# Formulation, Characterization, Study of Swelling Kinetics and Network Parameters of Poly (MA-co-VA-co-AA) Terpolymeric Hydrogels with Various Concentrations of Acrylic Acid

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**Abstract:** The ter-polymeric hydrogels of vinylacetate (VA), methacrylate (MA) and acrylicacid (AA) were prepared using ethyleneglycoldimethacrylate (EGDMA) as a cross linker and benzoylperoxide (BPO) as an initiator. The effect of acrylic acid concentration on various swelling parameters was studied at different pHs (1.0, 4.0, 5.5, 7.4 and 8.0). A promising relationship was found to exist between media penetration velocity and equilibrium media content of hydrogels at all pH values for various concentration of acrylic acid. The fastest dynamic swelling was observed for the highest concentration of acrylic acid (40 mol % of AA) at pH 8.0. In the kinetic study, during the first hours, a first order kinetics (Fick Model) was observed at pH higher than the value of $pK_a$ (4.75) of acrylic acid, the hydrogels exhibiting non-Fickian diffusion mechanism. Whereas, for the acidic media pH, a second order kinetics was observed (Schott Model). Network parameters strongly support the swelling out comes. The relaxations of the ter-polymeric chain were observed after swelling at pH 8.0 *via* SEM pictures. Thermo gravimetric analysis and differential scanning calorimetric analysis also agree with the above conclusions. Well controlled swelling behavior, network properties, SEM out comings and thermo-gravimetric analysis support the idea to use these hydrogels for targeted drug delivery in the colon part of the digestive tract.

**Keywords:** Hydrogels, acrylic acid, swelling, radical polymerization, ter-polymer.

## 1. INTRODUCTION

Hydrogels are interesting materials that being highly biocompatible and non-toxic in nature have become the centre of attention for extensive research areas especially biomedical, agricultural and pharmaco-biological. The hydrogels, depending on the hydrophilicity of the component polymers are capable of imbibing large quantities of water, maintaining their tridimensional structure. The capability of a macromolecular component to absorb the fluid medium depends upon the polarity of the chains and the polymer's disposition in the space. The physicochemical properties of the hydrogels are governed by the series of parameters: chemical composition, degree of cross linking, presence of functional groups and the variety of solvents that are used.

Hydrogels can be prepared from natural and synthetic polymers [1], but it is quite fortunate that synthetic polymers usually have well defined structures that can be modified to yield tailored degradability and functionality [2].

A quantitative mathematical analysis of material properties, interaction parameters, kinetic events and transport phenomenon within complex hydrogel systems supports network design by identifying the key parameters and mechanisms governing rate and extent of drug release.

The abrupt collapse of ionic hydrogel networks with respect to sudden changes in the swelling environment's ionic force has been studied and reported by different authors [3, 4]. In 1990 Grimshaw *et al*. developed a quantitative model to tract the swelling kinetics of gels sensitive to pH [5]. In 1998, Frusawa and Hayawaalsky devised the first work on the dynamic swelling of pH sensitive networks; they reported that adjusting the environment's pH, the poly-gels (methacrylic acid) (PMA) expanded and collapse reversibly [6].

Recent research has focused on characterizing hydrogels that exhibit specific absorption and network properties such as suitable thermal degradation, favorable porosity, environmental responsiveness to pH and mass transport control (that can be tuned to achieve very special pharmacological applications). For instance, a well-established hydrogel can help to decrease toxic 'burst' effect of a drug, protect fragile drugs in their releasing site and allow targeted dosing [7].

Although AA copolymers with significant concentrations of the cross linker (EGDMA) have been studied and characterized [8, 9], the effects of AA on swelling kinetics and network parameters off A-based ter-polymeric hydrogels have not been specifically

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investigated. In order for these materials to be seriously considered for use *in vivo*, they must be well studied with all aspects. The objective of present work was to determine the effect of the hydrophilic co-monomer, AA, on controlling the water absorption rate in MA-co-VA-co-AA ter-polymeric hydrogels.

## 2. EXPERIMENTAL PART

### 2.1. Materials

Acrylic acid (AA, Fluka), Vinylacetate (VA, Fluka), methacrylate (MA, MERCK), crosslinking agent, ethyleneglycoldimethacrylate (EGDMA, Fluka) and de-ionized water.

### 2.2. Synthesis of Hydrogels

Hydrogels were synthesized using Free Radical Polymerization method [10]. The two monomers Vinylacetate (VA ) and Methacryalte (MA) were mixed in equal volume ratio (1:1) whereas the concentration of Acrylic acid (AA) was used in different grades (0.6, 17.6, 32 and 40mol%) keeping the volume of EGDMA constant which was determined through preliminary swelling experiments. Benzoylperoxide (BPO) was added (1 % w/v) as an initiator to every sample. Ethyl alcohol (100%v/v) was used as solvent.

### 2.3. Swelling Kinetics

For the swelling characterization, five types of solutions (having pH 1.0, 4.0, 5.5, 7.4 and 8.0) were used. The swelling tests were carried out at the body temperature of man ($37^oC$), using a heating bath with controlled temperature. This weight is considered the initial weight or $m_o$. Each disk of a hydrogel was inserted into a beaker having a buffer of a certain pH value, inside a heating bath preset at $37^oC$. The sample was weighed after regular intervals until the sample stopped absorbing; it was the point where either there is desorption or swelling equilibrium is reached. At equilibrium, the quantity of water retained inside the hydrogel can be expressed mathematically in various forms [11, 12 and 13] and will be mentioned as weight swelling index of hydration percentage (eq. 1):

$$S\% = (m_t - m_o/m_o) \times 100 \quad (1)$$

Where, S% is the weight swelling index, $m_t$ is the disk's weight after swelling at time 't' and $m_o$ is the weight of the dry sample.

The adequate pH over the maximum swelling degree is determined by the gravimetric analysis in agreement with the maximum water retention and the determination of water absorbed by the hydrogel. The nature of water diffusion towards the inside of the gel was determined, using the following equation: (below 0.6, fractional swelling values)

$$\ln(W_t/W_e) = \ln k + n \ln t \quad (2)$$

Where $W_t$ and $W_e$ stand for the quantities of water absorbed by the gel in time 't' and at equilibrium respectively; k is constant and is characteristic of the system under consideration and n represents the diffusion exponent that throws light on the mode of water transport into the gel. A value of n up to 0.5 expresses the Fickian diffusion mechanism, and if lies between 0.5 and 1, it indicates that diffusion is of non-Fickian or anomalous type [14, 15]. If n=1, it is a special case where the transport mechanism is known by the name of Type II indicating that the migration of water into the disk occurs at constant speed and is purely controlled by the relaxation of chains.

