ZIBELINE INTERNATIONAL™ PUBLISHING

ISSN: 2576-6724 (Print)
ISSN: 2576-6732 (Online)
CODEN: ACMCCG

Acta Chemica Malaysia (ACMY)

DOI: http://doi.org/10.26480/acmy.02.2022.85.93

RESEARCH ARTICLE

IN-VITRO STUDY OF HYDROGEL FOR DICLOFENAC POTASSIUM RELEASE

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ARTICLE DETAILS

Article History:

Received 20 March 2022
Accepted 25 April 2022
Available online 10 May 2022

ABSTRACT

The delivery of drug has an incredible influence on treatment of chronic diseases. Various drugs are being used to treat such disease but are limited due to their side effects during their delivery to effective site. There is dire need to design such carrier molecules can cross blood–eye barrier, stay for long times, or mitigate side effects. By designing different drug carriers for site specific system for physiologically delivery of relevant concentration for long periods. By using cellular delivery systems, microelectromechanical (MEMs)-based devices, polymer matrices, or gene delivery systems, such issues can be solved. Stimulus-response polymers are gaining much attention of researcher for delivery of drug in a controlled way on specific sites of disease in human beings and to minimize deleterious effects and increase the frequency of drug. The polymer with novel combinations of monomers with stimuli responsive, biodegradable, and biocompatible can be synthesized. In current study, grafted polymers hydrogels were synthesized using acrylic acid, ethyl acrylate, hydroxy propyl methyl cellulose, benzoyl peroxide, and methylene bis-acrylamide to release the drug at the colon (pH=7). Hydrogels were characterized using various techniques FTIR-ATR, TGA, SEM, and XRD. Polymers were soft, transparent, foamy in touch, with high tensile strength, thermally stable till 300˚C and properly cross-linked. Swelling of hydrogels were observed at pH 1, 4, 7, 8, and 9.2, where optimum swelling was found at pH 7. The acrylic acid enhanced all Flory-Huggins solvent interaction parameters. The %age porosity and %age friction of sol-gel were measured as 91% and 35% respectively. The drug loading equilibrium was obtained in 3 hours. The kinetics of diclofenac potassium drug release were measured using Korsmeyer Peppas model and synthesized polymer showed maximum release (78-79%) at pH 7. Controlled release can easily be adjusted just by changing the percentage ratio of monomers used. Synthesized polymer is environment friendly, cost effective and easy to handle.

KEYWORDS

Stimuli-responsive polymers, Acrylic acid, benzoyl per oxide, diclofenac potassium.

1. INTRODUCTION

In past it has been observed that all drugs delivered to abnormal site of body and causes various side effects after passing through different pathway (Naseem et al., 2021). From last two decades a big revolution takes place in the field of medicine after the discovery of biodegradable polymeric materials. Polymers have been an important component in the development of drug delivery systems because of their ability to release active ingredients for a longer period of time without fluctuations in plasma levels. Drugs can easily be delivered to affected sites of the body through these stimuli responsive polymer materials. It improves its safety and efficacy by controlling the rate, time, and place of release of drugs in the body. They may be controlled release or target specific drug delivery system (Yong and Sung, 2020). The excellent solution of it is to deliver the drug on specific site of disease in a controlled way. A proper balance of physicochemical properties of polymers can be helpful to design several delivery technologies for various uses through different routes

The outcome of previous works over several decades proclaim that stimuli-responsive polymers can behave as an efficient smart material and makes drug capable to release fast, selectively, environment friendly, and uniformly on targeted area. Stimuli-responsive polymers are identified as materials with intelligent and smart sensation of environment through different stimuli (Wang et al., 2019). Sensitive polymeric materials has potential applications in many fields such as diagnosis, chemical storage, separation, transport, biosensors, gene, drug delivery, and catalysis (Zhifeng et al., 2009). The final properties of responsive material, structures, conformations, and also topologies can be alter by external or internal stimuli. These are some of chemical (ionic strength and pH) and physical (temperature, redox potential, light, ultrasound, electric, and magnetic fields) stimuli. There are many multiple natural triggers that can influence the response of polymeric material (Jiaxiang et al., 2018). The pH along with gastro-intestinal track (GIT) is the basic natural trigger and it varies with food conditions.

The pH of stomach, duodenum, jejunum, ileum, cecum, and colon during fasting remain as 1-3.5, 5-7, 6-7, 6.6-7.4, 6.4, and 6.8 whereas during eating 4.3-5.4, 5.4, 5.4-6, 6.6-7.4, 6.4, and 6.8 respectively (Enxian et al., 2017). Some of drug conveying forms commonly used are pellets, tablets, and capsules with protected coating of pH-sensitive material. pH sensitive

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	Website: www.actachemicamalaysia.com	**DOI:** 10.26480/acmy.02.2022.85.93

Cite the Article: Khadija Gillani, Saira Saeed, Syed M. Husnain, Surriya manzoor, Muhammad Rehan Hasan Shah Gilani, Naseem Abbas, Faisal Shahzad (2022). In-Vitro Study of Hydrogel for Diclofenac Potassium Release. *Acta Chemica Malaysia, 6(2): 85-93*.

polymers can accept or release protons upon change in pH. Polymers on passing towards the colon never loses integrity on its pathway. Mostly pH-sensitive polymers for basic medium were based on acrylic acid and their derivatives and these polymers mostly used in control drug delivery, can withstand numerous hours at pH ranges from 1.5 to neutral pH 7.5 (Kunal et al., 2013). Different drug delivery devices used in drug delivery system are dendrimers, polymeric-nano particulate systems, hydrogel system, solid lipid nanoparticles, magnetic nanoparticles, polymeric micelles, liposomes, and implants. As hydrogels are three-dimensional cross-linked networks of water-soluble polymers. They can be synthesized from both natural and synthetic polymers. They are highly absorbent and biocompatible.

