Original Article

Diffusion coefficient, porosity measurement, dynamic and equilibrium swelling studies of acrylic acid/polyvinyl alcohol (aa/pva) hydrogels

Nazar Mohammad Ranjha*[1], Muhammad Hanif[1], Zunaira Afzal[1], Ghulam Abbas[2]

[1]Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan.

[2] Faculty of Pharmaceutical Sciences, Government College University, Faisalabad, Pakistan

Abstract

Objective of the present work was to synthesize hydrogels of acrylic acid/polyvinyl alcohol (AA/PVA) by free radical polymerization by using glutaradehyde (GA) as crosslinkers. The hydrogels were evaluated for swelling, diffusion coefficient and network parameters like the average molecular weight between crosslink's, polymer volume fraction in swollen state, number of repeating units between crosslinks and crosslinking density by using Flory-Huggins theory. It was found that the degree of swelling of AA/PVA hydrogels increases greatly within the pH range 5-7. The gel fraction and porosity increased by increasing the concentration of AA or PVA. Increase in degree of crosslinking, decreased the porosity and inverse was observed in gel fraction. Selected samples were loaded with metoprolol tartrate. Drug release was studied in USP hydrochloric acid solution of pH 1.2 and phosphate buffer solutions of pH 5.5 and 7.5. Various kinetics models like zero order, first order, Higuchi and Peppas model were used for in vitro kinetic studies. The results showed that the drug release followed concentration dependent effect (First order kinetics) with non-Fickian diffusion. FTIR and SEM used to study the structure, crystallinity, and morphology of prepared and drug loaded hydrogels respectively.

Keywords: Acrylic acid, Polyvinyl alcohol, Diffusion coefficient, Metoprolol tartrate

Introduction:

Hydrogel is a hydrophilic mixture which has the properties of both solid and liquid (Li et al. 2006; Van et al. 2008). Hydrogel structure consists of networks that are formed from randomly cross-linked macromolecules (Barbucci 2009). It contains three phases: 1) polymeric-network matrix solid phase, 2) interstitial fluid phase, 3) ionic phase. The solid phase includes a network of cross-linked polymeric chains. Polymeric chains create a three-dimensional matrix with interstitial space filled up with water and often biological fluids. The cross-linked polymeric network can be formed physicochemically, for example by Vander Waals interactions, hydrogen bonding, electrostatic interactions and physical entanglements as well as by covalent bonds. The fluid phase fills in the pores of the polymeric matrix and makes that hydrogel wet and elastic. Due to these properties structure of hydrogel resembles to living tissue. The ionic phase consists of the ionisable groups that are bounded to the polymer chains and the mobile ions (counter-ions and co-ions). This phase exists due to the presence of electrolytic solvent. Hydrogels can be formed from both natural, synthetic and semi synthetic polymers (Lin and Metters 2006). Natural polymers have numerous advantageous properties like inherent biocompatibility, biodegradability, bacteriostatic and wound healing properties. Synthetic hydrogels do not have these inherent bioactive properties.

*Corresponding Author: *Nazar Mohammad Ranjha,*
e-mail: *drnazarmranjha@yahoo.com.*
Faculty of Pharmacy, Bahauddin Zakariya University
Multan
Ph: +92 3336103668

Poly vinyl alcohol (PVA) is a hydrophilic polymer with unique properties. It absorbs water, swells easily and it has extensively been used in controlled release applications (Peppas 1986). It has been used as a controlled drug delivery system for rectal propranolol, atenalol, indomethacin, phenylpropanolamine and emedastin/HCI (Morimoto *et al.* 1989; Morita *et al.* 2000). Swelling characteristics of this hydrogel depends to the presence of salts and the degree to which the acetate groups are replaced by hydroxyl groups (Morita *et al.,* 2000). However, as this hydrogel is quite a hydrophilic system, it releases the drug with a relatively high rate. To prolong drug release from such system, its macromolecular structure should be modified. This can be done by crosslinking and reducing the macromolecular mesh size available for drug diffusion (Kim and Lee 1992).