This equation is applied up to the fraction swelling values less than 0.6 [15]; these are the initial swelling states (where the density of the device remains almost constant), giving linearity when the ln ($W_t/W_e$) is related in function of the ln t. Above 0.6 (the fractional swelling values) for the second kinetic order, the reciprocal of the swelling average ($t/W_t$) is related to the treatment time't' using the following linear equation [16]:

$$t/W_t = A + Bt \quad (3)$$

In this equation, A and B are two coefficients having physical meanings which are interpreted in the following manner [17]:

$$A = 1/k_s W_e^2 \quad (4)$$

and

$$B = 1/W_e \quad (5)$$

Moreover, swelling studies of the hydrogels were also carried out for the determination of netwoek parameters like polymer volume fraction, molecular weight between the cross links and the mesh size at pH values changing from 1-8 at $37^oC$.

### 2.4. Scanning Electron Microscopy

The xerogels were cut to expose their inner structure used for SEM studies. The morphology and porous structures of the dried and swollen hydrogels (pH=8.0) were examined using a scanning electron microscope (Hitachi 3700N) with an operating voltage of 5.00 kV. The SEM photographs were obtained at two different magnification powers (1.00k and 5.00k) in order to specify the pore size and shape.

### 2.5. Thermal Behavior of Acrylic Acid Hydrogels

Thermal degradation of the samples was studied using a thermo-gravimetric analyzer [TA Instruments SDT Q.600 V20 .9 Build 20 simultaneous TGA-DSC], by heating them from room temperature to 600°C at a heating rate of 10°C/min under a nitrogen flow.

DSC was performed with a DSC instrument [TA Instruments SDT Q.600 V20 .9 Build 20 simultaneous TGA-DSC], at a scan rate of 10 degree $min^{-1}$ in a nitrogen atmosphere. The weight of $A_1$, $A_2$, $A_3$ and $A_4$ was 5.47, 7.9, 6.93 and 4.41 mg respectively. The second scan was taken into consideration.

## 3. RESULTS & DISCUSSION

### 3.1. Rate of Swelling & Equilibrium Swelling

In this case, the swelling experiments were carried out at three different pH values (1.0, 4.0, 5.5, 7.4 and 8.0). Since by changing the polymer composition, the swelling kinetics of hydrogels can be controlled [18], a variety of monomers was used to synthesize the hydrogels. The literature survey claims that there are three major elements which are responsible for the swelling process of hydrogels: the ionic content of the system and the surrounding, the cross-link content of the system and the hydrophilic ability of the system. All the three major elements mentioned above, are directly or indirectly depending on the presence of hydrophilic monomer units which are provided by acrylic acid (AA) in the gel systems in our case. The presence of free carboxylic groups in the polymer structure is the measure of swelling capacity of the system. The mechanism of swelling may be discussed at two different levels; macroscopically and microscopically. At macroscopic level, on exposure of a hydrogel to the aqueous medium, water was absorbed by the hydrogel. After a specific time of introduction of the sample disks into the surrounding medium, three regions were distinguishable within the hydrogel matrix (Figure **1**) [19].

The first region is highly swollen with water and obviously mechanically a weaker region. The outer layer of the highly swelled region works as a barrier for the new incoming water and now the second region appears that is moderately swollen and relatively stronger whereas the innermost region remains almost in its glassy state as mentioned in the Figure **1**. In short, across the matrix, water content of the hydrogel from the core to the surface increases with the decrease in the hydrogel content of the system.

In our case, the rate of swelling as well as the equilibrium swelling values increased with both the pH of the surrounding and AA content in the system.

The human body experiences variation of pH along the gastrointestinal tract and also in some specific areas like certain tissues, tumoral areas and sub-cellular compartments etc. In the case of pH-sensitive polymers, the key role played, is by the ionizable weak acidic or basic moieties attached to a hydrophobic backbone. The pendent acidic or basic functional groups added to the polymer backbone either accept or release protons in response to appropriate pH due the which the ionic strength changes in aqueous media [20]. When ionization occurs, the coiled chains extend dramatically, responding to the electrostatic repulsions of the generated charges. When the pH of the medium is changed, the ionic hydrogels exhibit changes in their

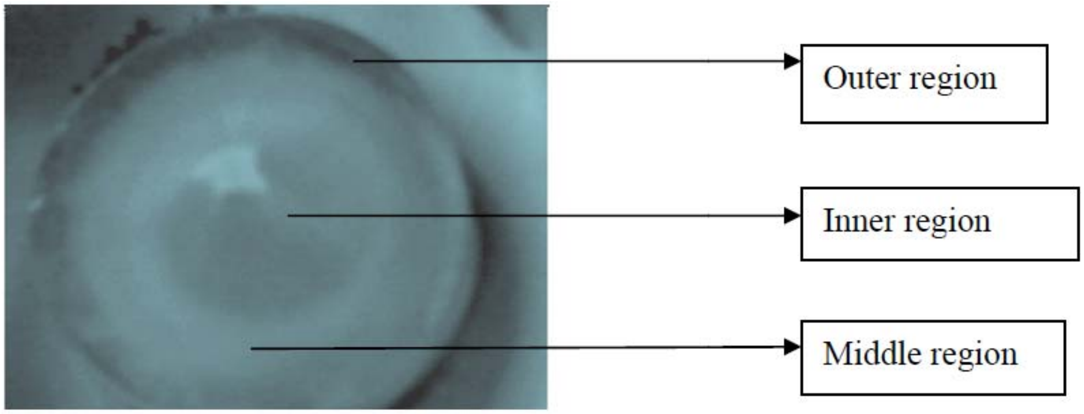

**Figure 1:** Swollen disk showing three regions during the process of swelling.

dynamic and equilibrium swelling behavior. As the degree of ionization of these hydrogels depends on the number of pedant acidic groups in the hydrogels, the electrostatic repulsions also increase between negatively charged carboxylic groups on different chains. This ultimately increases the hydrophilic ability of the network and the greater swelling ratio at high pH (Figures **2** and **3**). Whereas, at the pH lower than the $pK_a$ value of AA, the number of ionized carboxylic groups is not considerable and most of the free carboxylic groups are present in the unionized form which results in the formation of inter-polymer complexes based on inter-polymer hydrogen bonding. At pH higher than 4.5 -5.5 where the degree of ionization of weak poly-acid is higher than 10-15 %, the degree of dissociation is higher as compared to that at pH below 3-4, where the hydrogen bonds between the neighboring free carboxylic groups on the polymer chains, results in the formation of inter-polymer complexes [21].