2.1.1

Due to their inertness for many drugs biodegradable hydrogels are being used as carriers for controlled drug delivery. Hydrogels have immense porosity due to which the release rate of drug crucially depends upon the diffusion coefficient of the drug molecules. The tailoring of porosity of hydrogel can be done by controlling the level of cross-linking, which in turn affect the rate of delivery of the entrapped drug particles. The ability of hydrogels to rapidly swell in aqueous medium, promote the rate of

2.1.2

release of the entrapped drug and degradation of the polymer (Apurva et al., 2016). The polymer-solvent interaction can be studied by using different models such as: Flory-Huggins model, a classic mathematical approach for polymer systems, Korsmeyer Pappas model, and Higuchi model. These uses the balance between the entropic and enthalpy contributions regarding the size and form effect and the intermolecular interactions and the kinetics of the system used for synthesis (Laise et al., 2020).

2.1.3

The aim of study is to synthesize a biodegradable controlled release hydrogel polymeric material using both hydrophilic and hydrophobic monomers. To understand the versatile effect of different monomers of hydrogel; three-dimensional pattern ter-co-polymers were focused in this work. One of the monomers Acrylic acid is used as essential carrier in oral controlled delivery system due to its hydrophilic characteristics. The

2.1.4

important feature is high swell ability and well controlled drug release kinetics. The second component HPMC, a derivative of cellulose is mainly hydrophilic, bio-degradable, nontoxic, affordable, excellent bio-compatible polymer, and therefore being used in drug delivery devices as rate controlling polymer (Hossam et al., 2018). The third component Ethyl acrylate (EA) used for polymer synthesis, belongs to the acrylate family. It is hydrophobic in nature, volatile, clear liquid, slightly soluble in alcohol, but completely soluble in ethers, and organic solvents and being used to slow down the drug release for a uniform and longer period of time.

It is pH and electrically sensitive material, miscible with all organic solvents, and can readily polymerize with other monomer molecules (Argyrios et al., 2008). For this AA/EA/HPMC polymer of different composition was prepared by free-radical polymerization. Prepared polymeric hydrogels were characterized by using different techniques. pH sensitivity and swelling of the hydrogels were studied in different pH buffer solution. Flory-Huggins solvent interaction parameters of gels were studied. Kinetics of the hydrogels, %age porosity and %age friction of sol-gel were studied. A controlled medium was used for studying kinetics, swelling of the gel, drug loading and drug release in buffer solutions at different pH. Diclofenac potassium drug was used as controlled medium drug.

2. Material and Methods

2.1 Materials

Acrylic acid (> 99%) was acquired from Merck, Germany and Ethyl acrylate (> 99%) and HPMC were acquired from Sigma Aldrich. They were utilized as monomers for the synthesis of tercopolymer. N, N'-methylene bis-acrylamide (MBA) (Fluka analytical, USA) and benzyl peroxide (BPO) (Fisher-UK) were utilized as cross-linker and initiator respectively. Diclofenac potassium Drug for drug loading trial was acquired from Hisun pharmaceutical Industry Lahore, Pakistan. Distilled water was utilized throughout the experimental work.

2.2 Synthesis of Polymer Network AA/EA/HPMC

Five solution mixtures of polymer G1, G2, G3, G4, and G5, were prepared using ethyl acrylate (EA) 0.03, HPMC 0.0007, MBA 0.0006 moles and acrylic acid (AA) with varying concentration 0.10, 0.15, 0.23, 0.25 and 0.30 moles respectively and each solution were mixed with benzyl peroxide (BPO) 0.10/10 w/v separately. To avoid bubble formation, solutions were fluxed with nitrogen gas using screw caped glass test tubes. Then all sample solutions in test tubes were heated started from 45 for 1 hour with every 5°C rise for 2 hours up to 65 and then at 68 °C for12 hours respectively using water bath for uniform heating. The solution converted into gel and cylindrical shaped hydrogels were taken out from screw caped test tubes, cut into small discs, and dried in open air for 3 days. To remove unreacted chemicals, all the discs were washed with 50% ethanol/water solution for one week. After washing, all the hydrogel discs were first dried at room temperature and then in oven at 45°C. These were further stored in air tight containers.

2.3 Characterizations of AA/VA/EC Ter-co-polymeric Networks

Prepared hydrogels were characterized using techniques given below.

2.3.1 Fourier Transform Infrared: Attenuated Total Reflection (FTIR-ATR) analysis

Functional groups were identified using FTIR-ATR spectroscopy (Bruker Alpha, Germany) technique. The sample were analyzed directly by placing on crystal sample holder and scanned with a resolution of 4 cm^{-1} between the wavelength 4000-400 cm^{-1}.

2.3.2 X-ray diffraction (XRD)

The prepared samples were analyzed by diffractometer (D-8, Bruker, Germany) by using conventional copper target X- ray tube with Cu Kα radiations. The sample formulations were filled in the cavity with care and the surface was smoothen by using glass and radiation were fluxed with angle 10-80° @ 1°/min of 2θ value. The graph obtained was interpreted using the X'pert software. The results provided better information about the structures of the crystals.

2.3.3 Scanning Electron Microscopy (SEM)

Samples morphology and structural information at different magnification were analyzed by Scanning Electron Microscopy (SEM). Electrons were bombarded on the surface of samples by providing voltage.

2.3.4 Thermogravimetric Analysis (TGA)

To know the thermal stability of prepared samples, thermo-gravimetric analysis of hydrogel were carried out in thermo-gravimetric analyzer (SDT Q600 V20.9 TA instruments, USA). For this, 2.7 mg of samples were placed one by one in an Aluminum crucible under Nitrogen's atmosphere. All samples inside the furnace were subjected to control cooling and heating process. A sample under heat treatment show the quick weight loss as a function of time and/or temperature.

2.4 Swelling Behavior of AA/EA/HPMC hydrogels

The fluid amount incorporated into the hydrogel structure and polymer swelling volume fraction were determine by using the Flory-Huggins expression given in Equation 1 (Chien-Chi and Andrew, 2006).

