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Formulation, optimization and *in vitro* evaluation of sustained release oral hydrogels of diacerein to treat arthritis

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Abstract: The current study is aimed to formulate pH responsive polymeric hydrogels. Potassium per sulphate and Methylene bis acrylamide were employed as initiator and cross linker respectively. To determine the effect of substrate on degree of cross linking different ratios of the acrylic acid (AA), potassium per sulphate (KPS) and methylenebisacrylamide (MBA) were used. Swelling experiments were conducted in both basic and acidic media. Phosphate buffer of pH 7.4 and 0.1N HCl solution were used for swelling experiment of hydrogels. The hydrogels were more responsive towards basic medium as compared to acidic environment. Formulations were also evaluated for *In vitro* evaluation. Diacerein was selected model drug for hydrogel. Release pattern of the diacerein was studied both in acidic (0.1N HCl solution) and basic medium. Percentage drug release from M3 formulation showed as crosslinker concentration increase (0.03 %) drug release decrease Hydrogel samples were characterized by FTIR to confirm the functional groups of the hydrogels and their components and scanning electron spectroscopy (SEM) was performed to characterize the structure or morphology of the hydrogels. Finally, the dissolution studies were performed to evaluate the sustain release property of the hydrogel samples. Results show that all formulations of hydrogels are pH-sensitive and follow zero-order kinetics for drug release. Hence, optimized nexus (M3) serves as excellent carrier for target drug delivery.

Keywords: Hydrogel, polymer, monomer, diacerein, pH-sensitive, zero-order kinetics

INTRODUCTION

Diacerein (DC) is chondroprotective agent which belongs to DMOAD class is prodrug of rhein which inhabits synthesis of interleukin-1β (IL-1β) and cytokines. Furthermore, DC regulates MMPs (metalloproteinases), NF-kβ (NF-transcription nuclear factor kappa light-chain-enhancer of activated β cells, AP-1 (activator protein), MAPKs (mitogen-activated protein kinase), TGF-β1 and β2 (transforming growth factor-beta1 and 2) which provide protection to cartilage from degradation (Chattopadhyay *et al*., 2020). DC is sparingly soluble, low bioavailability (BCS class II drug) (Wang *et al*., 2022). Numerous strategies have been embraced to enhance solubility, dissolution and release out of which hydrogels are quite promising.

Polymeric hydrogels are hydrophilic crosslinked nexus (a connection or series of connections linking two or more things) which swell with significant fraction of water and biological fluids (Mahmood *et al*., 2022). Macromolecular design of engineered hydrogel furnishes tunable and versatile attributed like stimuli responsiveness. Traditionally, hydrogels are formulated via covalent bounding between polymer and monomer chain, thereby forming permanent crosslinked nexus (Bernhard & Tibbitt, 2021).

Recent researches in macromolecular science have ensured the development of fascinating drug delivery systems in order to achieve temporal control via programing the structure or responding to various stimuli (Internal and external) and drug release occur in controlled manner (Zafar *et al*., 2022). However, drug release from such system occur via passive manner following degradation, deformation, swelling of architecture. Another strategy is developing stimuli sensitive nexus. Stimulus can be temperature, pH, light, enzyme, ultrasound, biomolecules and electric or magnetic fields. Swelling and release profile of these architectures are influence by duration and intensity of stimuli which aids in controlled/ targeted drug delivery (Wang *et al*., 2021).

Novelty of current study is to investigate the potential of moringa gum for controlled drug delivery via polymeric

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network using vinyl monomer (acrylic acid) via free radical polymerization. Moringa oleifera is polysaccharide containing arabinose, xylose, rhamnose, manmose, galactose and glucoronic acid. Moreover, it executes swelling in water that's why employed as potential for colon targeting (Singh and Kumar, 2018). Swelling of polysaccharide is primary mechanism in diffusion controlled release system. Moreover, moringa gum is subjected to degradation by digestive enzyme and fluid. Literature review reported the fact that it improve the bioavailability of so it is need of time to use such polymers to improve bioavailability.

Maltodextrin (MD) is long chain polysaccharide derived from starch (corn and patato) via hydrolysis. Moreover, it is biocompatible, non-toxic, biodegradable and found application in controlled drug delivery system, cell cultures, tissue engineering, enzyme immobilization and so forth (Ghobashy *et al*., 2022). Literature survey supports the fact that MD is has low hydroscopicity which avoids partial aggregation thereby aids its use in synthesis of hydrogel (Paulino *et al*., 2011).

Sodium starch glycolate (SSG) is sodium salt of poly-α glucopyranose with hydroxyl groups are in the form of carboxymethyl ether. It has been reported in literature that SSG alter drug (ibuprofen) release (Puttipipatkhachorn *et al*., 2005). Acrylic acid (AA) is pH responsive synthetic monomer which is potentially employed for colon targeting. Attachment of anionic pendent group-COOH on to polymer makes matrix pH sensitive and aids in targeted drug delivery (Yadav *et al*., 2022). Moreover, intermolecular interaction like dipole-dipole interaction, electrostatic interaction and hydrogen bonding make these systems fascinating in terms of slow release system (Singh and Kumar, 2018). Chemical structures of drug and polymers are shown in fig. 1

Aim of current study was to formulate polymeric carrier in order to improve drug release by modified fascinating carrier. Formulated carrier was evaluated for swelling and drug release. Hence, preparation, characterization and optimization of modified carrier improve solubility and bioavailability of diacerein.

MATERIAL AND METHOD

Chemicals, reagents and solvents

All the chemicals were of high purity and analytical grade. Acrylic acid, potassium per sulphate, methylene bis acrylamide, maltodextrin and moringa oleifera obtain from Sigma Aldrich, Germany. Sodium starch glycolate was procured from Yung Zip Chemicals, Taiwan. Diacerein was obtained from Euticals SPA, Milano Italy. Ethanol, HCl and N-N methylene bis acrylamide were obtained from Merck, Germany.

Synthesis of hydrogels of different polymers with acrylic acid

Under continuous stirring weighed amount of polymer (1-2%) was added in distilled water (10mL) in test tube followed by addition of KPS. Other solution was prepared by adding varying quantity of acrylic acid (3-4 mL) along with different quantities of cross linker (MBA) (0,02-0.03 w/v) in a test tube. Both prepared solutions were mixed in test tube under continuous stirring, followed by addition of distilled water (Qs to make 100mL). Test tubes were kept in water bath with gradual increment in temperature. Nitrogen atmosphere was provided to remove air bubbles. When the clear solution was solidified, hydrogels were removed and cut (5mm each). Discs were washed with water/ethanol (90/10) solution for two weeks to remove unreacted monomers. Hydrogels then dried initially at room temperature and followed by in oven at 40°C. The dried discs were preserved in labeled and air tight containers for further studies.