In recent years, the polyacrylic acid (PAA) and its copolymers have been often used as carriers in drug release systems, because of their multifunctional nature, unique properties and good biocompatibility (Dimitrov *et al.* 2003). It has also been reported that the presence of polyacrylic segments in hydrogels significantly increase their ability to uptake water. It is predictable that due to the presence of carboxylic acid side groups, the swelling behavior of PAA hydrogels is highly dependent on the pH of the surrounding medium (Adnadjevic and Jovanovic 2008). Crosslinking is one of the important factors that affect the swelling of the hydrogels. Increasing the degree of the crosslinking results in decreasing the mesh size of polymer network. Crosslinking hinders the mobility of the polymer chain, hence lowering the swelling ratio. Furthermore, highly cross linked polymers are less acidic because, as the mesh size is reduced, the carboxylic group is concealed and that higher crosslinking ratios hinder the ionization process. Changing the degree of the crosslinking has been utilized to achieve the desired mechanical property of hydrogels. Increasing the degree of the crosslinking of the system will result in the stronger gel. However a higher degree of crosslinking creates a more brittle structure. Hence, there should be an optimum degree of crosslinking in hydrogels (Watts and Lllum 1997).

Drugs can be incorporated into hydrogel matrices by two ways (Lin and Metters 2006). In the post-loading method, drug is absorbed to the preformed hydrogel matrix. For an inert hydrogel system diffusion is the major force for drug uptake. Their porosity permits loading of drug into gel matrix and subsequent drug release at predesigned rate. In the in-situ loading a polymer precursor solution is mixed with drugs or drug-polymer conjugates.

In the present study, pH sensitive hydrogels were prepared through free radical polymerization from PVA and AA with different polymeric, monomeric compositions and degree of crosslinking. GA was used as crosslinking agent. Metoprolol tartrate, an antihypertensive drug was used as a model drug. Effect of pH on swelling and on drug release behavior of hydrogel was studied in USP phosphate buffer solution at various buffers. Sol-gel fraction, degree of cross linking and porosity were determined. Structure of these hydrogels was characterized by Fourier transform infrared (FTIR) spectroscopy. Average molecular weight between crosslinks Mc, volume fraction of polymer V2s, solvent interaction parameters, cross-linked density and diffusion coefficient were also calculated to characterize the structural parameters of PVA/AA hydrogels.

Experimental Materials

For the preparation of hydrogels, Acrylic acid (AA) (Merck, Germany) was used as monomer, polyvinyl alcohol (PVA), (Mw~72000) (Merck, Germany) with hydrolysis degree 98 % as polymer and Glutaraldehyde (GA) (Schlaru Chemie S.A. Spain) as cross linkers, Benzoyl peroxide

(BP) (Park Scientific, U.K.) as initiator and HCl (Fluka, Switzerland) as catalyst.

Synthesis of PVA/AA copolymer hydrogels

PVA solution (10%) was prepared using distilled water; first stirred at room temperature for 2 hour then stirring at 80°C for 30 minutes. Varying amounts of Benzoyl peroxide (1% w/v of AA) were dissolved in acrylic acid and then HCl, as a catalyst, was poured followed by the addition of varying amount of glutaraldehyde (GA) as mentioned in Table 1. Final weight of all the samples was made 100 gm with solvent and the reaction mixture was once again rapidly stirred to ensure homogeneity. The obtained solutions were introduced into the glass tubes and then deoxygenated with nitrogen gas bubbling for 10-20 minutes. The capped tubes were placed in the water bath at a temperature scheme of 45°C for 1 h, 50°C for 2 h, 55°C for 3 h, 60°C for 4 h, 65°C for 12 h. The temperature was raised gradually to avoid the process of extremes of bubbling due to auto acceleration during polymerization. Gels obtained were cut into 7 mm length and washed completely with distilled water. Cylindrical discs obtained were dried at 40°C to constant weight and stored in vacuum desiccators for further use.

Swelling studies

Dynamic and equilibrium swelling ratios were studied in 100 ml medium of pH 1.2, 5.5, and 7.5 at 37⁰C. Dynamic study was performed up to 12 hours while equilibrium study was continued until the samples reached the constant mass and it took almost 2-3 weeks. The swelling ratio of each hydrogels was calculated from the following relation (Ranjha and Mudassir 2008).

$$q = \frac{W_h}{W_d}$$

(1)

Where W_h is the weight of swollen hydrogels at time t, and W_d is the initial weight of dry hydrogels.

Diffusion coefficient

Diffusion coefficient (D) is the amount of a particular solvent that diffuses across a unit area in unit time under the influence of a gradient of one unit. It is an important parameter indicative of the diffusion mobility. It was determined by following relation (Mudassir and Ranjha 2008);

$$D = \pi \left(\frac{h.\theta}{4.q_{eq}} \right)^2$$

(2)

where q_{eq} is swelling of gel at equilibrium, θ is the slop of the linear part of the swelling curves and h is the initial thickness of gel before swelling.