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

Polymer and solvent densities (g/mL) are represented by dp and ds, where masses (g) of swollen and dry hydrogel were represented by Ma and Mb respectively. The volume fraction in equilibrium swollen state of hydrogel is given as V_{2s} (ml/mol). The compatibility of monomer and polymer hydrogel with surrounding media molecules were estimated by solvent interaction parameter using Equation 2 (Arkan et al., 2013).

$$X = \frac{\ln(1-V_2\,S)}{V_2 S^2} \quad (2)$$

The average molecular weight (M_c) between two adjoining crosslinks and degree of crosslinking in hydrogel network can be calculated by Equation 3 (Shahid et al., 2013).

$$M_c = \frac{d_p\, V_s\left(V_{2s}^{1/3} - V_{2s}/2\right)}{ln(1-V_{2s}) + V_{2s} + XV_{2s}^2} \quad (3)$$

Here V_{2s} is the solvent molar volume (mL/mol) of the hydrogel at equilibrium and Flory- Huggins solvent polymer interaction parameter was shown by χ. The average molecular weight of repeating unit was calculated using Equation 4 (Kashif et al., 2014).

$$Mr = \frac{m_{AA}M_{AA} + m_{EA}M_{EA} + m_{HPMC}M_{HPMC} + m_{MBA}M_{MBA}}{m_{AA} + m_{EA} + m_{HPMC} + m_{MBA}} \quad (4)$$

Here mAA, mEA, mHPMC, and mMBA are the masses while M_{AA}, M_{EA}, M_{HPMC}, and M_{BA} are the molar masses of acrylic acid, ethyl acrylate, hydroxy propyl methyl cellulose and N, N'MBA, respectively. The number of links

(N) between two crosslinks can be deliberated using Equation 5 (Peppas et al., 2000).

$$N = \frac{2M_c}{M_r} \quad (5)$$

2.5 Diffusion Coefficient

It is the amount of solvent diffuses through unit area (based on concentration gradient) per unit time. The dry polymer was inserted in different buffer solution at 25 °C and after every 15 minutes, swollen polymer was weighed after removing surface water till equilibrium achieved and diffusion coefficient was calculated using Equation 6 (Fahad et al., 2017).

$$D = \pi\left(\frac{h.\theta}{4.q_{eq}}\right)^2 \quad (6)$$

Where, q_{eq} is swelling of hydrogel at equilibrium, θ is slop of the linear part of swelling curves, and before swelling initial thickness of hydrogels was shown by h.

2.6 Sol-Gel Fraction Analysis

To estimate the extent of gelation of polymer by absorbing solution, 3-4 mm un-washed polymeric disc were inserted into Soxhlet extraction apparatus for 4 hours in de-ionized water and after formation of gel structure polymer was removed. A constant weight of the extracted gel was obtained by drying in vacuum oven at 45 °C. By measuring initial weight of the dry gel (W_0) and weight of extracted dry gel (W_1) gel fraction was calculated using Equations 7 and 8 (Murat and Esra, 2005).

$$Sol\ fraction\ (\%) = \left[\frac{W_0 - W_1}{W_0}\right] \times 100 \quad (7)$$

$$\text{Gel fraction (\%)} = 100 - \text{Sol fraction} \quad (8)$$

2.7 Porosity Measurement

Solvent absorption technique was used to determine Hydrogel porosity. In this process, dry hydrogel were immersed in absolute ethanol overnight. The surface water of hydrogel was removed using blotted paper and then hydrogel was weighed. The hydrogel porosity was calculated using Equation 9 (Wen-Jen and Chia-Hui, 2002).

$$Porosity = \frac{(M_2 - M_1)}{\rho V} \times 100 \quad (9)$$

Where M_1 and M_2 are the masses of hydrogels after and before immersing in ethanol solution.

2.8 Dynamic and Equilibrium Swelling of Hydrogels

To understand the swelling behavior of hydrogel at different pH, dynamic swelling was performed. For this process, all weighed dry discs were immersed in 100 ml phosphate buffer solutions having pH 1, 4, 7, 8, and constant ionic strength at 37 °C. All immersed hydrogel discs were weighed after each 30 min till the equilibrium was achieved. The dynamic and equilibrium swelling of each hydrogel was estimated using Equations 10 and 11 respectively (Ranjha et al., 2011).

$$q = \frac{W_t}{W_d} \quad (10)$$

$$q_{(eq)} = \frac{W_h}{W_d} \quad (11)$$

W_h, W_t and W_d are weights of swollen gel at equilibrium, at time t, and dry gel respectively.

2.9 Quantification of Diclofenac Potassium Loading of on Hydrogel

The drug was loaded on hydrogels by immersing them in 1500 ppm Diclofenac potassium solution. The hydrogel discs remained in drug solution till swelling equilibrium was achieved. The drug loaded hydrogels were then removed from drug solution, were dried until constant weight was obtained, firstly over night at 25°C and then in the oven at 45°C. The drug was remained stable up to 45°C. The drug concentration remained in solution extract was used to estimate percentage drug loading using spectrophotometer at 276 nm λmax (Vishal and Shivakumar, 2010). The percentage drug loading was also calculated by using Equations 12 and 13.

$$\text{Amount of drug} = W_D - W_d \quad (12)$$

$$Drug\ loading\ (\%) = \frac{W_D - W_d}{W_d} \times 100 \quad (13)$$

W_D and W_d are dry weight of hydrogel after and before loading respectively.