In vitro characterization

Swelling Studies

Swelling studies includes dynamic Swelling Studies and equilibrium Swelling Studies

Dynamic swelling studies

To evaluate the behavior of hydrogels towards dynamic swelling studies. We placed each formulation of hydrogel in 0.1 N HCl solution and similarly placed in 7.2 pH Buffer solution. Each hydrogel was weighted before placing in the solution and weighed after every 08 hours till hydrogels achieve constant weight (3 days). Swelling in hydrogels is calculated by using equation as under (Ijaz *et al*., 2018). Dynamic and equilibrium swelling was calculated from the following formulas.

$$q = \frac{Ws}{Wd} \quad (1)$$

$$\%\ ES\ = \frac{Ws-Wd}{Wd} \times 100 \quad (2)$$

Where, q is swelling ratio, Ws is the swelled disc weight at time "t" and Wd is the weight of dried hydrogel (Ijaz *et al*., 2019).

ON / OFF pulsatile phenomenon

To check the swellability of hydrogel discs in acidic and basic medium dry disc of each hydrogel formulation was placed in 100ml solution of 0.1 N HCl. After 08 hrs the disc was removed from the solution and removes the surface solution contents with the help of blotting paper, disk was weighted and then put the disc in solution of 100ml of 6.8 buffer solution and weighed the disc again after 08 hrs. Repeat the above procedure for all the hydrogels formulation and collect data for 72 hrs. From above experiments it reveals that all the discs of hydrogels swell and gain weight in phosphate buffer solution but in HCl solution they show reverse behavior. Hence it is concluded that the hydrogel formulations are pH dependent (Ijaz *et al*., 2020).

Sol-Gel fraction

Sol-gel study is a technique used to analyze the effect of cross-linking agent, degradation and gelation properties associated with characteristics both physical and chemical

characteristics of hydrogel formulations. In this technique unwashed hydrogel samples are used to study the amount of cross-linked polymer present in gels. Hydrogels are cut into several pieces of length 3-4 mm each and then first dried at ordinary temperature and followed by at 45°C in oven till the discs attain constant weight. Soxhelt extraction used to study the amount of un-crosslinked polymer. The sol-gel fraction of hydrogel discs is calculated by using the following equation (Sarfraz *et al*., 2019). Gel fraction was calculated by:

$$Sol\ Fraction(\%) = (Wo - Wi/Wo) \times 100$$

$$Gel\ Fraction(\%) = 100 - Sol\ fraction$$

Where, W1=initial weight of dried disc and W0= weight of the dried disk after extraction (Tulain *et al*., 2016, Shabir *et al*., 2017).

Porosity measurement

Porosity is fraction of the pores volume between 0 and 100 percent over the total volume of the hydrogel surface. Technique known as solvent replacement is utilized to calculate the porosity of the hydrogel discs. Weigh the dry discs and then put the discs in the absolute ethanol solution overnight, weigh the swelled discs after removing the removing the ethanol from the surface of the discs by using blotting paper. The porosity of the discs can be calculated by using the equation (Mahmood *et al*., 2022).

Porosity =M2-M1/ ρ V*100

M1 = Weight of dried discs

M2 = Weight of the swelled discs after immersion

ρ = Density of solution

V = Volume of the hydrogels

Loading of diacerein (Model drug)

Drug loading was conducted in pH 7.4 by placing the disk in buffer of pH 7.4 containing 1% w/v of drug. Drug was initially dissolve in N-N dimethyl acetamide. After drug loading, hydrogel were taken, washed with distilled water, blotted and oven dried at 40°C to constant weight.

Quantification of drug loading

Following three different methods are used for quantifying drug loading.

Weight method

Drug loaded can be calculated by weight method. Following equation is used to estimate the drug loading in hydrogel discs (Ijaz *et al*., 2018).

Drug loading = Ws-Wd/Wd*100

Ws = Weight of swell discs

Wd = Weight of dried discs

Spectrophotometric method

In this method repeated extraction is performed to evaluate drug loading in hydrogels. In every cycle 25ml of buffer solution is used until no residue is present in solution. Amount of the drug is calculated by spectrophotometrically. Total amount of the drug entrapped by hydrogels is equal sum of the drug in all portion.

In vitro dissolution studies

Dissolution apparatus and UV-Vis spectrophotometer were used for drug release studies. 900 mL Dissolution media (acid and basic) was taken in basket and hydrogel was kept at 37°C and stirred at 100 rpm. Sample was analyzed spectroscopically with regular intervals at λ max 258 nm (Qureshi *et al*., 2014).

Fourier transmission spectroscopic analysis (FTIR)

To conduct the FTIR spectroscopy, dried hydrogels were crushed by pestle and mortar. The hydrogel samples were powdered and dried at temperature 40°C.Then dried powder of hydrogel samples was applied on the disc of FTIR spectrometer (Bruker). Over the wavelength range of 4500-500cm-1 FTIR spectrum was obtained. (Sarfraz *et al*., 2019; Ijaz *et al*., 2018)

Scanning electron microscopy (SEM)

SEM was employed to observe surface topology and morphology of hydrogel discs. Both unloaded and drug loaded hydrogel discs were analyzed.

Drug release kinetics

Release of diacetin from hydrogels depends upon rate of diffusion and swelling of polymers use to synthesize hydrogels. Apply different kinetic models to evaluate the behavior of drug release from hydrogels (Azam *et al*., 2020).

