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Original Article

Design, Development and *in vitro* Evaluation of Hydrogels Prepared by Free Radical Polymerization of Acrylic Acid (AAc) Containing a Model Antidiabetic Drug

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ABSTRACT

Introduction: The controlled release of medicaments in the management of diabetes is desirable to have a better therapeutic activity of the drug. **Objectives:** In the present study hydrogels were prepared as a controlled drug delivery system taking Rosiglitazone as a model drug. **Materials and Methods:** Hydrogels were created using the Free Radical Polymerization approach, with the crosslinker N, N'-Methylene bisacrylamide serving as a binding agent for the polymerization. To create a polymeric network, ammonium persulphate has been used as a polymerization inducer for AAc to poly (acrylic acid) in the existence of polyvinyl alcohol (PVP). A maximum of fifteen formulations were created with various concentrations of polymers and crosslinking agents to test the swelling, diffusion coefficients, ESR, and *in vitro* drug release properties of the drugs tested. The FT-IR and DSC techniques were used to determine the drug's compatibility with the polymers. The XRD studies were carried out to understand the nature of the drug contained within the hydrogel formulation. The morphologies of the surface were determined using SEM. **Results and Discussion:** A greater swelling was observed in the basic pH range and a marginal swelling was observed in the acidic pH range according to the swelling studies. The ESR affirmed that the pH of the hydrogels was indeed a factor in the swelling of the gels. The results of the diffusion study revealed that the diffusion coefficient has risen as a result of the reduction in cross-linker concentration and the increase in acrylic acid concentration in the solution. The *in vitro* release of drug data revealed that the swelling has been increased as a result of the increased concentration of acrylic acid, which resulted in the increased release of the drug. However, when the concentrations of PVP and cross-linker were increased, it was discovered that the drug release was decreased. **Conclusion:** AAc-PVP based hydrogel was found to be a promising controlled drug delivery system for the treatment of Rosiglitazone, according to the findings of this study.

Keywords: Hydrogels, PVP Acrylic acid, Free Radical Polymerization, Antidiabetic Drug.

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INTRODUCTION

The most common and convenient route of drug administration is the oral route which is also suggested from the history of dosage form development.[1,2] The oral route is most widely used for sustained or for controlled-release systems. In comparison to the parenteral route, the oral dosage form offers greater flexibility in design because of high patient compliance, a safe administration route, and other factors. There is much significant modification in the oral drug delivery that has been made but the basic remains unchanged.[3] Many approaches are done as insoluble matrices, slowly erodible matrices, swelling matrices, polymer-coated tablets, osmotic delivery systems, controlled delivery systems through various approaches, etc. Wide extensive studies are conducted for the mean of controlled delivery of a drug by the use of hydrophilic 3D matrices which act as carried for the drug and can accumulate a large amount of biological fluid of water from the system.[4,5] Due to the presence of chemical or physical crosslinks between the polymeric structure, the hydrogel does not dissolve in the water instate it accumulates the water molecule in between the polymeric network. It's because the polymer contains hydrophilic groups like –OH, ––SO_3H, $CONH_2$– and –CONH. System that water can be absorbed. Both the natural and the synthetic polymer can be used to form the hydrogel which can be used extensively as a release retardant for the drug in controlled delivery systems.[4-7]

Diabetes is not new to Indian traditional medicine which is known as "Madhumeha".[8,9] The sweet nature of urine in diabetes mellitus was also mentioned in Ayurveda by Sushruta. The word "diabetes" which means "to flow through" was first described

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by Greek physician Aeretaeus in the 1st century A.D. in the 17th century.[10,11] To put it simply, diabetes is a condition in which our body is unable to adequately utilise the food we ingest for energy. Energy is required by our cells to survive and flourish. The food we eat breaks down into a molecule called "glucose" as it moves through our digestive system. The glucose enters into the blood and the blood sugar increases. A hormone named "Insulin" is made by the pancreas that helps the glucose to move from the blood into cells so that our body can produce energy. Diabetes mellitus has impacted the health care system and quality of life of the patient as it is a serious chronic metabolic disorder. Type 1 and Type 2 diabetes are categorised based on the fact that our bodies either don't create enough insulin or don't utilise it appropriately. The most prevalent type of diabetes is Type 2 diabetes and it is caused by a lack of insulin production or a failure Insulin is used to transport glucose from the bloodstream to the cells. Type 1 diabetes is due to the condition where our body does not produce any insulin at all. In this condition, we need to inject insulin from outside to the blood.[10-13]