2.10 Release Kinetic Analysis of Diclofenac Potassium

The drug release of drug loaded hydrogel was performed using dissolution apparatus (USP31-NF26 Apparatus II) with paddle speed at 100 rpm in 900 ml Phosphate-buffered saline solution (pH 7.5) at 37.5 °C. To estimate the extent of drug release, 4ml PBS solution was withdrawn after 0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, and 12 hours and analyzed using UV/Vis spectrophotometer (UV-7504, Xin Mao Instrument Company, Shanghai, China) at 276 nm. The absorbance results were compared with that of standard curve of pure drug. The drug release kinetics was calculated using following Equations 14-17 (Margaux et al., 2020).

$$\text{Zero order kinetics: } \frac{M_t}{M_\infty} = K_0 t \quad (14)$$

$$\text{First order kinetics: } ln\frac{M_t}{M_\infty} = K_1 t \quad (15)$$

$$\text{Higuchi model: } \frac{M_t}{M_\infty} = K_2 t^{1/2} \quad (16)$$

$$Korsmeyer\ Peppas\ model: \frac{Mt}{M_\infty} = K_3 t^n \quad (17)$$

Here amount of the drug released during time t is M_t and total amount of the drug is M_∞ while "K_0, K_1, K_2 and K_3" are apparent release rate constant for first order, zero-order, Higuchi model, and Korsmeyer-Peppas model respectively. Here 'n' explains release rates in terms of relaxation-controlled transport process and diffusion-controlled process.

2.11 Statistical Analysis

The mean percentages of Diclofenac Potassium released in phosphate buffer solutions (pH 7.5) was compared with others. To find out the statistical significance, One-way Analysis of variance (ANOVA) was used. The statistically significant value of $p < 0.05$ was considered. Dunnett-Tukey-Kramer (DTK) Pairwise Multiple Comparison Test was performed to understand the effect of buffer solution with different pH on drug release.

3. Results and Discussion

3.1 Synthesis of Hydrogel

Five hydrogel samples were synthesized through free radical polymerization with varying concentrations of Acrylic Acid (Figure 1). While the presumptive structure of ter-polymer (Figure 2). These synthesized hydrogels were transparent, elastic in touch, smooth in texture, and stable at room temperature. These were further used for characterization, swelling, drug loading, and drug release kinetic studies.

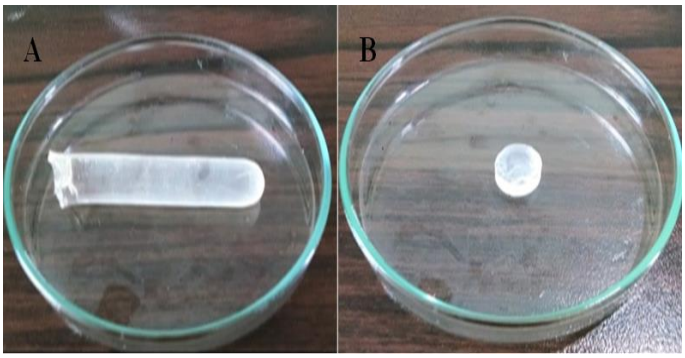


Figure 1: Prepared Hydrogels A Complete hydrogel removed from the caped tube B Disc shaped cut from hydrogel

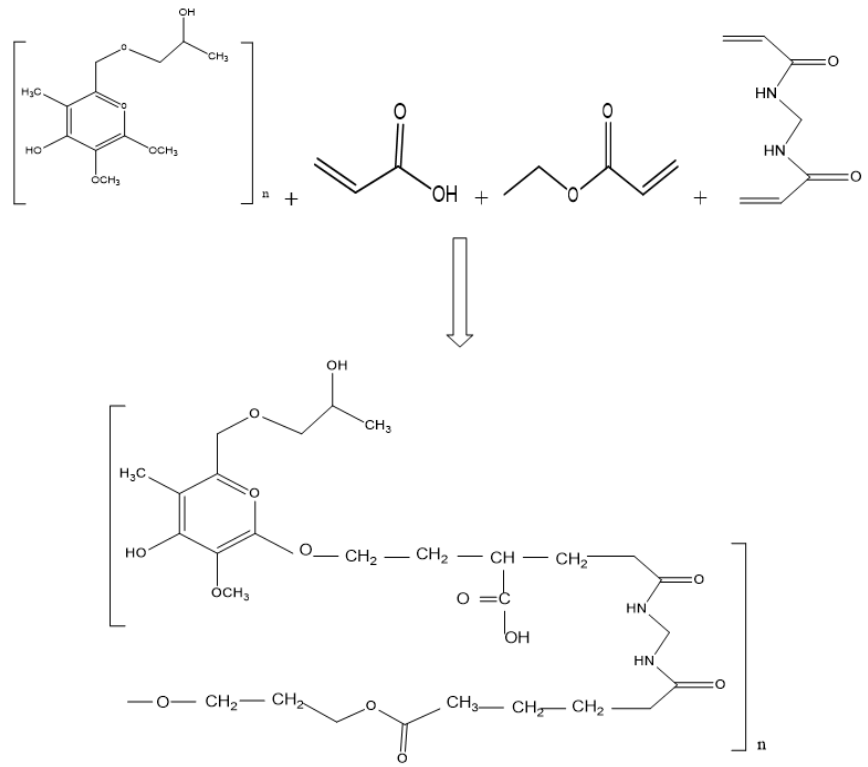
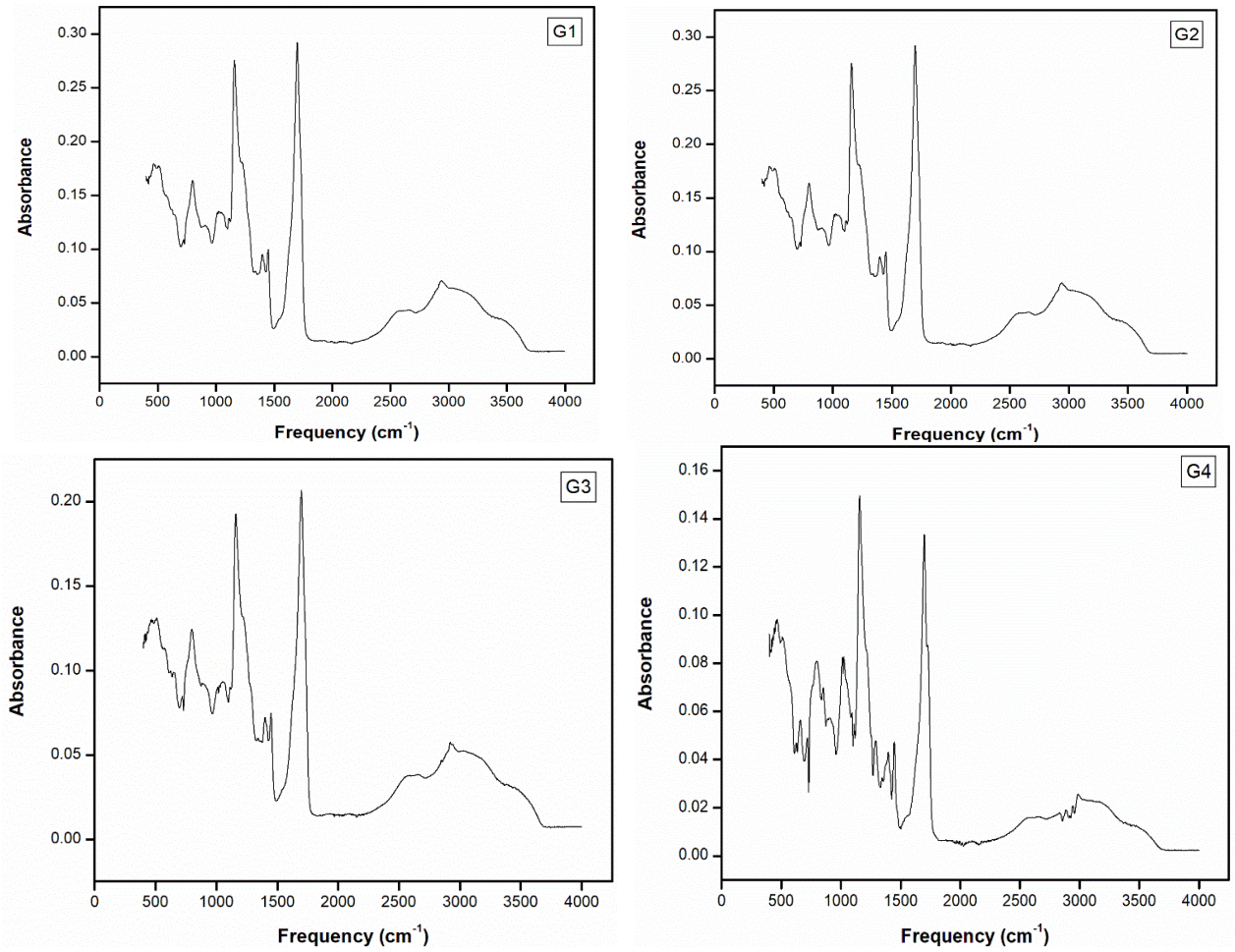