Characterization of network structure of AA/PVA hydrogels

The Flory-Huggins theory was used to obtain solvent interaction parameters χ. According to this theory:

$$\chi = \frac{\ln(1 - V_{2,s}) + V_{2,s}}{V_{2,s}^2}$$

(3)

where $V_{2,s}$ is volume fraction of swollen gel in the equilibrium state. Where $V_{2,s}$ (ml/mole) is volume fraction of swollen gel in the equilibrium state. Average molecular weight between two adjacent crosslinks represents the degree of crosslinking of hydrogels. Mc was determined using equilibrium swelling data through this equation (Flory 1953).

$$M_c = \frac{d_p V_s (V_{2,s}^{1/3} - V_{2,s}/2)}{\ln(1 - V2, s) + V2, s + \chi V_{2,s}^2}$$

(4)

Where dp and ds are the densities (gm/ml) of polymer and solvent respectively while χ is the Flory-Huggins polymer solvent interaction parameter. V2,s (ml/mol) is the volume fraction of swollen hydrogels in equilibrium state. It is the amount of fluid that hydrogel can incorporate into its structure in swollen state (Lin and Metters 2006);

$$V_{2,s} = \left[1 + \frac{d_p}{d_s} \left(\frac{M_a}{M_b} - 1 \right) \right]^{-1}$$

(5)

In this equation dp and ds are the densities of the polymer and solvent. Mb and Ma are

the masses (Li, Luo et al.) of the dry and swollen polymers respectively.

Cross-linked hydrogels are characterized by cross-linked density. The equation used for cross-linked density is given below (Peppas *et al.* 2006)

$$N = \frac{2M_c}{M_r} \tag{6}$$

Mc is the average molecular weight between crosslinks and Mr is the molar mass of the repeating unit and was calculated by the following equation;

$$M_r = \frac{m_{PVA}M_{PVA} + m_{AA}M_{AA} + m_{GA}M_{GA}}{m_{PVA} + m_{AA} + m_{GA}} \tag{7}$$

Where m_{AA}, m_{PVA}, and m_{GA}, are the masses of AA, PVA and GA while M_{AA}, M_{PVA}, and M_{GA} are the molar masses of AA, PVA and GA respectively.

Sol-gel analysis

For sol-gel analysis non washed samples were used. Samples were cut into pieces with 3-4 mm length, dried in a vacuum oven at 45 °C to constant mass, and subjected to soxhelt extraction for 4 hrs. De-ionized water with zero electrical conductivity was used as solvent. Uncross linked polymer was removed with this extraction from the gel structure. Extracted gels were dried again in a vacuum oven at 45°C to constant weight. The gel fraction was calculated by using initial weight of dry gel (W_0) and weight of extracted dry gel (W_1) according to the following equation (Yin *et al.* 2007);

$$\text{Sol fraction (\%)} = \left[\frac{W_o - W_1}{W_o}\right] \times 100 \tag{8}$$

$$\text{Gel fraction (\%)} = 100 - \text{Sol fraction} \tag{9}$$

Porosity measurement

Porosity is actually a measure of the fraction of the volume of voids over the total volume between 0-1, or as a %age between 0-100 percent. Solvent replacement method was used to determine porosity. Dried hydrogels were immersed in absolute ethanol overnight and weighed after excess ethanol on the surface was blotted. The porosity was calculated from the following equation (Lin and Lu 2002);

$$\text{Porosity} = \frac{(M_2 - M_1)}{\rho V} \times 100 \tag{10}$$

where M_1 and M_2 are the mass of hydrogel before and after immersion in ethanol respectively, ρ is the density of absolute ethanol and V is the volume of the hydrogel.

Metorolol tartarate loading and release analysis

Six samples were selected for drug loading and their release analysis. 1% (w/v) of metoprolol tartrate solution in distilled water was used for drug loading. Discs were immersed in this solution until equilibrium was achieved. After achieving equilibrium, fully swelled discs were removed from the drug solution and blotted with filter paper to eliminate the surface drug solution. The drug loaded disks were first dried at room temperature and then dried in oven at 40-45 °C until constant weight was obtained.

For determining the percent drug loading, weighed drug loaded disc were extracted repeatedly with the same solvent used for drug loading up to exhaustion and the concentration of drug in pooled extract was determined spectrophotometrically at λ_{max}222 nm. The quantity of drug loaded was also determined by swelling method (Ranjha *et al.* 2008).