The preparation of a hydrogel is the primary goal of this research consisting of a model antidiabetic drug, Rosiglitazone. Swelling tests, equilibrium swelling ratios, diffusion coefficients, *in vitro* dissolution tests, and drug compatibility tests were all performed on the produced hydrogel. The prepared hydrogels were characterized by FT-IR, DSC, SEM and XRD. The study was performed to know the effect of various polymers composition and crosslinking agents on the swelling and drug release profile from the hydrogels. Based on the evaluation parameter the optimized hydrogel formulation was selected carried out the stability studies of the selected formulations.

MATERIALS AND METHODS

Materials

Microlab Bangalore provided the Rosiglitazone as a complimentary sample. The other chemicals like AAc, PVP and N, N'-ethylene bisacrylamide was procured from Sigma-Aldrich, Steinheim, Germany. The potassium persulphate was procured from Fibe-Chem Limited, Mumbai. The Department of Pharmaceutics at the PES College of Pharmacy in Bangalore offered all other chemicals and facilities.

Methods

Preformulation Studies

Melting Point Determination[14]

For this study, we used a small quantity of Rosiglitazone in a capillary tube that was sealed at one end. We put the tube inside a melting point apparatus, and we noted the temperature at which the drug melts. The process was done three times and the average value was recorded.

Determination of Solubility of Rosiglitazone in Phosphate Buffer pH 7.4[14,15]

A study on the solubility of Rosiglitazone was conducted in a phosphate buffer solution at pH 7.4. To conduct the study, we used excess quantities of the medication in a volumetric flask that was shaken continuously for 24 hr. After 24 hr, the combination was examined spectrophotometrically at a wavelength of 276 nm (maximum absorbance).

Drug–Excipients Interaction Study[16,17]

Perkin Elmer Spectrum 100 FT-IR-spectrophotometer was used to generate the infrared spectra, which had been captured between the wavelength ranges of 4000 and 400 cm^{-1}, by using KBr pellet technique. Study looked at the spectra of pure Rosiglitazone as well as physical mixtures of Rosiglitazone and polymers in order to evaluate whether or not the drug and polymers were compatible with one another.

Formulation of Hydrogels[18-20]

The formulas of prepared hydrogels are given in Table 1. In the formulation of hydrogels both PVP and AAc were crosslinked. The N, N′-methylene bisacrylamide was acting as a crosslinking agent. Potassium persulphate was used as a free radical polymerization initiator. AAc was polymerized to poly (AAc) by N, N′-methylene bisacrylamide in presence of potassium persulphate by free radical polymerization. The drug-polymer ratio was kept constant which is 1:20 for all the formulations. The amount of AAc was varied from 75%-90% and PVP was varied from 10%-25%. The concentration of N, N′-methylene bisacrylamide was also varied with 7.5%, 10%, 12.5%, 15% and 20% range. The amount of Potassium persulphate was kept constant for all the formulations which is 5%. The concentration of crosslinking agent and polymer ratio was varied to achieve an optimized formulation, which gave a sustained release of Rosiglitazone over a period of 12 hr.

Preparation of Hydrogels[18-21]

Exactly 100 mg of rosiglitazone was accurately weighed out, and the solution was added to 10 mL of distilled water in a beaker. The specified amount of PVP and the AAc was added to the drug solution and mixed thoroughly. Potassium persulphate was dissolved in 10 mL of distilled water in a separate beaker. It was then introduced to the drug-polymer mix and mixed for 15 min with a precise amount of MBA. At 70°C for four hours, the mixture was moved to other Petri dishes and the entire bulk was transformed into thin white films. The crosslinked hydrogels obtained were then cut into 1cm x 1cm pieces and dried for 24 hr at 40°C. The dried hydrogels were powdered and passed through sieve no. # 60/85. The dried hydrogels remained on sieve no. # 85

Table 1: Formulation of hydrogels.