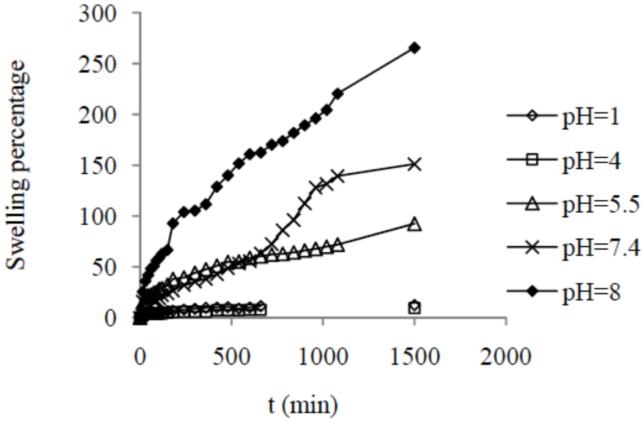

**Figure 2:** Effect of pH on swelling percentage and equilibrium swelling of terpolymeric hydrogels for optimized concentration of acrylic acid sample $A_4$.

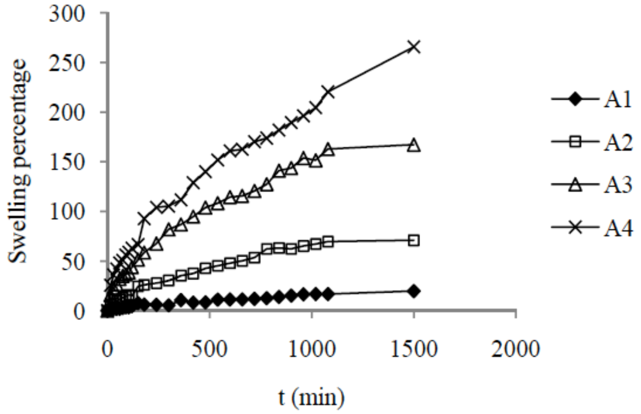

**Figure 3:** Effect of concentration of AA on swelling percentage and equilibrium swelling of terpolymeric hydrogels at pH=8.0.

Media penetration velocity (v) was calculated to determine the rate of advancement of glassy to rubbery front from the surface to the center of the polymer disk.

$$v = 1/2\rho A.\delta w/\delta t \quad (6)$$

Where ρ shows density of the swelling media, A is area of one disk face, w is weight of polymer after specific time t (the early time data at t<15 were used). It is reported that as the media penetrates the glassy polymer swelling starts to crate rubbery region in it [22]. Figure **4** exhibits that the media penetration velocity increased up to approximately 95% and the equilibrium media sorbed increased by an order of magnitude as the concentration AA was increased from 0.6 to 40 mol % (Table **1**).

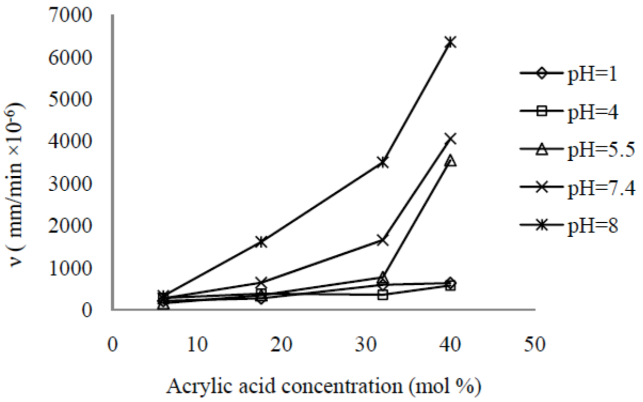

**Figure 4:** Media penetration velocity at pH 1-8 in polymers comprised of 0.6-40 mol % AA.

The pH of the acidic medium appeared to have less effect on the media penetration velocity and the equilibrium sorption but there was a pronounced increase in values of v as well as equilibrium media content, especially at the higher AA concentrations. The sample $A_4$ exhibited 90 % increase in the media penetration velocity when the pH was increased from 1 to 8. The change in penetration velocity with AA content and pH of the medium may be due to two possible mechanisms. First, if the media traveled primarily through the hydrophilic acrylic acid regions of these hydrogel, the increasing number of hydrophilic domains (-COOH) could facilitate the media diffusive pathway through ionization of free carboxylic groups in the basic media. Second, osmotic pressure caused by solvent molecules starts to relax the polymer network chains more effectively in basic media at higher AA concentrations.

The Figure **5** is indicating a good linear relationship between media penetration velocity and the equilibrium media content, a trend that has been observed in poly

**Table 1: Summary of Media Penetration Velocities, Equilibrium Media Contents, Schott,s Model and Power Law Parameters for the Polymers**

| Sample | Media penetration velocity (mm/min×$10^{-6}$) | Equilibrium media sorbed (mg media/mg polymer) | Schott,s Model | Fick's Model | |
|---|---|---|---|---|---|
| | | | $R^2$ | n | $R^2$ |
| pH =1 | | | | | |
| $A_1$ | 212 | 0.057 | 0.988 | 0.486 | 0.965 |
| $A_2$ | 272 | 0.060 | 0.964 | 0.475 | 0.925 |
| $A_3$ | 594 | 0.084 | 0.989 | 0.386 | 0.911 |
| $A_4$ | 637 | 0.124 | 0.975 | 0.790 | 0.721 |
| pH = 4 | | | | | |
| $A_1$ | 281 | 0.049 | 0.959 | 0.494 | 0.996 |
| $A_2$ | 382 | 0.07 | 0.985 | 0.225 | 0.976 |
| $A_3$ | 357 | 0.074 | 0.964 | 0.441 | 0.976 |
| $A_4$ | 577 | 0.094 | 0.981 | 0.286 | 0.991 |
| pH = 5.5 | | | | | |
| $A_1$ | 160 | 0.130 | 0.929 | 0.915 | 0.999 |
| $A_2$ | 348 | 0.142 | 0.159 | 0.566 | 0.996 |
| $A_3$ | 773 | 0.515 | 0.567 | 0.570 | 0.996 |
| $A_4$ | 3550 | 0.924 | 0.927 | 0.432 | 0.992 |
| pH = 7.4 | | | | | |
| $A_1$ | 272 | 0.085 | 0.902 | 0.347 | 0.999 |
| $A_2$ | 645 | 0.394 | 0.565 | 0.595 | 0.996 |
| $A_3$ | 1656 | 1.48 | 0.977 | 0.578 | 0.996 |
| $A_4$ | 1518 | 1.51 | 0.455 | 0.702 | 0.992 |
| pH = 8 | | | | | |
| $A_1$ | 331 | 0.197 | 0.762 | 0.638 | 0.999 |
| $A_2$ | 1614 | 0.71 | 0.873 | 0.612 | 0.996 |
| $A_3$ | 3499 | 1.671 | 0.928 | 0.545 | 0.996 |
| $A_4$ | 6353 | 2.656 | 0.963 | 0.502 | 0.992 |

(NIPA-co-FOSA) copolymers [23]. The Figure **5** clearly shows that the hydrogel sample with high media penetration velocity (i.e. permeability) also have high equilibrium media content (i.e. water solubility). It may be suggested that the slope of the Figure **5** (diffusion of water) was relatively constant through the polymers since the product of diffusivity and the solubility equals the permeability [24]. Again, this relationship looks important in the sense that the equilibrium media content may be predicted in very short experimental time (i.e. on the order of minutes vs. days) using the media penetration velocity.