Zero order model

$F=K_o t$……..… (10)

Where,

F = Cumulative amount of drug release

K0 = Zero-Order Kinetics release constant

t = Time for release of drug

First-order kinetics model

$Ln(1-F)=K_1 t$

Where,

F = Cumulative amount of drug release

t = Time for release of drug

K1 = Release constant of First-Order Kinetics

Higuchi release model

$F=k_2 t_{1/2}$

Where,

F = Cumulative amount of drug release

t = Time for drug release

K2 = Higuchi release constant

Korsmeyer-peppas kinetics model

$Mt/M\infty=K_3 t^n$

Where,

Mt = Time to require drug penetration

M∞ = Amount of water in drug at equilibrium

t = Time to require for drug penetration

K3 = Korsmeyer-Peppas Release kinetic constant

n = Exponent representing the swelling ratio

Hixson-crowell kinetics model

$W_o^{1/3}$-$W_t^{1/3}$= KT

Where,

W0 = Amount of drug in hydrogel disc at initial stage

Wt = Remaining amount of drug in hydrogel discs

t = Time for release of drug

k = Hixson-Crowell Model constant (Kappa)

RESULTS

Results are shown in fig. 4-16 and table 1-2.

DISCUSSION

Swelling behavior shows the controlled delivery of the drug from hydrogel discs. pH of the surrounding media is much important parameter when the hydrogels are pH-sensitive.

Effect of pH on swelling

At present, pH sensitive intelligent hydrogel have been studies and attracted the attention in many pharmaceutical researchers. Swelling behavior of the hydrogel discs are directly affected with pH of the medium. For maximum swelling ratios of the hydrogels pKa value of buffer solution component should be greater that the pKa value of the carboxylic group present in the hydrogel disc. At this condition when pKa of buffer solution is greater, buffer will accept a proton from carboxylic group of hydrogel disc and ionize the hydrogel. To determine the influence of pH on swelling behavior of hydrogels acidic and basic media were used. 0.1N HCl solution and phosphate buffer was used as acidic and basic medium respectively. The ionization of carboxylic group and swelling of Moringa hydrogels was increases when the pH of the medium or solution increases as shown in fig. 2. When pH of medium greatrer than pKa value of acidic, swelling ratios of the hydrogels increases. Same was reported by Ranjha *et al* while formulating pH responsive CS-co-AA based nexus for verapamil loaded hydrogel (Ranjha, *et al*., 2010). When the pH of the external environment increases, repulsion among the protonated carboxylic groups of hydrogel discs increases and hence the swelling ratios also increases. On the other hand, if the pH of the medium is decreases the repulsive power among the un-protonated carboxylic groups (-COOH) decreases hence the swelling ratio also decreases. Similar results were also obtained by Byun *et al* while studiing swelling and release of PVA-co-PAA based nexus (Byun *et al*., 2008). Water retention of hydrogel is shown in fig. 4-6 which increase with increase in time which is attributed to 3-D structure of traditional hydrogel. In fact, water retention is attributed to physical and chemical interaction.

Effect of AA on swelling

Hydrogels were prepared containing variable concentration of acrylic acid as monomer is shown in table 1. pKa of acrylic acid is 4.28, therefore acrylic acid chains are collapsed at pH 1.2 (0.1N HCl) solution, hence the swelling behavior and swelling ratio of hydrogels decreases. However, as the pH value increases up to 7.4 (phosphate buffer solution) carboxylate ions (COO-) produces by acrylic acid, hence swelling ratio increases due to increases in repulsion between network chains. Same results were obtained by Sullad *et al* while synthesizing PVA-co-AA based hydrogel for isoniazid controlled release (Sullad *et al*., 2010). Fig. 4-6 shows the effect of monomer (acrylic acid) concentration on swelling ratios of hydrogels keeping the concentration of polymers and cross linking agent remains constant. Swelling ratios of samples M1, MD1 and SSG1 increases at higher pH values (7.4) and higher acrylic acid concentration as compared to the same samples at lower pH values (1.2) showing less swelling ratios as shown in fig. 4-6 respectively. Environmental responsive nexus depicted dimensional changes with change in pH of surrounding environment. Swelling of hydrogel increase from 29.34 to 70.34% in pH 7.4 which is attributed to porous nature of the nexus. However, swelling decrease in pH 1.2 due to strong H-bonding which do not impart swelling to the network. Moreover, this hydrogen bonding weakened with increases in pH. Carboxylic acid group formation occurs from amide moiety in basic environment. Hence, repulsive interaction between nexus was significant. It means formulated hydrogel has good pH sensitivity, strength and swelling degree (Suhail *et al*., 2022).

Effect of concentration of polymer on swelling

Hydrogel swelling occur as function of polymer concentration, reaction parameters and nature of media. Swelling of hydrogel was conducted to determine influence of polymer on swelling. As the concentration of polymer increases swelling increases. In order to evaluate the influence of polymer concentration on swelling ratio of hydrogels, the gels were subjected to place in a solution of different pH values. The concentration of polymer effect conversely to the concentration of monomer on hydrogels. The swelling ratio of hydrogels increases as we increase the concentration of polymer in hydrogels. Furthermore, swelling is attributed tomented hydrophilicity and cross-linked density. However, swelling of nexus is attributed to feed composition and cross-linked density. Furthermore increase in swelling is attributed to increase in pH. Moreover, swelling results increase in pore size and decrease cross-linked density during polymerization reaction as reported by Singh, B., & Kumar, A. (2018) while formulating moringa and acrylamide crosslinked pH sensitive nexus (Singh & Kumar, 2018)

Effect of cross-linker

Swelling ratio of the hydrogels increases as we decrease the concentration of cross linking agent because the physical entanglement of the network chains decreases. As the concentration of cross linking agent increases swelling ratio of hydrogels decreases, it is because of reduced mesh size of nexus. High concentration of cross linking agent

decreases the ionization of acrylic acid chains and remains less acidic as shown in fig. 4-7. Same results were obtained by Ijaz *et al*., 2019 while synthesizing xanthan gum based hydrogel for controlled release of perindopril erbumine. Due to increase in crosslinking density, the media absorbency of the nexus has been decreased. Chavada and Patel 2011 studied the influence of crosslinker concentration on swelling of hydrogel which supported the fact that water absorbency decreases with increase in cross-linked density (Chavada and Patel 2011).

On-off switching

pH responsive behavior of optimized formulation (M4) was evaluated in acidic and basic pH. Fig. 8 showed reversible on off switching in acidic (pH 1.2) and basic (pH 7.4) media. At pH 7.4 anion-anion repulsion aids in swelling due to electrostatic force of repulsion, while at pH 1.2 shrinkage occur which is attributed to screening effect of cation. Sharp and rapid swelling at different pH make the system pH responsive and subsequently results in fascinating controlled drug delivery system. Similar pH dependent swelling was reported previously by ijaz *et al*., 2019.