Drug release was measured with USP paddle apparatus type-II associated with spectrophotometer (IRMECO, UV-Vis. U2020. The weighed polymer disk was immersed in 500 ml dissolution medium at 37 °C and stirred at a rate of 100 rpm for maintaining a uniform drug concentration in the medium. With each sampling, the solution was changed with fresh medium in order to maintain the total volume constant. Metorolol tartrate release was observed at λ_{max} 222 nm with readings taken up to 12 h. Drug release was conducted in USP hydrochloric acid solution of pH 1.2 and phosphate buffer solutions of pH 5.5 and 7.5.

Analysis of release pattern

Swelling-controlled release occurs when diffusion of drug is faster than hydrogel swelling. Drug diffusion time and polymer chain relaxation are two key parameters determining drug delivery from polymer matrices. Zero order, first order, Higuchi and Korsmeyer-Peppas models were used to analyze the drug release pattern. Equations used for these models are as follows;

Zero-order kinetics (Najib and Suleiman 1985):

$$Ft = K_0 t \qquad (11)$$

Where Ft is the fraction of drug release in time t and K_0 is the apparent rate constant for zero-order release constant.

First order kinetics (Najib and Suleiman 1985):

$$\ln (1-F) = -K_1 t \qquad (12)$$

Where F represents the fraction of drug release in time t and k_1 is the first order release rate constant.

Higuchi model (Najib and Suleiman 1985)

$$F = K_2 t^{1/2} \qquad (13)$$

F represents the fraction of drug release in time t and K_2 is Higuchi constant. This model is based on several hypothesis: (1) initial drug concentration in the matrix is much higher than drug solubility, (2) drug diffusion takes place only in one direction, (3) drug particles are much smaller than system thickness, (4) matrix swelling and dissolution is negligible (Mudassir and Ranjha 2008).

Korsmeyer-Peppas model (Peppas 1984);

$$Mt/M\infty = K_3 t^n \qquad (14)$$

where K_3 is constant incorporating the structural and geometric characteristics of the gels and n is the release exponent. This expression describes the release rates in terms of relaxation-controlled transport process and the diffusion-controlled process. The diffusion exponent, n, is dependent on the geometry of the device as well as the physical mechanism for release.

FTIR spectroscopic analysis

Crosslinked hydrogel samples were crushed with pestle in an agate mortar. The crushed material was mixed with potassium bromide (Merck IR spectroscopy grade) in 1:100 proportions and dried at 40°C. The mixture was compressed to a 12 mm semitransparent disk by applying a pressure of 65 kN (Pressure gauge, Shimadzu) for 2 min. The FT-IR spectrum over the wavelength range 4,500-400 cm-1 were recorded using FTIR spectrometer (FT-IR 8400 S, Shimadzu).

Scanning electron microscopy (SEM)

Morphology of the selected hydrogels was observed by using the Scanning electron microscope. Hydrogel samples having drug (Figure 6) and without drug was randomly selected and their combined structure were observed.

Table 1 Feed composition for the preparation of AA/PVA hydrogels

Sample code	PVA content	GA content	AA content
	(g/100g Solution)	(g/100g solution)	(g/100g Solution)
S1	5.5	22	0.22
S2	6.572	22	0.262
S3	7.34	22	0.293
S4	6.572	17.76	0.293
S5	6.572	23.3	0.293
S6	6.572	32.08	0.293
S7	6.572	32.08	0.1314
S8	6.572	32.08	0.197
S9	6.572	32.08	0.329

RESULTS AND DISCUSSION

Effect of pH on swelling and drug release from PVA/AA hydrogels

Eficient swelling was obtained in buffer solution having pH values more than pKa values of AA (4.26). When pH of buffer solution rises above its pKa, the buffer will accept protons and carboxylic groups within the network will be ionized. As a result of this ionization, an electrostatic repulsion along the chain takes place causing an expansion of the originally coiled molecule. Thus, the ionic swelling

Table 2 Flory-Huggins network parameters of AA/PVA interpenetrating networks

| Samples	$V_{2,s}$	X	Mc	Mr	N	$D\ 10^{-5}$ (cm^2/sec)
S_1	0.1332	0.5509	448.00	85.21	10.51	**5.**32
S_2	0.1154	0.5415	686.12	81.69	16.79	7.21
S_3	0.0915	0.5323	1171.16	79.90	29.32	8.89
S_4	0.1255	0.5458	527.28	86.47	12.19	3.26
S_5	0.1165	0.5320	584.08	82.99	14.07	5.49
S_6	0.0970	419	945.93	79.24	23.87	6.11
S_7	0.0676	0.5225	1698.49	81.54	41.65	4.87
S_8	0.0954	0.5341	951.00	81.62	23.32	1.42
S_9	0.0977	0.5349	762.42	81.77	21.53	0.95

pressure will increase and so does the swelling. With increasing pH, the polymeric network becomes more hydrophilic as the degree of ionization increases. Similar attitude has been reported by Ranjha and Mudassir who observed that by increasing the pH, swelling and drug release increases in hydrogels of vinyl acetate-co-acrylic acid (Ranjha and Mudassir 2008).