## 3.2. Kinetic Order of Swelling

The hydrogel's swelling order can be determined through the kinetic studies of swelling of hydrogels. The order may be either 1st (if it obeys Fick's model), or 2nd (if it follows Scott model), even it may follow both of the laws mentioned above, exhibiting the 1st as well as the 2nd order kinetics at a particular time of swelling [25].

In our studies, the Fick's law was applied for the first swelling times, due to the reason that for longer time, there is a deviation in this behavior. So the swelling fraction values ($W_t/W_e$) less than or equal to 0.6 were established in accordance with bibliographic data [26]. The Schott model was used for longer times when the density of the sample has been increased.

As can be observed in the first order (Fick's model) of Table **1**, for the study of swelling at pH 1.0 and 4.0, with the varying concentration of AA content the n values are below 0.5 except in the sample $A_4$ at pH 1.0.

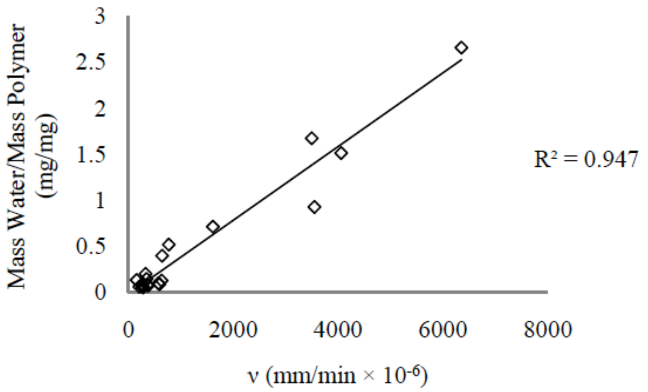

**Figure 5:** Equilibrium media content at pH 1-8 as a function of media penetration velocity in the polymers comprised of 0.6-40 mol% AA.

On the other hand values of n exceed 0.5 in pH medium higher than $pK_a$ value of acrylic acid. Likewise, the Table **1** deals with the results when Schott model ($2^{nd}$ order) is applied for determination of the swelling degree of hydrogels. All the cases show an excellent correlation coefficient (Figures **6** and **7**). These results are indicative of the fact that the systems show diffusion controlled mechanism in earlier times but demonstrates that the system's swelling behavior follows a second order diffusion kinetics and the swelling process for the longer times is not governed by the diffusion, but by the relaxation of the polymer chains.

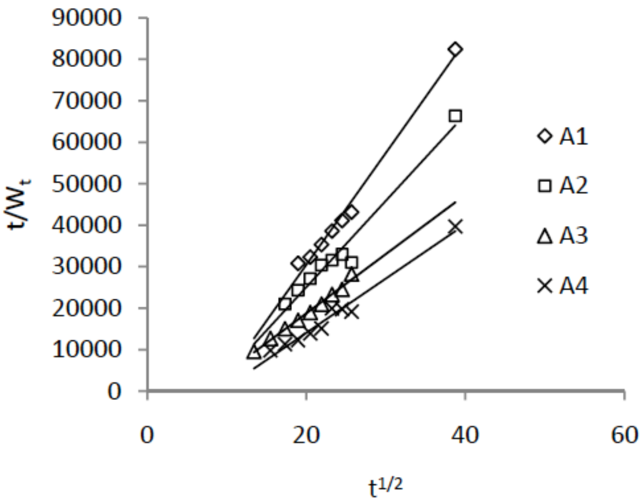

**Figure 6:** Graphic of Schott Model for the four hydrogels studied at pH=8.0.

### 3.3. Network Parameters

When a cross linked polymer is placed in a good solvent, rather than dissolving completely, it will absorb a portion of solvent and subsequently swells. To characterize polymers, swelling is a simple and low cost technique. That is why; the equilibrium swelling values of these hydrogels were used to determine the influence of concentration of acrylic acid, the major swelling component in these gels, on their network parameters. The following well known Flory-Rehner equation was used to calculate $M_c$, the molecular weight between the cross links, one of the important parameters characterizing the cross linked parameters:

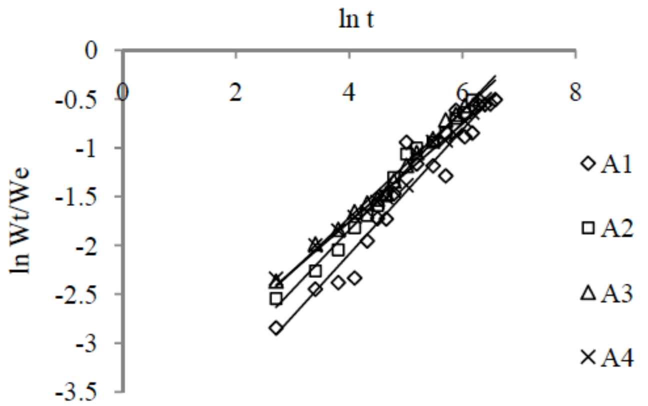

**Figure 7:** Graphic of Fick Model for the four hydrogels studied at pH=8.0.

$$M_c = -d_p V_s / (v_{2,s}^{1/3} - v_{2,s}/2)\ [\ln(1 - v_{2,s}) + v_{2,s} + \chi\, v_{2,s}^{2}] \qquad (7)$$

Whereas, the following equation was applied to calculate the volume fraction $v_{2,s}$

$$v_{2,s} = [1 + d_p/d_s\ (W_a/W_b - 1]^{-1} \qquad (8)$$

Where, $d_p$ and $d_s$ (1g/ml) stand for the densities of the polymer and the solvent respectively. The density of the polymer was determined by the solvent displacement method using n-hexane as a non-solvent. $M_b$ and $M_a$ represent the masses of xerogel and the hydrogel after equilibrium swelling has been attained. $V_s$ stand for the molar volume of the solvent (18.0 ml/mol) and $\chi$ is the Flory-Huggins polymer-solvent interaction parameter. To study the effect of pH of the medium on the network parameters, equilibrium swelling results of poly (AA-co-MA-co-VA) hydrogels, named as $A_1$, $A_2$, $A_3$ and $A_4$ were used to determine $M_c$ values at various pH values (1.0 – 8.0) at 37°C. Experimental values of $M_c$ were tabulated in the Table **2** for hydrogels of varying concentration of acrylic acid.