Sol gel fraction

Polymeric hydrogel contain significant amount of loosely bounded un-crosslinked polymeric macromolecules. Sol gel fraction was employed to elucidate the cross-linked and loosely bond nexus. Moreover, significant increase in gel fraction was observed with increase in polymer and monomer concentration. Higher concentration of moringa (M4), lead to higher degree of intra and inter chain H-bonding, resulting in minimum sol fraction as shown in fig. 9. At higher pH-COOH group of acrylic acid ionize resulting in weaker H-bonding between-COOH (monomer) and-COOH (acrylic acid) (Nawaz *et al*., 2018).

Porosity measurement

Porosity of hydrogel is related to volume of pores in hydrogel. Fig. 10 showed porosity increases as we increase the concentration of moringa and acrylic acid. As viscosity of the solution increases with increase the concentration of polymer and acrylic acid, therefore porosity also increases. Viscous consistancy prevents the bubbles to escape from the solution hence develop interconnected channels and results in the porosity enhancement. While increasing the concentration of cross linking agent (MBA) porosity decline due to increment in entanglement between acrylic acid and polymer molecules. Decrease in porosity is also attributed to higher cross-linked density as reported previously (Nanda *et al*., 2013).

Drug loading and release kinetics

Drug loading was conducted in pH 7.4 and shown in fig. 11. To evaluate the effect of pH on drug release from hydrogels was investigated by conducting the dissolution studies in the in acidic and basic medium. It was observed that drug release is better in basic medium as compared to acidic medium. In acidic medium pH 1.2 of 0.1N HCl solution, swelling ratios of the hydrogels decreases and the drug release from hydrogels also decreases, when the pH of the medium increases to basic pH 7.4 (phosphate buffer solution) swelling ratios of the hydrogels increases due to increasing repulsive forces among the protonated carboxylic groups (COO-) and ultimately drug release from hydrogel discs also increases as shown in fig. 12-14 for M1-M4, SSG1-SSG4 and MD1-MD4 respectively. Percentage drug release from M3 formulation showed as crosslinker concentration increase (0.03 %) drug release decrease. Increase in polymer concentration cause thicker matrix, thereby controlling the drug release form the system which is directly related to drug loading.

Drug release pattern was observed by employing phosphate buffer solution of pH 7.4 as dissolution medium. The dissolution data fitted in zero-order, first-order, Higuchi, Korsmeyer-Peppas and Hixon Crowell models to evaluate release of drug pattern from hydrogels. The release data which shows the desired values was calculated by the regression co-efficient [R^2].The most appropriate model that fits the data is selected for which the value of regression co-efficient [r] is near to 1. Results of drug release kinetics are shown in table 2 showing that drug release from all formulations follows Zero-Order Kinetics. ANOVA showed p-value of 0.055 ($p \leq 0.1$) which showed that all results were significant

FTIR spectroscopy

FTIR-Spectroscopy was performed to confirm the functional groups in the components of hydrogel discs. Pure model drug (Diacerein) and drug loaded hydrogels were evaluated by FTIR-spectroscopy. FTIR spectra of drug and hydrogels loaded with drug (Diacerein) (fig. 15). By comparing the FTIR of drug and drug loaded hydrogels it is observed that there is no marked shift in major peaks of their spectra, which showed that no chemical reaction is occurred between the components during hydrogels formation. All major peaks observed in individual component spectra are retained in hydrogel formulations. Similar facts was reported by Ijaz *et al*., 2022 while formulating CS-coAA based nexus for targeted delivery of perindopril erbumine (Ijaz *et al*., 2022).

Scanning electron microscopy

SEM was applied to study the morphology of interpenetrating hydrogels. From SEM micrograph results of unloaded hydrogel it was observed that pores are present in hydrogel sample, these pores facilitates the interpenetrating hydrogels to adhere drug as much as possible. White dispersed particles were observed in SEM graph results of loaded hydrogel as in fig. 16, which indicates that model drug is loaded successfully in the interpenetrating hydrogels containing pores on their surface. These facts and finding were reported by Akhtar and his coworkers while formulating losartan potassium loaded guar gum based nexus (Akhtar *et al*., 2022).

Table 1: Composition of different formulations of hydrogels

Formulations	Polymer (w/v)	Monomer (mL) (Acrylic Acid)	Cross Linker (w/v) (MBA)	Initiator (w/v) (KPS)
M1	1 .0	3	0.03	0.04
M2	1.5	3	0.03	0.04
M3	2.0	3	0.03	0.04
M4	2.0	4	0.02	0.04
SSG1	1 .0	3	0.03	0.04
SSG2	1.4	3	0.03	0.04
SSG3	2.0	3	0.03	0.04
SSG4	2.0	4	0.02	0.04
MD1	1.0% (w/v)	3ml	0.03 % (w/v)	0.04 % (w/v)
MD2	1.5% (w/v)	3ml	0.03 % (w/v)	0.04 % (w/v)
MD3	2.0% (w/v)	3ml	0.03 % (w/v)	0.04 % (w/v)
MD4	2.0% (w/v)	4ml	0.02 % (w/v)	0.04% (w/v)

Table 2: Release kinetics from prepared hydrogel

Sample Code	Zero Order Model	First-Order Model	Higuchi Model	Korsmeyer Peppas Model	Hixson Crowell Model
Expression	$F=K_ot$	$Ln(1-F)=K_1t$	$F=k_2t_{1/2}$	$Mt/M\infty=K_3t^n$	$W_o^{1/3}-W_t^{1/3}= KT$
M1	0.9845	0.9878	0.9956	0.57	0.9953
M2	0.9799	0.9889	0.9920	0.54	0.9958
M3	0.9901	0.9849	0.9900	0.64	0.9927
M4	0.9824	0.9909	0.9929	0.50	0.9967
MD1	0.9926	0.9891	0.9822	0.66	0.9876
MD2	0.9927	0.9966	0.9969	0.53	0.9936
MD3	0.9782	0.9945	0.9958	0.58	0.9942
MD4	0.9931	0.9825	0.9920	0.74	0.9914
SSG1	0.9381	0.9743	0.9675	0.62	0.9679
SSG2	0.9783	0.9954	0.9936	0.67	0.9945
SSG3	0.9651	0.9876	0.9813	0.76	0.9892
SSG4	0.9933	0.9650	0.9750	1.03	0.9774

