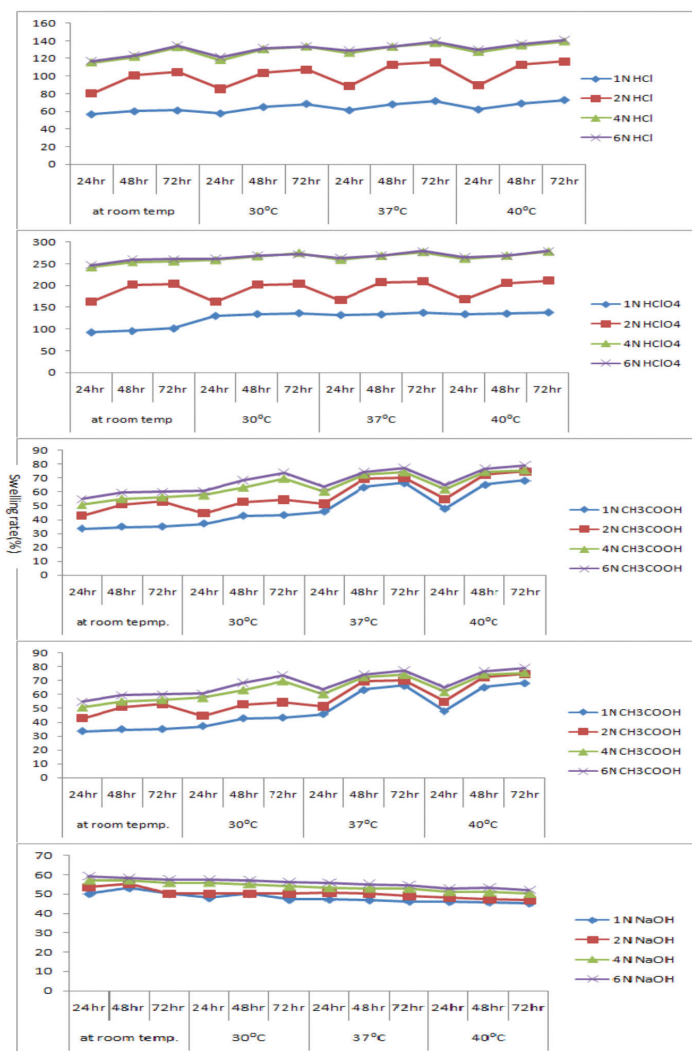


Figure 4. Swelling rate of 10 mL glutaraldehyde crosslinked hydrogels

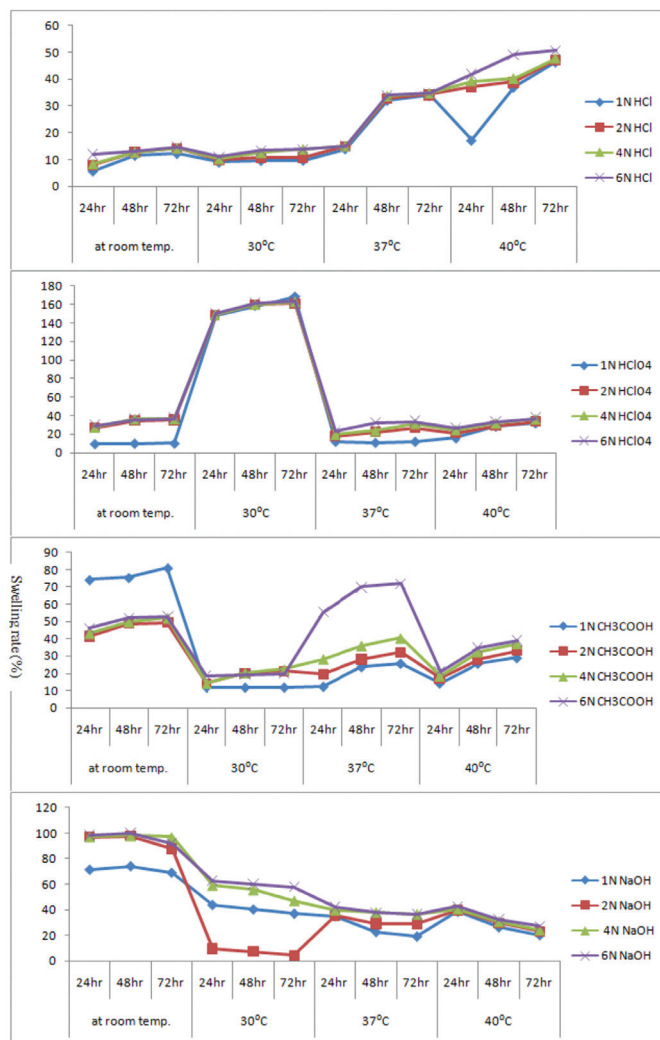


Figure 5. Swelling rate of 12 mL glutaraldehyde crosslinked hydrogels

Table 2. Data of swelling studies of hydrogels in different pH solutions at 37°C

	8 mL glutaraldehyde			10 mL glutaraldehyde			12 mL glutaraldehyde		
	24 h	48 h	72 h	24 h	48 h	72 h	24 h	48 h	72 h
pH 2	120.2	121.56	122.01	75.65	76.92	77.15	75.19	76.08	77.33
pH 3.2	109.2	113.2	116.07	72.01	74.1	76.12	73.24	74.19	75.28
pH 7	70.37	77.78	83.34	67.92	68.12	69.12	66.27	67.19	68.92
pH 10	69.24	71.34	73.45	65.26	66.74	67.05	65.48	66.47	67.19