It is clear from the table that $M_c$ value increased with decreasing cross linking ratio and volume fraction of the swollen hydrogel. Additionally the effect of the external medium pH on the network parameters was also investigated and it was found that, as the pH was raised, the molecular weight between the cross links

**Table 2: Net Work Parameters Determined from Equilibrium Swelling Studies of Hydrogels in Various pH Media at 37°C**

| Sample | Cross linking ratio | Volume fraction of the swollen polymer ($V_{2,s}$) | Molecular weight between cross links ($M_c$) | Cross link density (q) | Mesh size ($10^2$) (ξ) |
|---|---|---|---|---|---|
| pH =1 | | | | | |
| $A_1$ | 6.6 | 0.93 | 31 | 2.87 | 3.40 |
| $A_2$ | 6 | 0.92 | 39 | 2.26 | 3.87 |
| $A_3$ | 5.13 | 0.90 | 47 | 1.83 | 4.32 |
| $A_4$ | 4.3 | 0.86 | 63 | 1.3 | 5.21 |
| pH =4 | | | | | |
| $A_1$ | 6.6 | 0.925 | 32 | 2.78 | 3.45 |
| $A_2$ | 6 | 0.91 | 43 | 2.05 | 3.95 |
| $A_3$ | 5.13 | 0.90 | 47 | 1.83 | 4.17 |
| $A_4$ | 4.3 | 0.88 | 57 | 1.44 | 4.90 |
| pH =5.5 | | | | | |
| $A_1$ | 6.6 | 0.85 | 58 | 1.53 | 4.80 |
| $A_2$ | 6 | 0.84 | 71 | 1.24 | 5.37 |
| $A_3$ | 5.13 | 0.592 | 585 | 0.147 | 15.59 |
| $A_4$ | 4.3 | 0.445 | 997 | 0.08 | 25.89 |
| pH =7.4 | | | | | |
| $A_1$ | 6.6 | 0.89 | 50 | 1.78 | 4.41 |
| $A_2$ | 6 | 0.65 | 232 | 0.379 | 10.53 |
| $A_3$ | 5.13 | 0.5 | 655 | 0.131 | 19.71 |
| $A_4$ | 4.3 | 0.48 | 765 | 0.107 | 35.91 |
| pH =8 | | | | | |
| $A_1$ | 6.6 | 0.79 | 98 | 0.9 | 6.44 |
| $A_2$ | 6 | 0.65 | 289 | 0.304 | 11.81 |
| $A_3$ | 5.13 | 0.30 | 3989 | 0.021 | 57.36 |
| $A_4$ | 4.3 | 0.27 | 54450 | 0.0015 | 223.7 |

increased significantly. For example $M_c$ value of the sample $A_4$ reached 54450 g/mol from 63 g/mol when the pH was changed from 1.0 to 8.0. This relatively higher change in $M_c$ can be attributed to the fact that as the pH of the swelling medium changes from 1.0 to 8.0, the –COOH groups attached to the polymer chains ionize completely to produce charged carboxylate, –$COO^-$, groups and $H_3O^+$ counter ions within the hydrogel. Since free counter ions remain inside the hydrogel to neutralize the fixed charges on the polymer chain, a high osmotic pressure is resulted which causes enhanced swelling percentage. Moreover, carboxylate groups experience electrostatic repulsive force, which are responsible for the relaxation of the polymer network. It was also determined that $M_c$ changed depending upon the composition of the hydrogel. Mole percent of ionizable monomer, AA, based on their total monomer, for example $A_1$, $A_2$, $A_3$ and $A_4$ were 0.6, 17.6, 32 and 40 mol% respectively. Due to the presence of the highest number of ionizable groups, the sample $A_4$ swelled to thee greatest extent and owing to this swelling behavior, its $M_c$ value was found to be 54450 g/mol which is the highest one as compared to those of other samples.

Characterizing cross linked polymers, is another significant parameter called cross linking density, q

$$q = M_r / M_c \tag{9}$$

Where $M_r$ is the molar mass of the repeat unit and is calculated as

$$M_r = m_{VA}\ M_{VA} + m_{MA}\ M_{MA} + m_{AA}\ M_{AA} /\ m_{VA} + m_{MA} + m_{AA} \tag{10}$$

Here $m_{AAm}$, $m_{MA}$ and $m_{AA}$ are the masses of the monomers VA, MA and AA; whereas, $M_{VA}$, $M_{MA}$ and $M_{AA}$ are the molar masses of the monomers VA, MA and AA respectively.

The mesh size, ξ, describing the available space for solute transport within the polymer network, is also an important parameter in analyzing cross linked polymers and was calculated using following equation:

$$\xi = v_{2,\,s}^{-1/3}\,(2Mc/Mr)^{1/2}\,Cn^{1/2}l \qquad (11)$$

Where, $M_r$ represents the molecular weight of the repeating unit, *l*, the C-C bond length (1.54 Ǻ for C-C) and $C_n$, the characteristic ratio taken 6.7 for AA [27]. ξ and q values for these hydrogel systems are represented in Table **2** as a function of pH and acrylic acid concentration. It is indicated that as the swelling of the medium increased with pH, the values of ξ for the sample $A_4$ increased from 5.21 Ǻ to 223.7 Ǻ and q decreased from 1.3 to 0.0015. Thus, with pH, greater swelling resulted more space available between the cross links. It is also noticed that the cross linking decreased with increasing external medium pH, again, indicating the availability of more space for solute transportation. More over, the concentration of AA exhibited marked effect on mesh size at all the pH of the media especially at pH 8.0, the value increased from $6.44A^o$ for $A_1$ to 223.7 Ǻ for $A_4$.