Ingredient Formulatiom	Rosiglitazone (mg)	AAc (%)	PVP (%)	N,N`-methylene bisacrylamide (%)	Potassium persulphate (%)
FH1	100	75	25	20	5
FH2	100	85	15	20	5
FH3	100	90	10	20	5
FH4	100	75	25	15	5
FH5	100	85	15	15	5
FH6	100	90	10	15	5
FH7	100	75	25	12.5	5
FH8	100	85	15	12.5	5
FH9	100	90	10	12.5	5
FH10	100	75	25	10	5
FH11	100	85	15	10	5
FH12	100	90	10	10	5
FH13	100	75	25	7.5	5
FH14	100	85	15	7.5	5
FH15	100	90	10	7.5	5

were taken and 100 mg equivalent amount of hydrogels was filled into empty capsules and taken for further studies.

Evaluation of Prepared Hydrogels

Drug Content[21]

Following the preparation of the hydrogel, it was finely powdered which were permitted to pass through sieve # 60/85 to obtain the final product. The hydrogels that were retained on sieve # 85 were collected for the purpose of studying content uniformity. From the manufactured hydrogel powder, an amount equal to 10 mg of the drug was collected and placed in a standard volumetric flask of 100 mL volume. The hydrogel powder was mixed with approximately 75 mL of pH 7.4 buffer solution and allowed to sit overnight. It was necessary to dilute the final volume with pH 7.4 buffer solution and filter it after it had been allowed to stand for the proper amount of time. A 10 mL sample was pipetted into a 100 mL volumetric flask and volume was made up with pH 7.4 buffers before estimating the amount of drug contained in the sample.

In vitro Drug release Studies[15,22]

Analytical approach used in Rosiglitazone Determination

TheUltraviolet-spectrophotometric technique was used for the *in vitro* drug analysis using the double beam spectrophotometer having model number Shimadzu 1601.

Standard Curve for Rosiglitazone in 0.1 N HCl[23]

As a starting point for the final stock solution, we used 100 mg of Rosiglitazone carefully weighed into 100 mL of 0.1% sodium hydroxide to get a final concentration of 1000 g/mL. Final concentrations ranged from 1 g/mL to 10 g/mL after a second dilution of the initial stock solution. Absorbance at a wavelength of 230nm was measured using an UV-visible spectrophotometer. In order to determine the regression coefficient, it was also calculated.

Standard Curve for Rosiglitazone in phosphate buffer of pH 7.4[23]

One hundred milligrammes of Rosiglitazone were properly weighed and diluted in one hundred millilitres of phosphate buffer at pH 7.4 to form the first stock solution with a 1000g/mL concentration. It was necessary to make several dilutions of the original stock solution before achieving the desired final concentrations, which varied from 1 mg/mL to 10 mg/mL. In order to measure absorbance, an Ultraviolet spectrophotometer was used with a wavelength of 245 nm and recorded the results. The regression coefficient had to be calculated.

Drug release studies[21,23]

The *in vitro* drug release study from the hydrogels were done at 37°C ± 0.1°C using dissolution apparatus type II with a rotating basket at 50 rpm rotation speed. The drug release from the hydrogels was investigated in two different solutions: 900 mL of 0.1 N HCl for 2 hr and pH 7.4 buffer for 10 hr. The event lasted a total of 12 hr. The samples were taken out of the system at one-hour

intervals and examined in a UV-visible spectrophotometer for the presence of the drug.

To determine the influence of pH on drug release from hydrogels, the drug release from the hydrogels was tested separately in 900 mL of 0.1N HCl for 12 hr and in pH 7.4 buffer for 12 hr. The drug release from the hydrogels was examined in both solutions for 12 hr.

Mathematical Model Fitting[15,21,24-26]

Various mathematical models were studied to know the best fitted mathematical models for the drug release data. Various parameters like the time exponent (n), release rate constant (k) and regression coefficient (R^2) were evaluated to identify the release mechanism. When the value of n is around 0.5 for a non-swellable polymeric system, diffusion is predicated as the mechanism for water absorption and drug release from the polymeric system, which is known as the Fickian diffusion system. When the value of n is 0.5 to 1, the release of the drug from the polymeric system follows an anomalous diffusion which is a time-dependent mechanism, which is called a non-Fickian diffusion system. And when the value of n is equal to 1 the release of the drug from the system follows a zero-order release profile. The various models studied were:

Zero Order Kinetics

The equation $\boldsymbol{Q_t = Q_o + Kt}$ predicts the rate of drug release from the polymeric system, which is independent of drug concentration.