F=Cumulative amount of drug release, K0=Zero-Order Kinetics release constant, t=Time for release of drug, K1=Release constant of First-Order Kinetics, K2=Higuchi release constant, Mt=Time to require drug penetration, M∞=Amount of water in drug at equilibrium, K3=Korsmeyer-Peppas Release kinetic constant, n=Exponent presenting the swelling ratio, W0=Amount of drug in hydrogel disc at initial stage, Wt=Remaining amount of drug in hydrogel discs, k=Hixson-Crowell Model constant (Kappa)

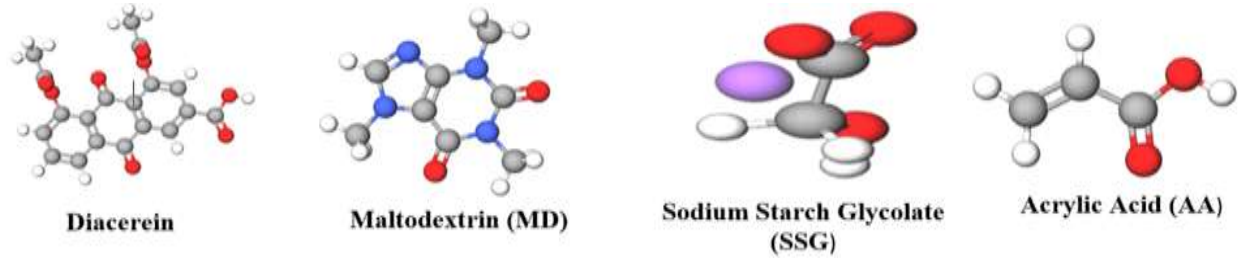

Fig. 1: Chemical structure

Fig. 2: Un-cut and unwashed base hydrogel (A), Hydrogel disk (B), Swell hydrogel (C)

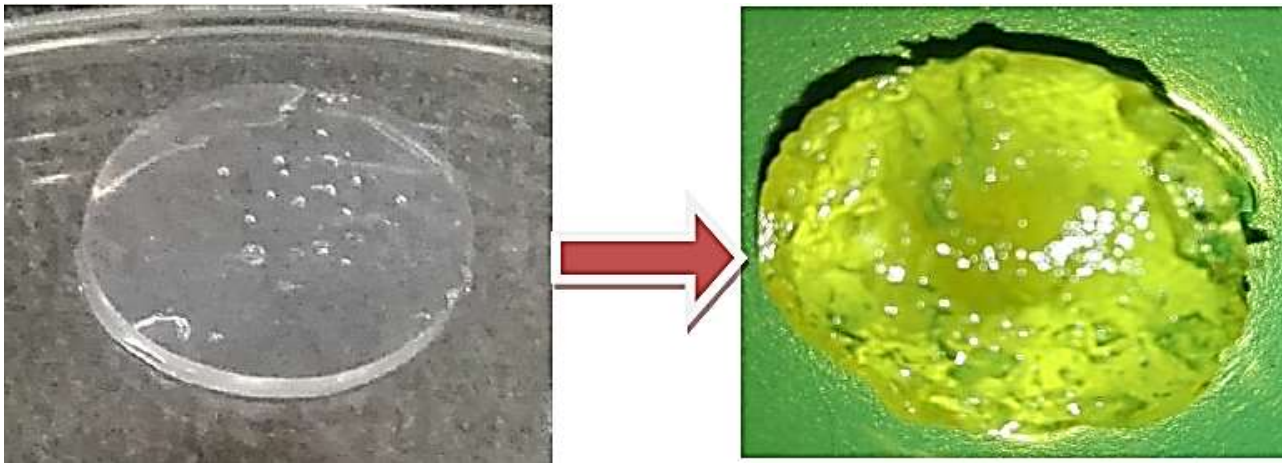

Fig. 3: Unloaded hydrogel dried disk (A), Drug loaded disk (B)