### 3.3. Scanning Electron Microscopy

SEM photomicrographs of optimized formulations with respect to the concentration of the cross linking agent as well as the acrylic acid and pH, are shown in the Figures **8** and **9** at two different magnifications in dried as well as swollen states. In the dried state the large number of small pores is observed in the

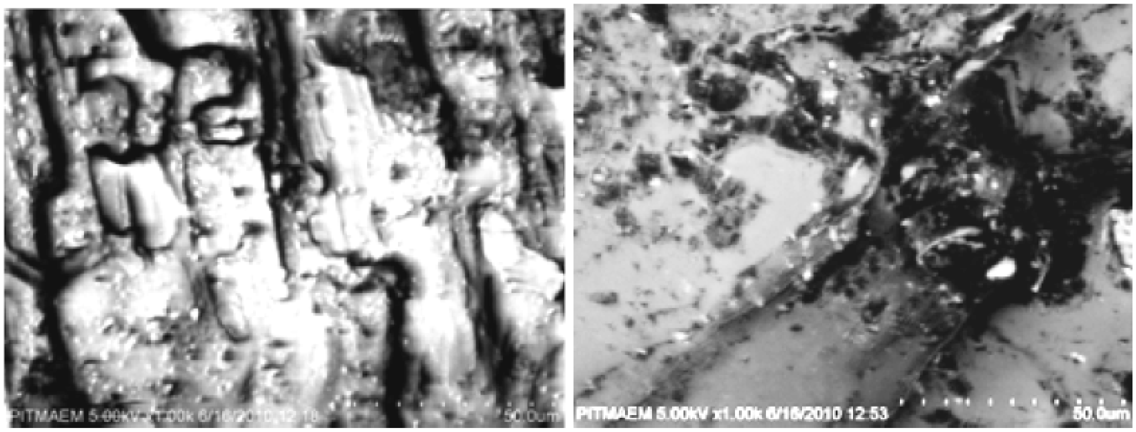

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**Figure 8: a**: SEM structures of the optimized batch [A- 3] inner surface in dry state at low magnification power.
**b**: SEM structures of the optimized batch [A- 3] inner surface at equilibrium state at low magnification power.

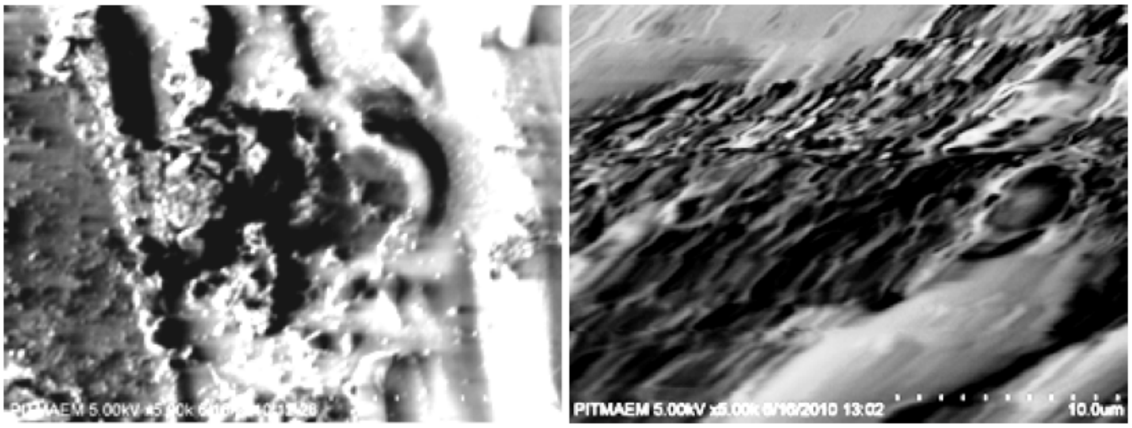

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**Figure 9: a**: SEM structures of the optimized batch [A- 4] inner surface in dry state at high magnification power.
**b**: SEM structures of the optimized batch [A- 4] inner surface at equilibrium state at high magnification power.

structure of the gels. The presence of large number of pores is clear indication of swelling ability of hydrogels.

Whereas, the SEM photographs of the same hydrogel sample at pH 8.0 swollen up to its equilibrium stage exhibits more or less smooth surface which is due to the water retention inside the porous structure of the gel. Moreover, it is clear from the micrographs that at higher magnification power, the surface is more uneven indicating the presence of pores of variable size in the ter-polymeric hydrogels. We can conclude that the pore size is not uniform inside the structure of the gel. The most probable reason may be the presence of different moieties inside the gel structure due to the use of a variety of monomers in composition of the hydrogels. The higher degree of freedom allows the formation of cross links at different distances thus creating a variety in size as well as shapes of the pores. Whatever the size and shape of the pore are, it is confirmed that the hydrogels present a porous structure capable of retaining and transferring fluids after swelling, which is to be expected since the porosity of the material yields a better swelling degree.

### 3.4. Thermal Behavior of Acrylic acid Ter-polymeric Hydrogels

Figure **10** presents the results form the thermo gravimetric analysis of the ter-polymeric hydrogels with four different concentrations of AA content of hydrogels. Thermal degradation proceeds in two steps in all the cases. It was observed that no significant degradation occurred before 200°C in any case. The temperatures, at which the first step started and then ended, are in increasing order with the concentration of AA in the hydrogel systems. This increasing order may be attributed to the fact that with the concentration of AA, the number of inter-polymer hydrogen bonds is also increased resulting in the higher thermal stability. As the concentration of AA exceeds the certain stoichiometric limit, the formation of PAA may appear inside the hydrogel systems. The formation of a variety of polymers inside the gel systems, not only disturbs the surface morphology of the hydrogels but also the thermal properties, which are in clear agreement with the swelling behavior as discussed earlier. The temperatures at which the final and full weight loss (up to 97%) occurs, also exhibited the similar trend just like the first step. Finally, almost complete degradation of the cross-linked polymer occurred near 600°C in all cases. In Figure **11**, the thermo grams of samples $A_1$, $A_2$, $A_3$ and $A_4$ having the concentration of acrylic acid as 0.6, 17.6, 32 and 40 mol % respectively, is observed. The figure indicates that all the gels are showing a high $T_g$ value approaching to 300°C. As we used the samples as xerogels and there was no chain relaxation in the dry state, so covalently formed cross links as well as the presence of hydrogen bonds are the key factors for the high values of $T_{g.}$ According to Ortiz *et al*. and Murali, the films of certain hydrogels obtained a $T_g$ of 79°C before swelling [28, 29, 30, 31], whereas the same sample films gained a $T_g$ of approximately 40°C after swelling.