In zero-order kinetics, Q_t is the amount of drug dissolved in time t, Q_0 is the initial amount of drug in the solution (typically Q_o=0), and K is a constant.

First Order Kinetics

The following is the reaction rate, which is dependent on the concentration of the drug and predicted by the equation: $\boldsymbol{Q_t = Q_o e^{-kt}}$

In this equation, Q_t denotes the amount of drug released in time t, Q_0 is the initial quantity of drug present in the solution, and K denotes a constant for first-order release kinetics.

Higuchi Kinetics

It is calculated by constructing a graph between the quantity of drugs released and the square root of time. The data is inputted to the equation $\boldsymbol{f_t = F_H t^{1/2}}$ by using a linear fit.

Where ft represents the cumulative per cent of drug release, KH represents the Higuchi constant, and t represents the time.

Korsmeyer–Peppas Model

If the amount of drug released (M_t) at time t is proportional to the total amount of drug released (M) from a thin slab, the following equation can be used to calculate the amount of drug released (M_t):

$$\frac{M_t}{M_\infty} = \boldsymbol{k t^n}, \text{ for } 0 < M_t/M_\infty < 0.6$$

In this equation, M_t/M_∞ refers to the fraction of drug released at time t, and K is a constant that incorporates the structural and geometric characteristics of the drug-polymer interaction. The diffusion exponent of the release is denoted by the letter n.

Swelling Studies[27-29]

The hydrogels are having pH-dependent swelling properties which is studied in both pH 1.2 and pH 7.4 buffer at 37± 1°C. A specific weighed piece of hydrogels was placed separately in 0.1 N HCl and pH 7.4 buffers separately. The hydrogels were removed from the solution at every half an hour interval and the excess solution on the surface of the hydrogel was removed by blotting. After the solutions were removed completely the hydrogels were weighed. The swelling investigations were carried out in 0.1N HCl for 8 hr, and the studies in pH 7.4 buffer were carried out for 12 hr, respectively. The weight before swelling (Wb) and weight after swelling (Ws) were used to calculate the percentage swelling.

The percentage swelling (S) was calculated by an equation as follows:

$$S = \frac{\text{weight of swollen hydrogels} - \text{weight of dry hydrogels}}{\text{weight of dry hydrogels}} \times 100$$

Equilibrium swelling studies[28-29]

A specific amount of prepared hydrogels was swelled in different buffer solution pH ranging of 1.2, 2, 3, 4, 5, 6 and 7.4 pH at 37± 1°C for all the formulations. The swelling was continued for 24 hr until no changes in weight. The weight of the swelled hydrogel was measured and it was used to calculate the Equilibrium Swelling Ratios (ESR). The equation used for the calculation of equilibrium swelling studies was as below:

$$S = \frac{\text{weight of swollen hydrogels} - \text{weight of dry hydrogels}}{\text{weight of dry hydrogels}} \times 100$$

Studies of diffusion co-efficient[27,30]

In the present study, the prepared hydrogels were passed through sieve number 85 before the drug release studies. Thus, the diffusion of the drug from the hydrogels can be calculated considering the powders as particles. Both the diffusion of the drug from the formulations and the water diffusion into the hydrogels were calculated based on the following equation:

$$\boldsymbol{D} = \left(\frac{r\theta}{6M_\infty}\right)^2 \pi$$

Where θ refers to the slope of the linear portion of the plot between M_t/M_∞ and *t*, *r* refers to the radius of the hydrogel particle and M_∞ refers to the maximum swelling value. Both the calculation of solution absorption into the hydrogels and drug release from the formulation was calculated from the above equation.

Differential Scanning Calorimetry (DSC)[17,31]

Differential scanning calorimetry (Universal V4 2E instruments) was used to determine the physico-chemical compatibility of pure Rosiglitazone and the polymeric mixtures.

X-ray diffraction (XRD) studies[16,17]

In order to determine the polymeric structure of the hydrogels, they were subjected to X-ray diffraction using Siemens 5005 model in the diffraction angle range spanning 5.00 and 60.00, 2, using C_u K_α radiation produced at 40 kV and 40 mA.

Scanning Electron Microscopy (SEM)[29,17]

The scanning electron microscope JSM 6100 JEOL made in japan was used to analyse the surface morphology of the hydrogels that had been manufactured. Samples were put onto the stubs and delicately coated with a gold-palladium alloy before being examined under the scanning electron microscope in this experiment.