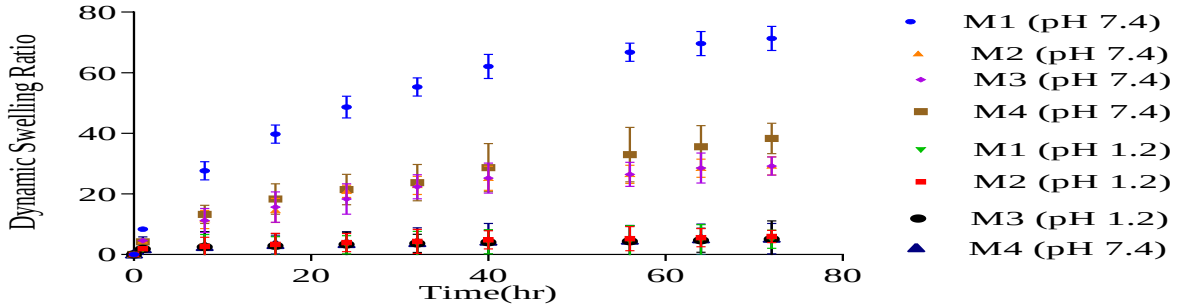

Fig. 4: Dynamic swelling ratio of M1-M4 in pH 1.2 and pH 7.4

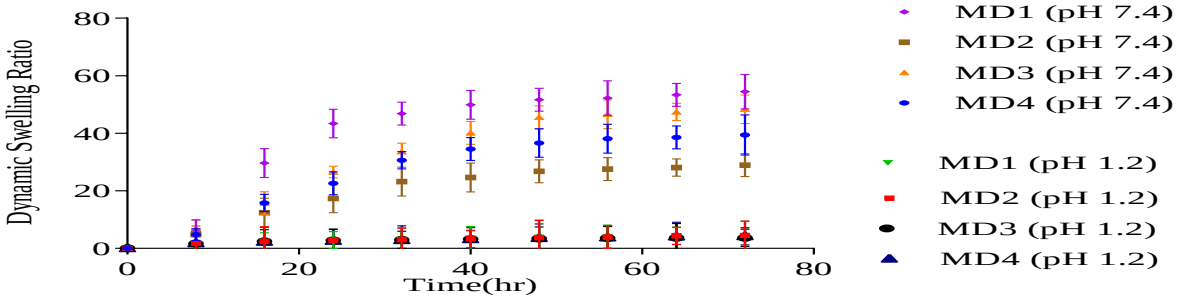

Fig. 5: Dynamic swelling ratio of MD1 to MD4 in pH 1.2 and pH 7.4

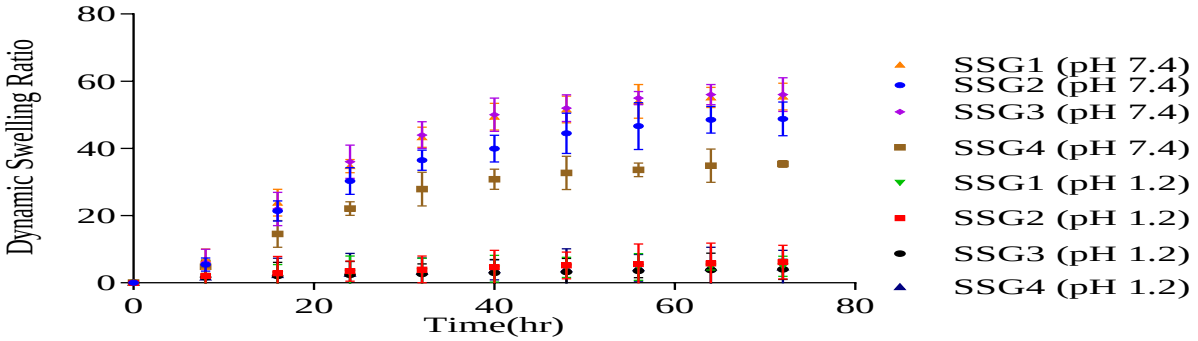

Fig. 6: Dynamic swelling ratio of SSG1 to SSG4 in pH 1.2 and pH 7.4

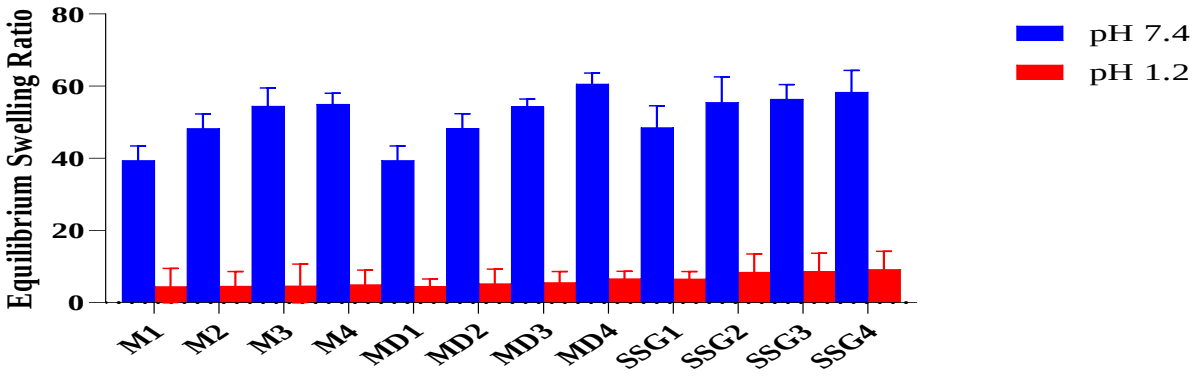

Fig. 7: Equilibrium swelling ratio in pH 1.2 and pH 7.4