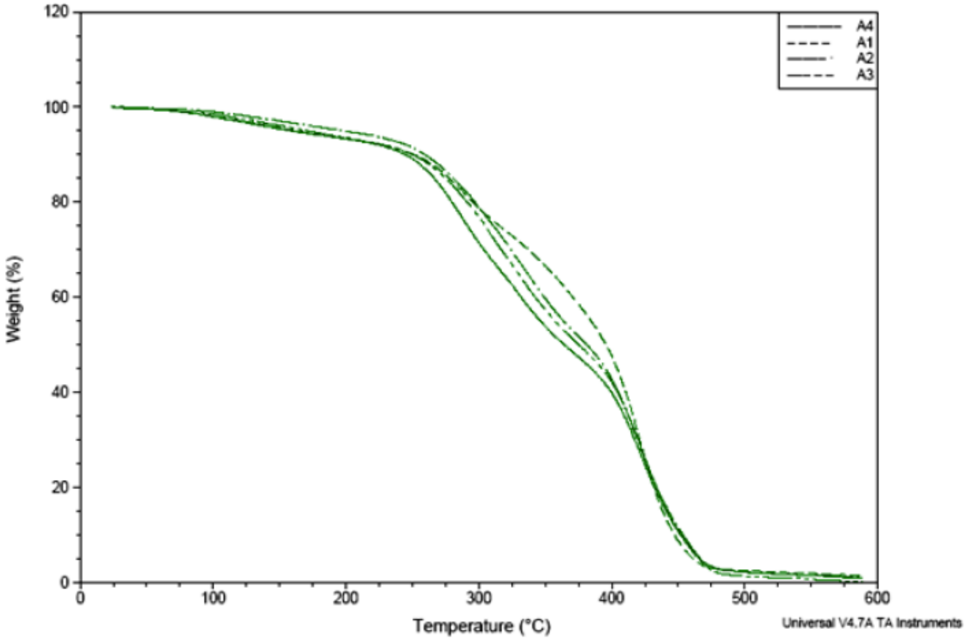

**Figure 10:** TGA curves of Acrylic acid terpolymeric hydrogels.

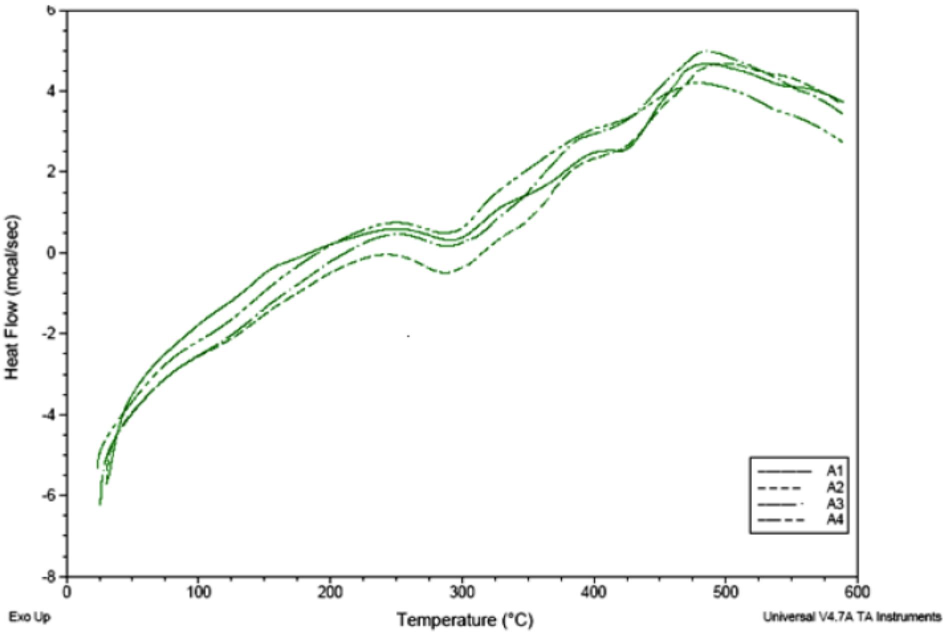

**Figure 11:** DSC curves of Acrylic acid terpolymeric hydrogels.

## CONCLUSIONS

The chemically crosslinked hydrogel copolymer comprised of a hydrophilic monomer (AA) with MA and VA has proven to be effective in controlling the sorption of the swelling medium into the gel matrix. Copolymerizing the AA in chemically cross linked hydrogel increased (1) the media penetration velocity through the copolymers, (2) the change in disk volume during swelling, (3) the equilibrium media content in the gel matrix, (4) and molecular weight between the cross links. The pH of aqueous media showed a marked effect on the dynamic as well as equilibrium swelling behavior of hydrogels. Increasing the media pH enhanced the diffusion of swelling medium by increasing swell-ability of the hydrogels. This is a desirable attribute for a hydrogel when subjected to environments of varying pH of human digestive tract. Diffusion models fitted to the experimental data showed that the media diffusion rates through the copolymers were primarily Fickian in acidic medium but non-Fickian in basic environment, as shown by the values of the diffusion exponents (Table **1**). Furthermore, hydrogel mesh size is of special significance in the drug release behavior because of the screening effect of the hydrogel. So, the hydrogel mesh size should be large enough for the drug molecules to pass through the hydrogel mesh. The experimental values of the mesh size of the hydrogels were in the range of 3.40-223.7 Ǻ at the pH value of 1.0-8.0. This mesh size range is large enough for the most on piptide and protein drug molecules will pass easily through the polymers. It should be emphasized that pH-sensitive behavior of sample $A_4$ is of importance in oral drug delivery to target colon part of gastrointestinal tract of human body.

## REFERENCES

[1] Devis KA, Anseth KS. Controlled release from crosslinked degradable networks. Crit Rev Ther Drug Carr System 2002; 19: 385-23. http://dx.doi.org/10.1615/CritRevTherDrugCarrierSyst.v19.i45.30

[2] Chien LC, Andrew TM, Hydrogels in controlled release formulation network design and mathematical modeling. Adv Drug. Delivery Rev 2006; 58: 1379- 408. http://dx.doi.org/10.1016/j.addr.2006.09.004

[3] Ohmine I, Tanaka T. Salt effects of phase transitions of polymer gels. J Chem Phys 1982; 77: 5725-29. http://dx.doi.org/10.1063/1.443780

[4] Brandon-Peppas L, Harland RS, Eds. Absorbent polymer technology. Elsevier, Amsterdan-Oxford-New Cork-Tokio 1990; pp. 159-170.

[5] Grimshaw PE, Grodzinsky AJ, Yarmush ML, Yarmush AM. Selective augmentation of macromolecular transport in gels by electro-diffusion and electro- kinetics. Chem Eng Sci 1990; 45: 2917-29. http://dx.doi.org/10.1016/0009-2509(90)80183-F

[6] Frusawa H, Hayakawa R. Swellling mechanism unique to charged gels: Primary formulation of the free energy. Phys Rev 1998; E58: 6145-54. http://dx.doi.org/10.1103/PhysRevE.58.6145

[7] Kashyap N, Kumar N, Kumar M. Crit Rev Thermal Drug Carr. Syst 2005; 22: 107-49.