Effect of monomer concentration on swelling and drug release from PVA/AA hydrogels

Incorporation of AA contents during gel formation renders the swelling of AA/PVA interpenetrating networks pH-dependant. Figure 1 remarkably shows the effect of acrylic acid concentration on the dynamic swelling behavior as a function of pH of swelling medium; keeping cross-linkers concentrations constant to 0.5% of AA. Dynamic and equilibrium swelling coefficients do not increase considerably at low pH because carboxyl groups remain associated and form hydrogen bonding with PVA chains but at higher pH there is significant increase in swelling coefficient with increase in AA concentration due to development of large number of carboxylate ions, which cause repulsion between them (Ranjha *et al.* 2011).

Effect of GA concentration on swelling and drug release from PVA/AA hydrogels

The swelling of the hydrogel samples (S_7 to S_9) was studied as a function of different

Figure 1 Dynamic swelling coefficient of
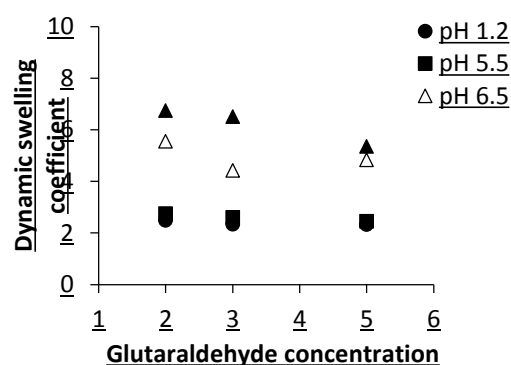
AA/PVA interpenetrating networks with different concentration of acrylic acid (17.76, 23.3 & 32.08 gm) using GD as crosslinking agent (0.5 % of acrylic acid) in solutions of different pH in 0.05M USP phosphate buffer at 370C
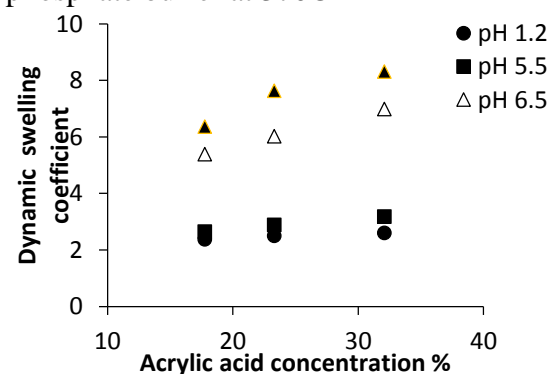
Figure 2 Dynamic swelling coefficient of AA/PVA interpenetrating networks with different concentrations of GD as crosslinking agent (2 %, 3% and 5% of acrylic acid) in solutions of different pH in 0.05M USP phosphate buffer at 37 C^0 of AA) at different pH values ranging from 1.2 to 7.5.

feed cross linker concentrations (2, 3, 5 wt
 Figure 2 shows the effect of cross linker
concentration on the dynamic swelling
coefficient keeping PVA and AA content.
Here a clear picture is seen that the %age
swelling decreased as the amount of GA
was increased. This is due to the fact that as
the concentration of crosslinking agent was
increased, there was a decrease in the mesh
size of the polymer network and the
stability of the polymeric network was
increased which resulted in the tighter
structure and showed low swelling values
as compared to samples with low degree of
crosslinking. Also crosslinking hinders the
mobility of the polymer chain, hence
lowering the swelling ratio. It is now
obvious here that the swelling behavior also
depends upon the crosslinking density
(Varshosaz and Koopaie 2002).

In order to evaluate the effect of
crosslinking agent concentration on drug
release, three samples with different
crosslinking agent concentrations keeping
PVA/AA concentrations constant were
used. Figure 3 shows the effect of GA
concentration on drug release. It was
observed that with increase in GA
concentration, there was decrease in drug
release at all pH values.
This was due to increase in stability, small
pore size and tighter structure in samples
with higher crosslinking ratios which
retarded the expansion of network and
chain relaxation.