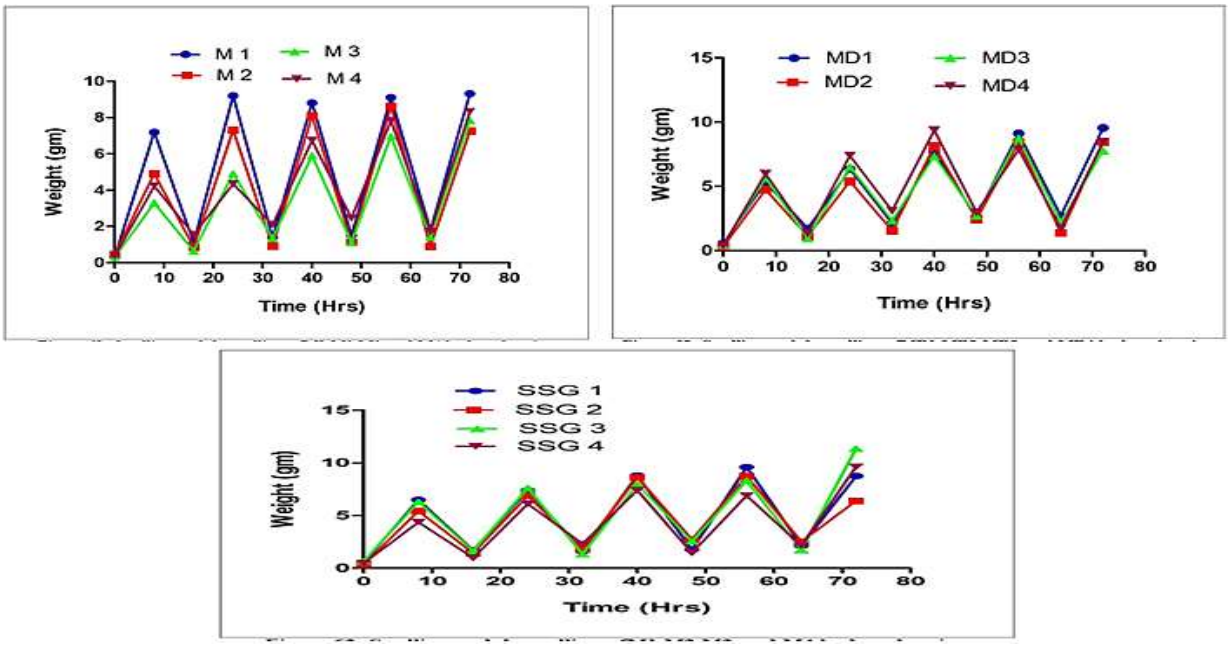

Fig. 8: On-off switching in pH 1.2 and pH 7.4

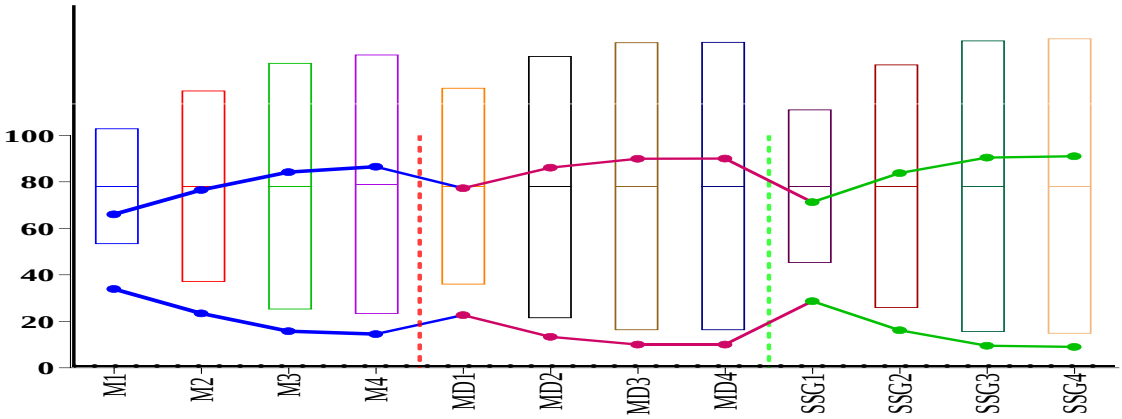

Fig. 9: Sol Gel analysis in pH 1.2 and pH 7.4

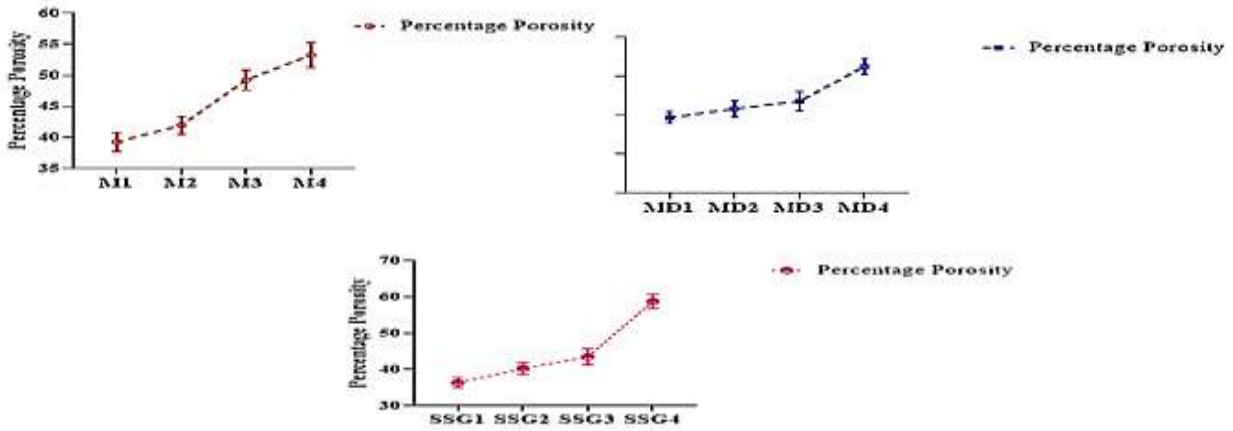

Fig. 10: Porosity measurement of all formulations

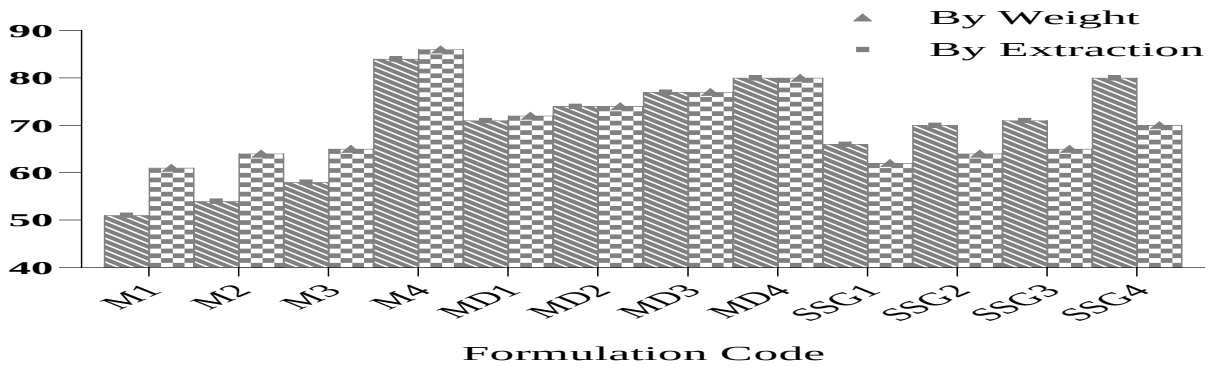

Fig. 11: Drug loading in pH 7.4

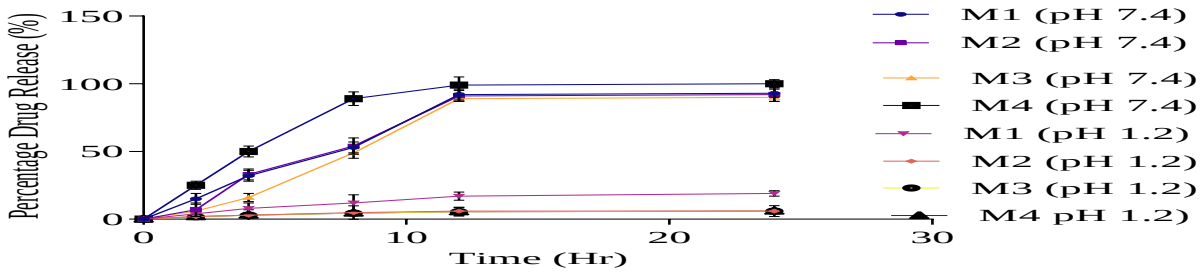

Fig. 12: Percentage drug release from M1-M4 in pH 1.2 and pH 7.4.