Figure 2: Presumptive structure of cross-linked N'N MBA interpenetrating networks of AA/EA/HPMC hydrogels.

3.2 Characterization of Synthesized Hydrogels

3.2.1 FTIR Analysis of Hydrogels

The composition and nature of both functional groups i.e. consumed during polymerization and available on the surface of hydrogel were illustrated using FTIR-ATR technique (Figure 3). In spectra, the stretching vibrations were observed for C-H and N-H bonds in the region of 2940-3070 cm^{-1}. Due to stretching vibrations of methylene (CH_2) group and carbonyl group of carboxylic acid, small peaks were observed in region of 1440-1470 cm^{-1} and 1700-1730 cm^{-1} respectively. Peaks in region of 1150-1170 cm^{-1} indicated presence of C-O-C group. The peaks in the range 1010-1065 cm^{-1} were due to presence of anhydride groups i.e. CO-O- and CO. The obtained peaks of spectra justified expected structure of hydrogels.



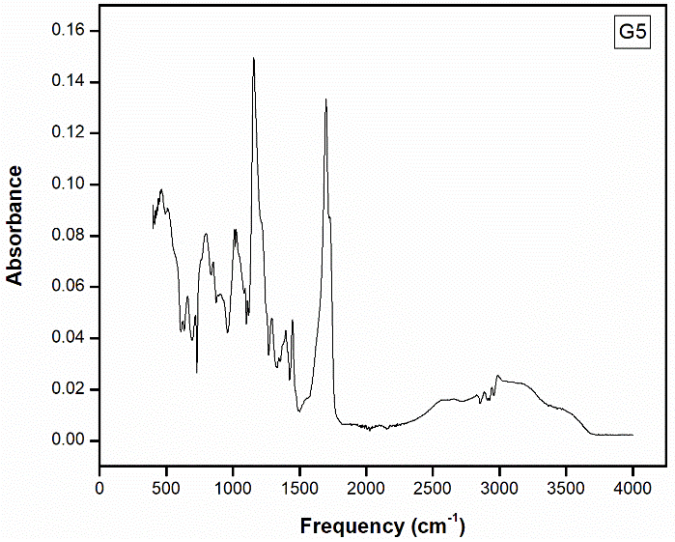


Figure 3: FTIR-ATR of the samples G1, G2, G3, G4 and G5 having frequency ranges from 4000-400cm-1 on x-axis and absorbance on y-axis.

3.2.2 XRD analysis of hydrogels

The amorphous nature of synthesized hydrogels were confirm by single peak in X-ray diffraction analysis (Figure 4).

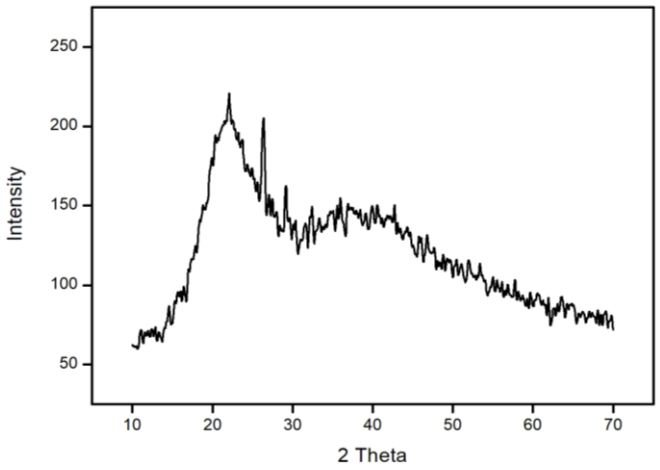


Figure 4: XRD graph of the prepared hydrogel.