reduced in swelling compared to those measured in deionized water. This results from a charge screening effect of the additional cations causing anion-anion electrostatic repulsion, which leads to a decreased osmotic pressure difference between the polymer network and the external solution. At a given ionic strength, Mg^{2+} and Ca^{2+} contribute more charge than monovalent cations like Na^+ and K^+ and induce a bigger drop in intermolecular repulsion and increased interaction between molecules, which, in turn, cause to a large extent the hydrogel collapse. In addition, Mg^{2+} and Ca^{2+} can chelate COO^- groups, leading to a compact network and causing further shrinking from the hydrogel; on the other hand, we also find that the smaller the radius of atoms of some valent monoatomic cations, the more the water absorption capacity if different cations were $K^+ > Na^+ > Ca^{2+} > Mg^{2+}$ (Table 3 and Figure 7).⁴⁵

CONCLUSIONS

In this work the authors studied the swelling degree in different acids and bases. It is concluded that the degree of

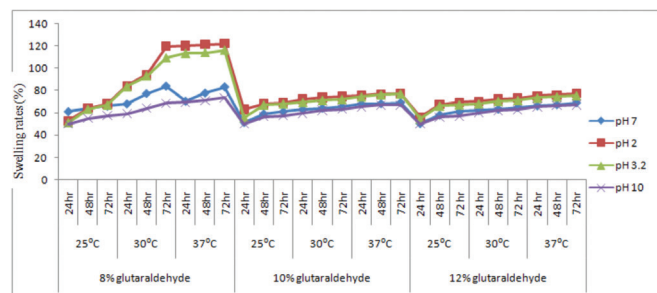


Figure 6. Swelling studies of hydrogels at different pH values of phosphate buffer solutions

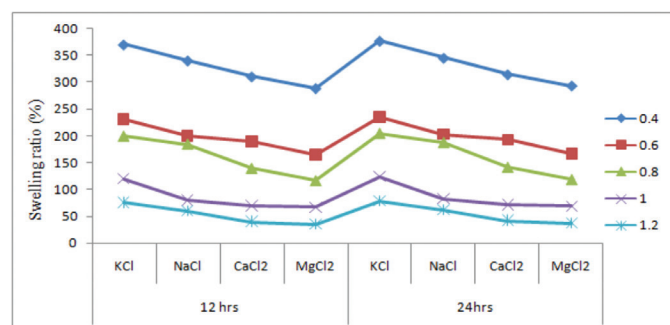


Figure 7. Swelling studies of different concentrated salt solutions at different times

swelling decreases with an increase in the concentration of the glutaraldehyde and also depending on the concentration of the acids. Here the swelling degree of PVA/SA hydrogels gradually increases with increases in the concentrations of acids. The aldehyde groups are covalently bonded with the COO^- and OH^- groups of PVA/SA and consequently the swelling degree is significantly reduced. In different concentrations of different salts the swelling rates decreased with increasing concentrations of salts. The swelling rate is in the order of $K^+ > Na^+ > Ca^{2+} > Mg^{2+}$.

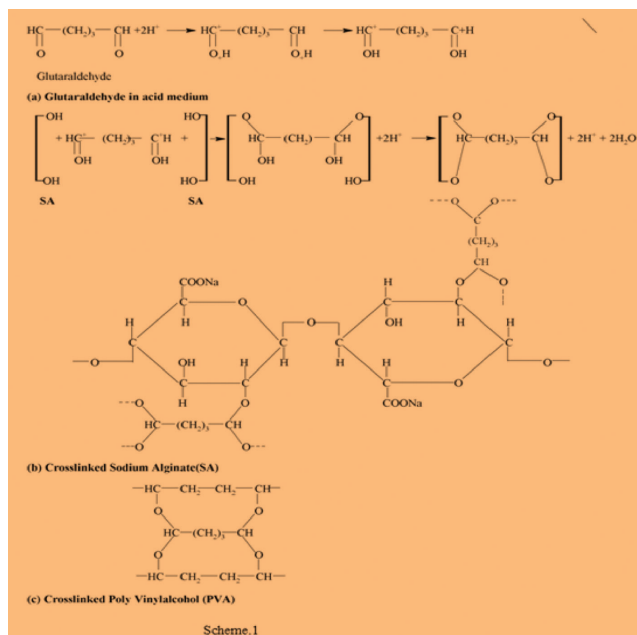
Further extension of the work

This swelling study is to be extended for biomedical and agricultural applications such as drug delivery and controlled release fertilizers.⁴⁵

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Conflict of Interest: No conflict of interest was declared by the authors.



Scheme 1. (a) Glutaraldehyde in acid medium, (b) crosslinked sodium alginate, (c) crosslinked poly(vinyl alcohol)

Table 3. Data of swelling studies of hydrogels in different salt solutions

Conc.	12 h				24 h			
	KCl	NaCl	CaCl ₂	MgCl ₂	KCl	NaCl	CaCl ₂	MgCl ₂
0.4	370.42	340.16	310.72	288.02	377.72	345.45	314.7	293.6
0.6	230.17	200.36	190.64	165	235.46	203.8	193.4	167.9
0.8	200.23	185.34	140.39	117.79	205.0	188.1	142.9	119.2
1.0	120.14	80.08	70.06	67.58	124.19	82.5	72.01	69.1
1.2	75.09	60.63	40.46	35.96	78.20	62.04	42.02	37.4

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