**Structural parameters of PVA/AA
hydrogels**
As the key parameters to characterize cross-
linked swollen network are the number
average molecular weight between
crosslinks Mc and polymer volume fraction
V2,s because Mc is a measure of degree of
crosslinking of the polymer while V2,s
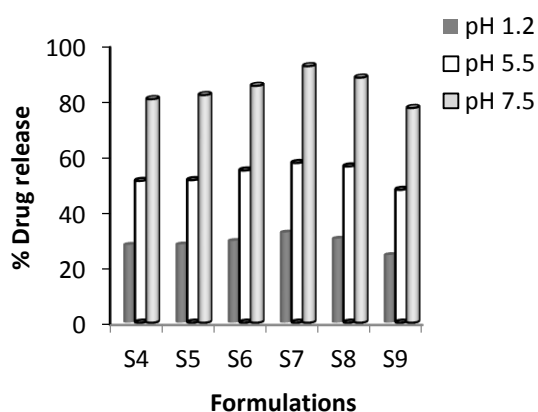evaluates the amount of fluid absorbed and
retained by the network.

Figure 3 Percentage drug release of
different formulations S4 to S6 (17.76/6.57,
23.3/6.57, 32.08/6.57 AA/PVA) and S7 to
S9 (0.13, 0.2, 0.33, % w/w GD) at pH 1.2,
5.5 and 7.5

During mathematical modeling,
equilibrium swelling data at pH 5.5 was
used as most of samples broke at higher pH.
Numerical values of Mc and volume
fraction of polymer V2,s, solvent
interaction parameter χ, number of links
between crossliks N and diffusion
coefficient D, has been elaborated in Table
2. A critical overview of these results
clearly depicts that values of V2,s and χ
decreased by increasing concentration of
AA and increased by increasing
concentration of PVA and crosslinking
agent. Mc and

Table 3 Porosity and amount of drug
loaded in selected samples

	Porosity (%)	Gel fraction (%)	Amount of metoprolol tartrate loaded g/g of dry gel		
			By swelling extraction		By By weight
S$_1$	13.22	89.93	-	-	-
S$_2$	18.39	91.95	-	-	-
S$_3$	20.39	93.56	-	-	-
S$_4$	35.69	91.07	0.1281	0.1179	0.1245
S$_5$	26.38	88.58	0.1298	0.1215	0.1205
S$_6$	18.72	85.23	0.1373	0.1323	0.1345
S$_7$	28.84	89.56	0.1638	0.1587	0.1612
S$_8$	17.46	91.01	0.1494	0.1403	0.1425
S$_9$	12.25	93.27	0.1134	0.1092	0.1074

number of links N are directly proportional to concentration of AA and inversely proportional to concentration of PVA and cross linker. This can be explained as the average molecular weight between crosslinks Mc is related to cross-linked density. If cross-linked density is higher than Mc will be lower. By increasing the concentration of cross linker, cross-linked density increased and as a result the value of Mc decreased (Jianqi and Lixia 2002).

Sol- Gel fraction

When the sol-gel fraction of different formulations of PVA/AA was calculated, it was noticed that the gel fraction increased with increasing the concentration of AA, PVA and GA while the sol fraction decreased. Figure 4 show effects of AA, PVA and crosslinking agent concentrations on the gel fraction of different formulations of PVA/AA. As with increasing polymer, monomer and GA concentration, there will be more crosslinking which will ultimately increase the gel strength.

Porosity

It was observed that by increasing AA and PVA concentrations porosity also increases as shown in Table 3. It can be explained as by increasing the concentration of polymer and monomer; the viscosity of solution increased which prevented the bubbles to escape from solution forming interconnected channels thus porosity increased. Figure 4 elaborates the effect of polymer, monomer and crosslinking agent on porosity. By increasing the concentration of GA (S_7 to S_9) porosity was decreased. As molecular entanglement between PVA and AA increased by increasing cross-linking density, there was a decrease in mesh size of hydrogen and less pore formation which resulted in decreased porosity.
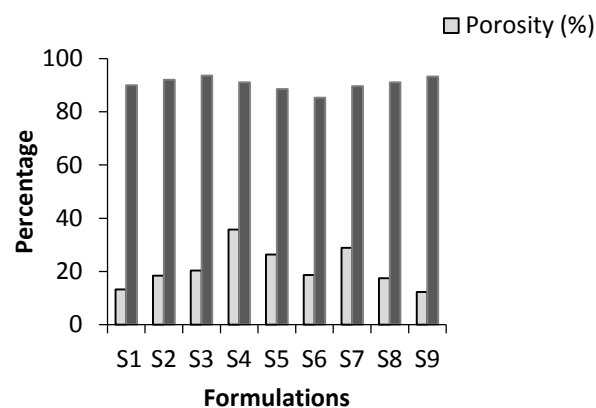

Figure 4 Percentage drug porosity and gel fraction of different formulations S1 - S9

Drug release mechanism

The release of water soluble drugs loaded in hydrogels occurs only after penetrate gets into the polymer networks to swell and dissolve the drug, followed by that drug diffuses out through the aqueous pathways to the surface of the device. The drug release is closely related to the swelling characteristic of the hydrogels, which in turn, is a key parameter of chemical architecture of the hydrogels. The method that best fits the release data was evaluated by the regression coefficient (r). A criterion for selecting the most appropriate model was based on the ideal fit indicated by the values of regression coefficient (r) near to 1.