3.2.3 SEM Analysis of Hydrogels

The morphology of hydrogels before and after loading of drug, were studied by obtaining SEM images (Figures 5). The images showing smoothness of a hydrogel. In second image B it is clearly seen that drug has loaded perfectly. As the hydrogels are amorphous and shows a good swelling behavior and it is cleared from the SEM image.

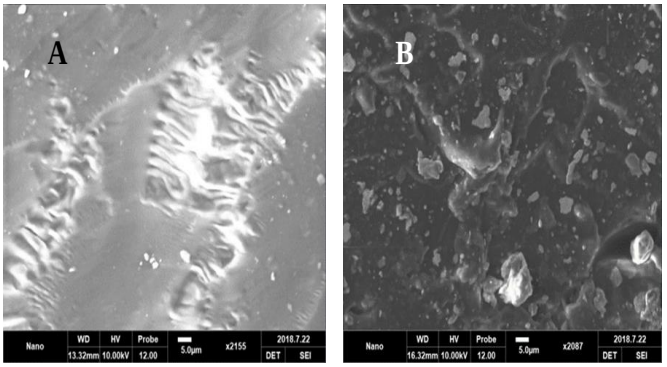


Figure 5: SEM image of the prepared sample, (A) Image of the sample without drug loading and (B) Image with drug loaded

3.2.4 TGA Analysis of Hydrogels

To understand the shelf life of hydrogel at different temperatures were studied by TGA (Figure 6). The results shown remarkable stability of synthesized hydrogels and they remained stable up to 130 °C and then hydrogels started decomposing slowly in temperature range of 130-250 °C. AA is hydrophilic in nature, so it contain significant amount of water content. Due to loss of water and inorganic impurities first transition can be attributed then decomposition of carboxylic group and further. It was also observed that maximum weight loss (85%) occurred in the temperature range of 250-450 °C. Residual polymers and side chains of polymer were responsible for stepwise degradation attitude of AA/EA/HPMC hydrogel (Osvaldo et al., 2004).

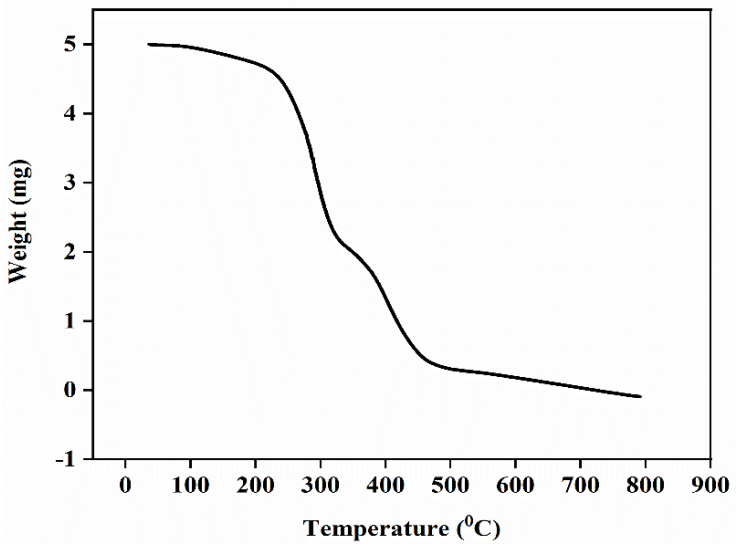
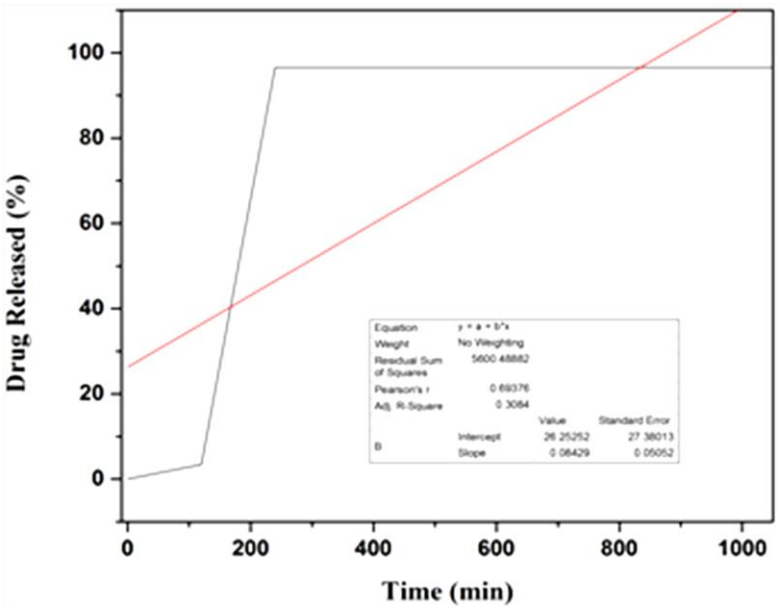


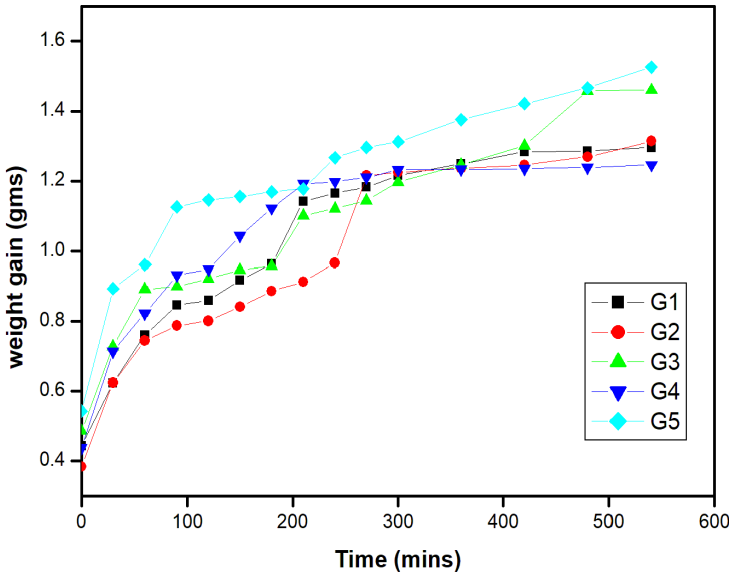
Figure 6: Thermal stability of the Drug delivery polymer ranges from 0°C to 900°C.