[8] Malana MA, Zafar ZI, Zuhra R. Effect of Cross Linker Concentration on Swelling Kinetics of a Synthesized Ternary Co-Polymer System. J Chem Soc Pak 2012; 34: 793-801.

[9] Malana MA, Zohra R. The release behavior and kinetic evaluation of tramadol HCl from chemically cross linked Ter polymeric hydrogels. DARU J Pharm Sci 2013; 21.

[10] Zafar ZI, Malana MA, Pervez H, Shad MA, Momina K. Synthesis and swelling kinetics of a cross linked pH-sensitive ternary co-polymer gel system. Polym (Korea) 2008 32: 1-11.

[11] Chen J, Belvins WE, Park H, Park K. Gastric retention properties of super porous hydrogels composites. J Control Release 2000; 64: 39-51. http://dx.doi.org/10.1016/S0168-3659(99)00139-X

[12] Chen J, Park K. Synthesis and characterization of superporous hydrogels composites. J Control Release 2000; 65: 73-82. http://dx.doi.org/10.1016/S0168-3659(99)00238-2

[13] Dorkoosh FA, Verhoef JC, Ambagts MHC, Rafiee TM, Borchard G, Junginger HE. Per oral delivery systems based on superporous hydrogels polymers: release characteristics for the peptide drugs buserelin, octreotide and insulin. Eur J Pharma Sci 2002; 15: 433-39. http://dx.doi.org/10.1016/S0928-0987(02)00028-3

[14] Ximming L, Yindgde C. Study on synthesis and chloral-mphenicol release of poly (2-hydroxyethynemethacrylate-co-acrylamide) hydrogels. Chinese J Chem Eng 2008; 16: 640-45. http://dx.doi.org/10.1016/S1004-9541(08)60134-2

[15] Kumar A, Pandey M, Koshy MK, Shubhini AS. Synthesis of fast swelling superporous hydrogels: effect of concentration of crosslinker and acdisol on swelling ratio and mechanical strength. Int J Drug Del 2010; 2: 135-40. http://dx.doi.org/10.5138/ijdd.2010.0975.0215.02022

[16] Schott H. Swelling kinetics of polymers. J Macromol Sci Phys Part B 1992; 31: 1-9. http://dx.doi.org/10.1080/00222349208215453

[17] Jabbari F, Nozari S. Strain induced clustring in polyelectrolyte hydrogels. Eur Polym 2008; 36: 2685-92. http://dx.doi.org/10.1016/S0014-3057(00)00044-6

[18] Houwei T, Yi Q, Xiaohua H, Yihua X, Hua Z, Peihu X, Filiang X. Study of the sigmoidal swelling kinetics of carboxymethyl chitosan-g-poly(acrylic acid) hydrogels intended for colon-specific drug delivery. Carbohydrate Polym 2010; 82: 440-45. http://dx.doi.org/10.1016/j.carbpol.2010.04.086

[19] Omidian H, Park K. Swelling agents and devices in oral drug delivery. Crit Rev J Drug Del Sci Tech 2008; 18: 83-93.

[20] Langer R, Peppas NA. Advances in biomaterials. Drug Deliv Bionanotechnol AIChEJ 2003; 49: 2990-3006. http://dx.doi.org/10.1002/aic.690491202

[21] Khutoryanskiy VV, Dubolazov AV, Nurkeeva ZS, Mun GA. pH effects in complex formation and blending of poly (acrylic acid) with poly (ethylene oxide). Langmuir 2004; 20: 3785-90. http://dx.doi.org/10.1021/la049807l

[22] Davidson III GWR, Peppas NA. Solute and Penetrant Diffusion in Swellable Polymers. V. Relaxation-Controlled Transport in P(HEMA-co-MMA) Copolymers. J Controlled Release 1986; 3: 243-58. http://dx.doi.org/10.1016/0168-3659(86)90096-9

[23] Tia Q, Zhao Z, Tang X, Zhang Y. Hydrophobic association and temperature and pH sensitivity of hydrophobically modified poly(n-isopropylacrylamide-co-acrylamide) gels. J Applied Polym Sci 2003; 87: 2406-13. http://dx.doi.org/10.1002/app.12122

[24] Geankoplis CJ. Transport process and unit operations. 3rd ed. Englewool Cliff, N.J: Perentice Hall 1993.

[25] Vazquez NM, Antonio-Cruz RDC, Castillo AA, Mendoza-Martinez AM, Morales-Cepeda AB. Swelling kinetics of hydrogels from methyl cellulose and poly (acryl amide). Rev Max De-Eng Qui 2007; 6: 337-45.

[26] Woerly S, Plant G, Harvey AR. cultured rat neuronal and glial cells entrapped within hydrogel polymer material: a potential tool for neutral tissue replacement. Neurosci Lett 1996; 205: 197-201. http://dx.doi.org/10.1016/0304-3940(96)12349-1

[27] Gudeman LF, Peppas NA. pH-Sensitive Membranes from Poly(vinyl alcohol)/Poly(acrylic acid) Interpenetrating Networks. J Membr Sci 1995; 107: 239-48. http://dx.doi.org/10.1016/0376-7388(95)00120-7

[28] Sezen Y, Hasan B. Swelling Behavior of Poly(2-hydroxyethyl Methacrylate-co-acrylic Acid-co-ammonium Acrylate) Hydrogels. J Macromol Sci Part A: Pure and Applied Chemistry 2007; 44: 939-46. http://dx.doi.org/10.1080/10601320701424198

[29] Murali YM, Keshava PSM, Sudhakar H, Kumar NBV, Mohana RK, Padmanabha RM. Swelling and diffusion properties of poly(acrylamide-co-maleic acid) hydrogels: A study with different crosslinking agents. Int J Polym Mat 2006a; 55 : 1-23.

[30] Murali YM, Sudhakar K, Keshava PSM, Mohana RK. Swelling properties of chemically cross linked poly(acrylamide-co-maleic acid) hydrogels. Int J Polym Mat 2006b; 55: 513-36. http://dx.doi.org/10.1080/00914030500208246

[31] Ortiz LE, Morals AB, Antonio R, Cruz AM, Sintesis Y. Caracrerizacion de hidrogeles obtenidos a partir de acrilamida y metilceluiosa. Revista Iberoamericana de Polimeros 2006; 7: 247-53.

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