Values of regression coefficient (r) for zero order and first order obtained from drug loaded PVA/AA hydrogels at varying content of AA and the degree of crosslinking are given in the Table 4. For most of the samples, the value of regression co-efficient (r) obtained for zero order release rate constants were found higher than those of the first order. It is therefore attributed to the fact that drug release from the samples of varying monomeric compositions and the degree of crosslinking are according to zero order release.

In Higuchi model the value of the regression coefficient (r) at different monomeric composition and at different degree of crosslinking indicated that the drug release mechanism is diffusion

controlled. As for diffusion controlled system, the plot of drug released versus the square root of time is linear, which indicates diffusion controlled system.

Effects of AA and GA on release exponent "n" values are given in a Table 5. The value of 'n' for the release of metoprolol tartrate different pH has been evaluated from the slope and intercept of the plot ln M_t/M_∞ versus ln t and the results presented that the values of 'n' are between 0.5 and 1.0 which indicates a non-Fickian or anomalous diffusion mechanism. It also clarifies that the rate of polymer chain relaxation and the rate of drug diffusion from these hydrogels are comparable (Singh *et al.* 2008).

Fourier Transform infrared spectroscopy (FTIR)

In order to confirm PVA/AA interactions, samples were analyzed by FTIR. Figure 5 shows spectra of pure PVA, PVA/AA hydrogel and drug loaded PVA/AA hydrogel. The FTIR spectra of pure PVA showed a broad peak at 3425 cm^{-1} indicating stretching of hydroxyl groups (–OH) and peaks at 2923 cm^{-1} 2850 cm^{-1} are due to –C-H stretching vibration. The peaks at 1485 cm^{-1} and 1342 cm^{-1} could be assigned to –CH2 scissoring and –OH bending vibration, respectively. The peak at
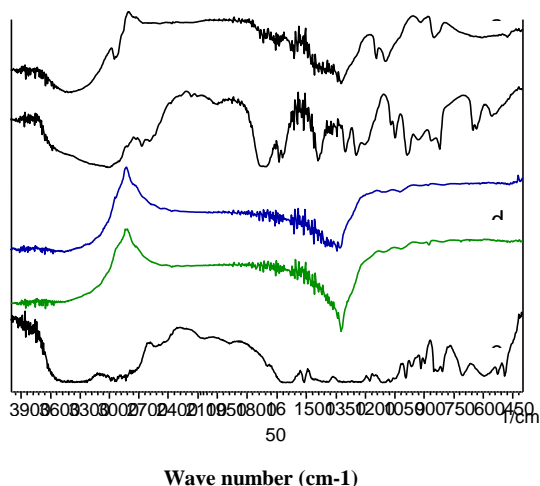

Wave number (cm-1)

Figure 5 FTIR spectrums of pure polyvinyl alcohol (a): acrylic acid (b): PVA/AA hydrogel (c): PVA/AA hydrogel loaded with Metoprolol Tartarate (d): Metoprolol.

1150 cm-1 suggested the presence of –CH-OH goup. The peaks at 1090 cm^{-1} and 917 cm^{-1} showed C-O stretching vibration of secondary alcohol and O-H bend respectively. The FTIR spectra of AA showed a broad peak at 3000 cm-1 for –OH stretching and at 2922 cm-1 for -CH group. The intensity of the esterified carboxyl group at 1751.92 cm^{-1} which decreased and shifted to a lower frequency i.e. 1742.63 cm^{-1} following interaction between PVA and acrylic acid**.**

Scanning Electron Microscopy (SEM)