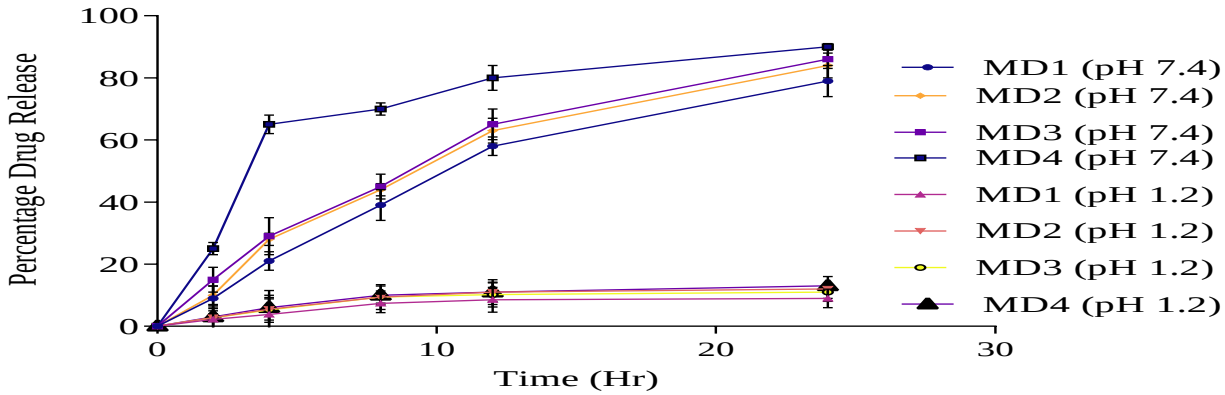

Fig. 13: Percentage drug release from MD1-MD4 in pH 1.2 and pH 7.4.

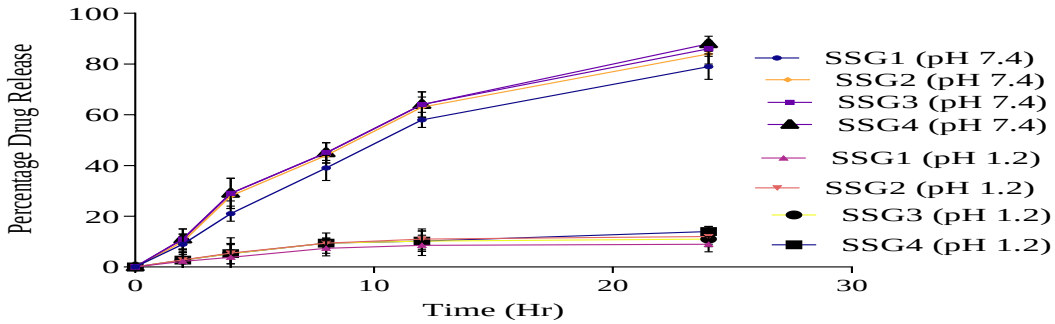

Fig. 14: Percentage drug release from SSG1-SSG4 in pH 1.2 and pH 7.4.

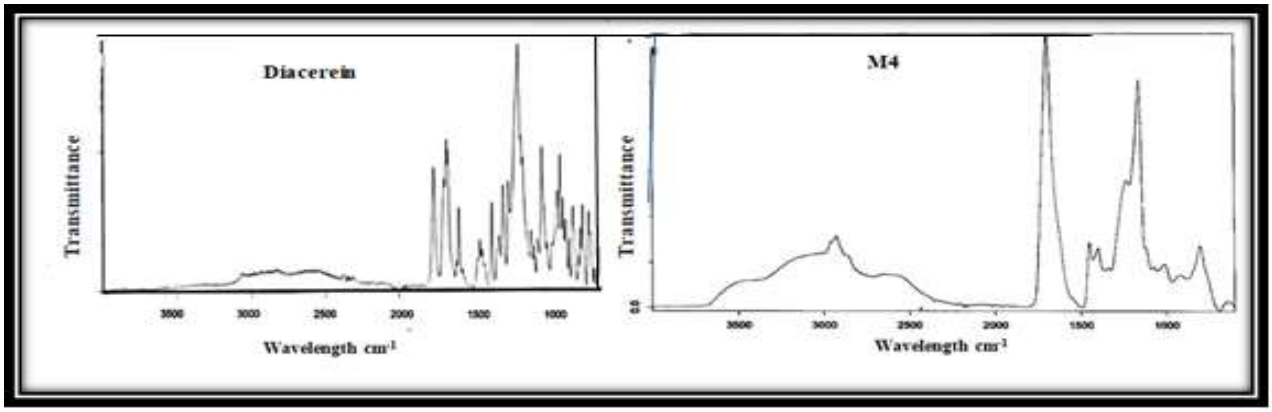

Fig. 15: FTIR of drug and formulation M4

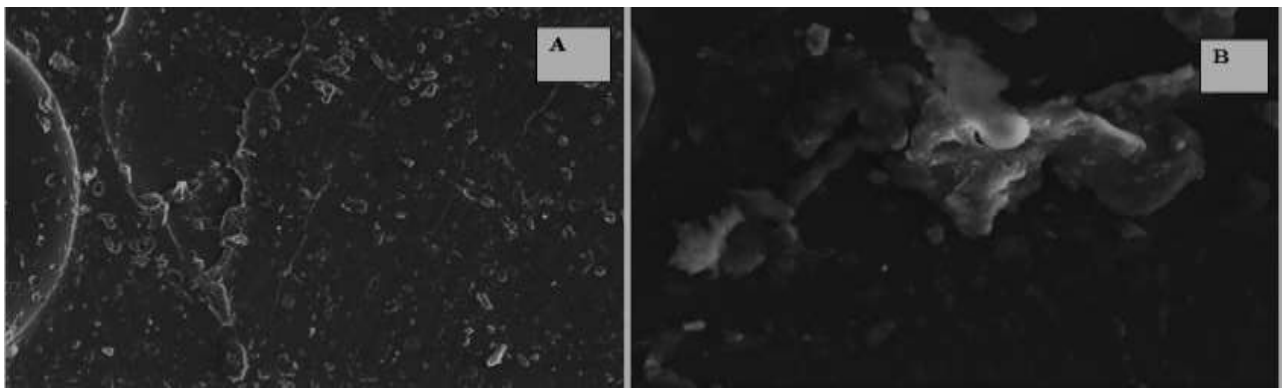

Fig. 16: Scanned micrographic image of M4 hydrogel at magnification 100X (A), 500X (B)

CONCLUSION

Ph-sensitive polymer containing hydrogels were prepared by free radical polymerization. Acrylic acid (AA) used as monomer, Moringa (M), Sodium Starch Glycolate (SSG) and Maltodextrin (MD) used as polymers. Methylene bis Acrylamide (MBA) and Potassium per Sulphate (KPS) used as cross-linking agent and initiator respectively. Drug release kinetics were applied on all the formulation, these all formulations follow Zero-Order Kinetics and found non-Fickian. Present study shows that hydrogels are sensitive to pH values and are able to respond changes in external environment or body fluids.

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