3.3 Optimization of Acrylic Acid Concentration on Swelling Behavior Of Hydrogel

The swelling and drug release equilibrium was observed and calculated for 4 hours at pH 7 (Figure 7). The water retained in swollen hydrogel cross-linked network were characterized by using Flory-Huggins formula. The data obtained for M_c, V_{2s}, X, M_r, D, and q are given in table 1. The V_{2s}, X, M_c, and q showed a direct relation with acrylic acid concentrations. The increase in acrylic acid concentration enhances crosslink density and consequently M_c. Hydrogels which polymerize in less amount of solvent, possess low degree of polymerization along with high cross-linked density network. Due to hydrophilic nature of AA, with increase in AA concentration, water diffusion increases and swelling enhances. While any hydrophobic component of hydrogel e.g. ethyl acrylate decreases its swelling ability (Zubaida et al., 2017).



(A)



(B)

Figure 7: (A) shows the % age drug release with the passage of time whereas (B) shows the weight gain with the passage of time all 5 hydrogel at pH 7.5

3.4 Diffusion Coefficient

For membrane permeation study Fick's law of diffusion was used. For the measurement of solute diffusion in hydrogel, indirectly applied diffusion coefficient (Table 1). Swelling of polymer increases by increasing acrylic acid concentration and diffusion coefficient decreased due to hydrophilic behavior of monomer. The remaining monomers and linker were kept constant in all the five samples, so they don't show any effect on diffusion.

Table 1: Flory-Huggins's network parameters of AA/EA/HPMC hydrogels in phosphate buffer solution. V2s: Volume fraction of the polymer at swelling equilibrium, X: solvent interaction parameter, Mc: average molecular weight between crosslinks, Mr: molar mass of the repeating unit, q: crosslinking density, D: diffusion coefficient.

Sample	V_{2s}	X	M_c	M_r	q	D 10^{-3} (cm^2/s)
G1	0.375998	-0.676244	1705.23	183.657	9.2848	0.95833
G2	0.383958	-0.681589	2014.90	156.650	12.8624	0.99245
G3	0.378854	-0.678165	2104.66	133.038	15.8199	1.91786
G4	0.385797	-0.682837	2220.44	129.060	17.2047	1.95168
G5	0.379519	-0.678598	2223.96	121.068	18.3693	2.05284

3.5 Sol-Gel Fraction Analysis

The sol-gel fraction of various composition of AA/EA/HPMC hydrogels were increases in with AA concentration (Table 2). The AA concentration decreases the viscosity which result in formation of fine gel structure due to further polymerization by free movement radical.

Table 2: Porosity measurement and sol-gel analysis of all five synthesized AA/EA/HPMC hydrogels.

Sample Code	Porosity (%)	Gel fraction (%)	Sol fraction (%)
G1	-93.634	100.7185115	-0.718511467
G2	-92.118	96.67268155	3.327318447
G3	-90.989	185.5955919	-85.59559194
G4	-90.156	183.5631516	-83.56315156
G5	-90.356	96.22493405	3.775065948

3.6 Porosity Measurement

The porosity of synthesized hydrogels were increases by increasing the AA concentration (Table 2). Due to increase in AA monomer concentration in polymer solution, viscosity decreased by formation of interconnected channels which allow bubbles to get escape from solution.

3.6 Effect of Ph on Swelling Behavior of Hydrogels

The results indicate that the increases in AA concentration and pH, swelling coefficient of prepared hydrogel were increased (Figure 8). The comparative study showed that polymers swelling increases with the increase in pH of solution which might be due to ionization of acidic group in basic medium and diffusion of water increases due to hydrophilic character of AA and hydrogen bonding of water with acrylate ion (Ranjha, 1999). The swelling coefficient increased in basic medium and made hydrogels elastic and rubbery.