Stability Studies[15]

The optimized formulation (FH 15) was filled into capsules and then packed in aluminium foil. The formulation was stored at 25°C with 60% RH, 30°C with 65% RH and 40°C with 75% RH for 3 months and samples were withdrawn on the interval of 0th, 15th, 45th and 90th days and were examined for drug content and drug release studies.

RESULTS AND DISCUSSION

Results

Standard plot data of Rosiglitazone

The standard graph for rosiglitazone was prepared separately in 0.1N HCl and pH 7.4 phosphate buffer. The graph between absorbance and concentration was plotted for both the medium and for HCl the regression (R^2) value was found as 0.9984 and for phosphate buffer, the R^2 value was found as 0.9981.

Preformulating Studies

Melting Point

The melting point of Rosiglitazone was found to be 120-121°C. The reported melting point for the Rosiglitazone is 122-123°C as per references.

Solubility Study

From the solubility studies, the solubility of Rosiglitazone was found to be 0.834 mg/mL in phosphate buffer pH 7.4. Due to this reason the phosphate buffer was selected as the dissolution media for further studies as a sufficient amount of drug dissolved in the phosphate buffer, which is essential to keep the sink condition.

Drug-polymer interaction studies

The IR spectra were recorded between 4000 and 400 cm^{-1} for pure drug, formulation with the drug (FH 15) and formulation without the drug. The spectra were given in the following Figures 1-3.

Evaluation of Prepared Hydrogels

Drug Content

This test was carried out to determine whether the drug is uniformly distributed in the formulations. The release of the drug from the hydrogel was evaluated for 24 hr the amount of Rosiglitazone was determined spectrophotometrically at 245 nm. The results obtained are reported in Table 2.

Swelling Studies

The swelling studies for hydrogels were evaluated in both acidic and basic media for their pH sensitivity. The swelling was carried out in acidic pH until there was a constant weight. In the same way, the swelling was checked in pH 7.4 phosphate buffer until a constant weight was obtained. The results of the swelling studies are shown in Figures 4-8.

FTIR Analysis

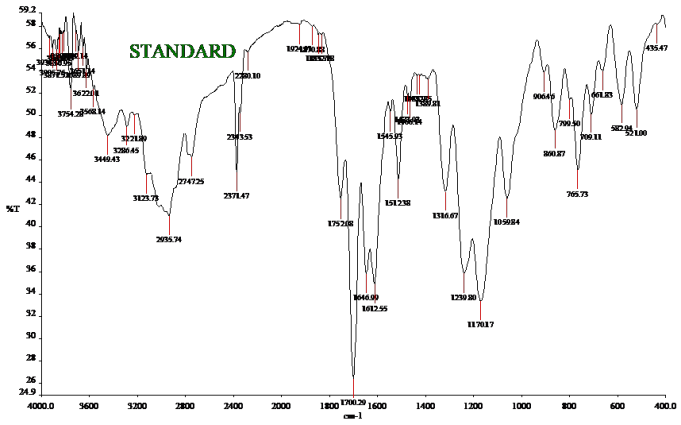

Figure 1: FT-IR spectra of Rosiglitazone pure drug.

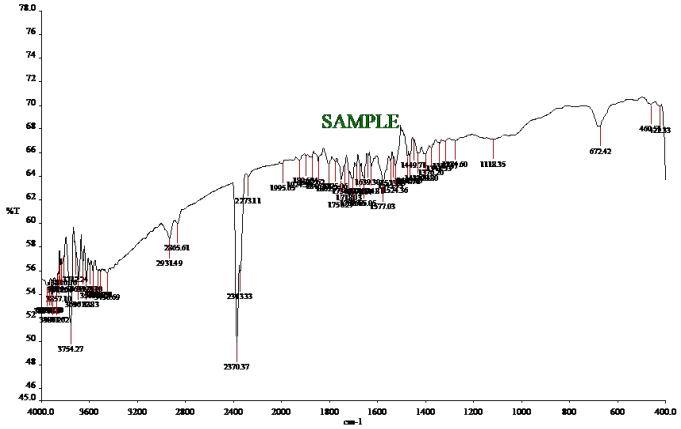

Figure 2: FT-IR spectra of Rosiglitazone in the formulation.