The results of scanning electron microscopy show that the drug is uniformly distributed in the hydrogels (Figure 6). The hydrogel loaded with drug showed the compact structure which is attributed to the filling of pores with drug and removal of the solvent from the hydrogel when it was dried after swelling.
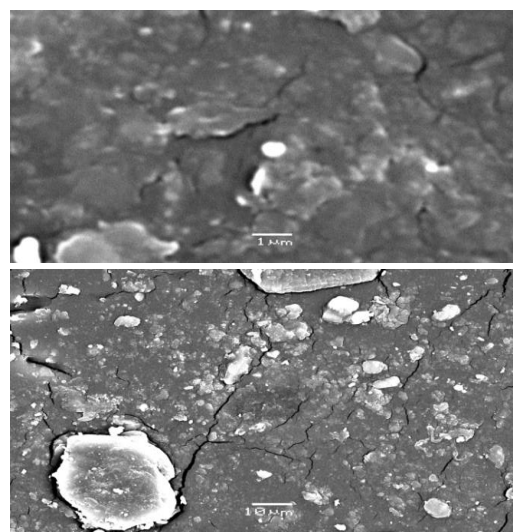

Figure 6 SEM Micrographs of (a) unloaded AA/PVA hydrogel, (b) drug loaded AA/PVA hydrogel

Conclusion

Above mentioned characters reveal the successful formation of pH-sensitive hydrogels of AA and PVA. Moreover

Table 4 Effect of AA and GD contents on release kinetics (zero order, first order and Higuchi models) from AA/PVA hydrogels in solutions of different pH.

Samples	AA contents	pH	Zero order kinetics		First order kinetics		Higuchi model	
			K_0 (h⁻¹)	r	K_1 (h⁻¹)	r	K_2 (h⁻¹)	r
S_4	17.77	1.2	2.158	0.9959	0.0256	0.9939	0.0916	0.9884
		5.5	4.273	0.9963	0.0608	0.9861	0.1841	0.9957
		7.5	6.233	0.9992	0.1331	0.9741	0.2722	0.9975
S_6	32.08	1.2	2.459	0.9939	0.0295	0.9888	0.1056	0.9950
		5.5	4.227	0.9979	0.0622	0.9914	0.1812	0.9957
		7.5	6.423	0.9973	0.1458	0.9835	0.2722	0.9904
GD contents (wt% of AA)								
S_7	2	1.2	2.5099	0.9673	0.0312	0.9535	0.1113	0.9907
		5.5	4.5545	0.9974	0.0693	0.9954	0.1925	0.9859
		7.5	7.2083	0.9955	0.2119	0.9716	0.3141	0.9922
S_8	3	1.2	2.5151	0.9869	0.0305	0.9796	0.109	0.9947
		5.5	4.3521	0.9978	0.0657	0.9894	0.1867	0.9946
		7.5	6.6397	0.9931	0.1664	0.9875	0.2859	0.9966
S_9	5	1.2	2.0486	0.9830	0.0239	0.9773	0.089	0.9948
		5.5	3.6981	0.9913	0.0518	0.9783	0.1608	0.9972
		7.5	5.8038	0.9959	0.1158	0.9918	0.2488	0.9965

Table 5 Effect of AA and GD contents on release mechanism by applying Peppas model on AA/PVA hydrogels in solutions of different pH.

Samples	AA	pH	Release exponent (n)		Order of release
S_4	17.77	1.2	0.765	0.9918	Non-Fickian
		5.5	0.8666	0.9937	Non-Fickian
		7.5	0.705	0.9957	Non-Fickian
S_5	23.30	1.2	0.8729	0.9894	Non-Fickian
		5.5	0.797	0.9781	Non-Fickian
		7.5	0.6486	0.9881	Non-Fickian
S_6	32.08	1.2	0.8317	0.9965	Non-Fickian
		5.5	0.7407	0.9952	Non-Fickian
		7.5	0.6428	0.9882	Non-Fickian
GD Contents (wt% of AA)					
S_7	2	1.2	0.7503	0.9825	Non-Fickian
		5.5	0.6903	0.9785	Non-Fickian
		7.5	0.6562	0.9847	Non-Fickian
S_8	3	1.2	0.8077	0.9925	Non-Fickian
		5.5	0.6916	0.9944	Non-Fickian
		7.5	0.6293	0.9942	Non-Fickian
S_9	5-	1.2	0.8097	0.9949	Non-Fickian
		5.5	0.7285	0.9945	Non-Fickian
		7.5	0.6542	0.9969	Non-Fickian

various parameters like gel fraction, porosity, swelling ratio etc. proved to be linked to the concentration of various variables like AA, PVA and cross linker concentrations. Analysis of swelling kinetic and drug release data showed zero order kinetics and non-Fickian diffusion behavior. FTIR spectroscopy studies revealed the presence of hydrogen bonding between PVA and AA in hydrogels while SEM revealed the sponge like porous structure. So it is concluded that prepared pH-sensitive hydrogels are suitable candidate for orally controlled drug delivery systems.

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