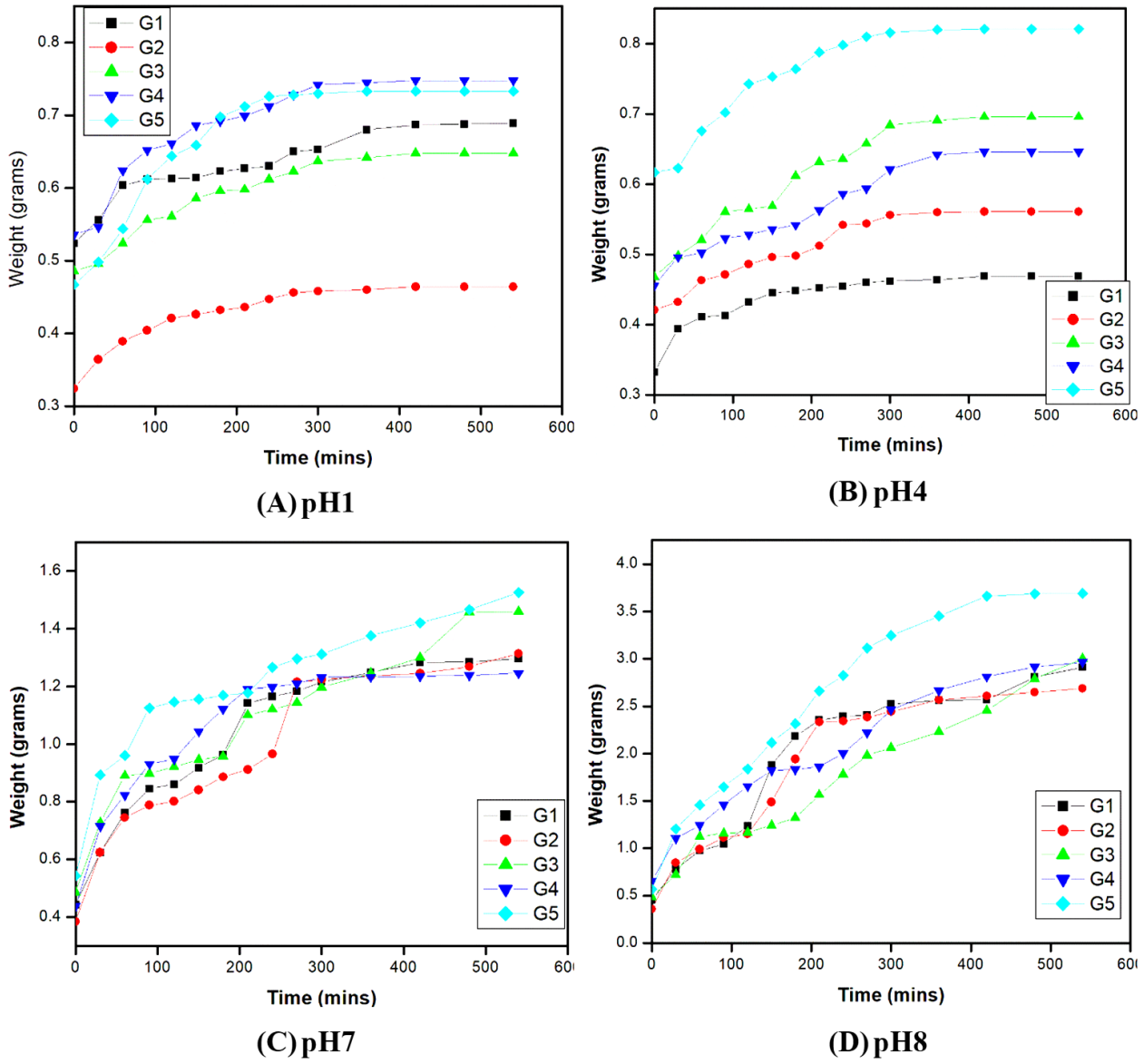


Figure 8: Study of effect of pH on swelling behavior of hydrogels with varying concentration of Acrylic Acid (A) pH1 (B) pH4 (C) pH7 (D) pH8.

3.7 Quantification of Diclophenic Potassium on hydrogel

The loading and release studies of Diclofenac potassium drug on hydrogel were performed and dynamic swelling coefficients of hydrogels with different AA concentrations at pH 7.5 (Figure 7) respectively. According to penetration theory, drug release occurs by dissolution of active ingredients through capillaries and the pore network composinmg of interconnecting drug particle clusters, when a matrix composed water insoluble polymer and water-soluble drug. The drug loading and release was increased with acrylic acid due to increased penetration of solvent. When solvent enters into the polymer network, the drug diffusion occurs from the drug loaded hydrogel to water and moves toward the surface. The swelling behavior of the hydrogel directly controlled the drug release mechanism (Gi-Ho et al., 2017).

3.8 Statistical analysis

By using regression coefficient (r) swelling and drug release kinetics can be studied. The most appropriate model was selected based upon ideal fit of regression coefficient which is ≈ 1. Regression coefficient values for zero order, first order, Higuchi model, and Korsmeyer-Peppas model obtained from drug loading (Table 3). Effects of AA concentration on release exponent (n) for the Diclofenac potassium were evaluated from the slope and intercept of plot drawn between ln M_t/M_∞ versus ln t. The regression

coefficient values were obtained by applying Higuchi model. The drug release mechanism followed diffusion controlled and non-fickian diffusion mechanism because all calculated values of 'n' were between 0.5 and 1.0 (Jianghua et al., 2011). For the most of samples, regression coefficient (r) values were supported the drug release through first order kinetics. It was cleared that drug diffusion rate and polymer chain relaxation rate are interrelated. Table 3 shows drug release pattern of samples, synthesized with different concentrations of AA.

Table 3: Study of effect of Acrylic acid concentration on release kinetics of hydrogel at pH 7.5 keeping the remaining monomers concentration contant.

Sample	Acrylic Acid Cons.	pH	Zero-Order Kinetics		First-Order Kinetics		Higuchi Model		Korsmeyer-Peppas Model	
			K_0	r^2	K_1	r^2	K_2	r^2	K_3	r^2
G1	0.10	7.5	5.137	0.985	0.101	0.980	0.221	0.986	0.802	0.979
G2	0.15	7.5	5.155	0.988	0.105	0.983	0.225	0.989	0.811	0.980
G3	0.23	7.5	5.162	0.991	0.107	0.985	0.229	0.995	0.817	0.982
G4	0.25	7.5	5.167	0.992	0.115	0.987	0.232	0.997	0.821	0.984
G5	0.30	7.5	5.177	0.995	0.119	0.988	0.236	0.998	0.828	0.985

4. Conclusion

Acrylic acid based hydrogels were synthesized for site specific transport of drug in a controlled manner through GI tract. The characterization confirmed that synthesized hydrogels were amorphous in nature and thermally stable up to 130 ˚C. The XRD, SEM, and FTIR confirmed the smooth polymerization with availability of required functional groups at the surface for swelling, drug loading, and drug release at the required pH in a controlled way. The results also indicated that hydrogels were swollen, and drug was released only at pH 8 in 4 hours following diffusion-controlled model. So, hydrogels formulations with varying concentrations of AA were very suitable for drug loading at pH 7 and release at colon with pH 8 after passing through gastrointestinal tract.

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