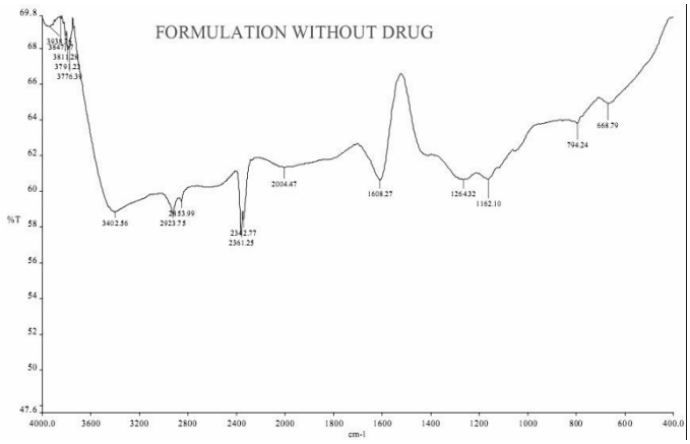

Figure 3: FT-IR spectra of formulation without drug.

Swelling Studies

Equilibrium swelling studies

The equilibrium swelling studies was evaluated in different pH. The Equilibrium Swelling Ratios (ESR) were calculated for the formulations. The results of the studies showed in Figures 9-13.

Equilibrium swelling studies of the hydrogels

Studies of Diffusion Coefficient

The diffusion coefficients of the formulations were calculated both for acidic and basic mediums. The diffusion coefficients were found to be more basic than the acidic medium. The values of the diffusion studies were shown in Table 3.

In vitro Drug Release Studies

In vitro, drug release studies were done in both 0.1 N HCl and pH 7.4 phosphate buffer for all the formulations. The studies were conducted in acidic pH i.e. 0.1N HCl for the initial 2 hr which mimicked the stomach condition. For subsequent 10 hr, the studies were done in basic pH i.e., in 7.4 pH buffer which mimicked the intestinal conditions. The *in vitro* drug release data for the hydrogels containing Rosiglitazone are given in Tables 4 and the corresponding graphs are represented in Figures 14-18.

In vitro Drug Release Studies

Mathematical Model of Data Obtained Drug Release studies

In order to determine the release mechanism, the *in vitro* drug release data for all of the formulations was analysed. The model with the highest R^2 value was chosen as the best-fitting model based on the data set that has been collected so far. Table 5 show the outcomes of the study that was conducted.

DSC Analysis

The DSC analysis of formulation FH 15 (melting point 122°C) and the pure drug Rosiglitazone demonstrated a molecular distribution of the crystalline drug in an amorphous state. There was no extra endothermic peak was observed which showed that the polymer did not interact with the drug. DSC thermogram is shown in Figures 19 and 20.

XRD Analysis

The XRD study of the pure drug, Formulation (FH 15) and formulation without drug indicated that the crystalline drug was well distributed in the formulation at its molecular level in the amorphous state and there was no extra peak which confirmed that there was no drug-polymer reaction took place. The XRD thermogram is shown in Figures 21-23.

SEM Analysis

The XRD study of the pure drug, Formulation (FH 15) and formulation without drug indicated that the crystalline drug was well distributed in the formulation at its molecular level in the amorphous state and there was no extra peak which confirmed that there was no drug-polymer reaction taken place. The SEM is shown in Figures 24 and 25.

Stability Study

The stability studies of optimized formulation FH 15 were carried out for 90 days at 25°C with 60% RH, 30°C with 65%RH and 40°C with 75% RH. Every 30 days, the percentage drug content and the percentage drug release were evaluated, and the results revealed that there was little change in the percentage drug content and the percentage drug release profile. These are the outcomes, which are presented in Tables 6 and 7.

DISCUSSION

In the present study, Rosiglitazone was employed as a model anti-diabetic medication in the creation of hydrogels for the treatment of type 2 diabetes. The dissolution media utilised in this investigation were 0.1N HCl and pH 7.4 phosphate buffer. According to the research, the solubility of Rosiglitazone in phosphate buffer at pH 7.4 was reported to be 0.834 mg/mL. The melting point of pure Rosiglitazone was discovered to be 120-121 degrees Celsius. As a result, the sample collected was reported to be pure Rosiglitazone and was used for future research.

The standard curves for Rosiglitazone were generated in two distinct solutions: 0.1N HCl and pH 7.4 phosphate buffer. The maximum absorbance of Rosiglitazone in 0.1N HCl was found to be at 230 nm, whereas the maximum absorbance in pH 7.4 phosphate buffer was found to be at 245 nm. In the case of 0.1N HCl, the coefficients of regression, the slope, and the Y-intercept were found to be 0.9984, 0.0365, and 0.0082, according to the results. The regression coefficients, slope, and Y-intercept for pH 7.4 phosphate buffer HCl were found to be 0.9981, 0.0407, and 0.0071, respectively, in the instance of this solution. It was decided to adopt the values from the standard curve for the *in vitro* drug dissolution investigations after that.

FT-IR Analysis

For the FT-IR analysis the pure drug Rosiglitazone, formulation FH 15 and formulation without drug was subjected for the analysis. The test was performed to study whether there was any drug-polymer interaction. The pure Rosiglitazone shows characteristic peaks at 1705, 1640, 1514, 1379, 1163 and 866 cm^{-1}.

The characteristic peaks of Rosiglitazone were compared with the formulation containing drug and the formulation without the drug. The formulation with drug and pure drug shows similar characteristic peaks. The IR spectra show the characteristic peaks for C=O stretching at 1700.5 cm^{-1}, N-H stretching at 3449.43 cm^{-1} and N-H bending out of plane vibration at around 860 cm^{-1}. It also shows C-H stretching at 2935 cm^{-1} and at 2747 cm^{-1} along with CH2 bending at 1512 cm^{-1} and CH3 bending at 1389 cm^{-1}. It also shows C=N stretching at 1646 cm^{-1}, C-N stretching at 1170 cm^{-1}. It conforms to a monosubstituted aromatic ring with numerous peaks from 1924 to 1800 cm^{-1}. Thus all the characteristic peaks were similar in both the drug-containing formulation (FH 15) and the pure Rosiglitazone. There were no variations in the main peaks of Rosiglitazone in the presence of Acrylic acid and polyvinylpyrrolidone. It seems that there was no chemical interaction between the drug and the polymers. Hence, it can be concluded that the drugs were in the Free State and can release easily from the interpenetrating polymeric network

Formulation of Hydrogels

In this study, hydrogels containing Rosiglitazone were prepared. The drug-polymer ratio was kept constant for all the formulations. The polymers used were Acrylic acid and polyvinylpyrrolidone. Potassium persulphate was used as initiator and N, N′-methylene bisacrylamide was used as the crosslinker in the formulation.

A total of fifteen formulations were prepared where the crosslinker was varied within 7.5, 10, 12.5, 15 and 20 and its effect on release pattern along with polymer ratio varied within 75:25, 85:15 and 90:10 was studied. During formulation, hydrogels were kept at 70°C for 4 hr for complete crosslinking to get a white thick mass and then dried for 24 hr at 40°C.

Drug Content

An investigation into the uniformity of drug content was conducted in order to ensure that the drug was evenly distributed throughout the formulations. The results of the investigation demonstrated that the drug content in the various batches of manufactured hydrogels was highly consistent and that the results were within acceptable limits. In conclusion, the results demonstrated that the technique used in the current investigation was capable of creating hydrogels with consistent drug concentrations.

Swelling Study

From the swelling studies, it was perceived that the swelling of the hydrogels was pH-dependent and the swelling varied to a large extent in both acidic and basic pH. The swelling of the hydrogels in the dissolution media may be due to the dissociation of the carboxylic acids groups present in the acrylic acid, which increases the osmotic pressure inside the hydrogels leads in swelling of the hydrogels.

The degree of percentage of swelling of the hydrogels was strongly dependent on the crosslinker concentration. It was observed that the percentage of swelling of the hydrogels formulations was decreased with an increase in cross-linker concentration.

It was also found that the swelling of the hydrogels was also dependent on the concentration of acrylic acid in the formulation. As the concentration of acrylic acid increased the swelling of the hydrogels also increased for various cross-linker concentrations. This behaviour can be attributed to the higher hydrophilic character of PAAc than PVP polymer. In this study, the swelling studies were carried out and the results were interpreted for the effect of crosslinker on various polymer ratios and the effect of polymer on cross-linker ratio.

The maximum swelling of the hydrogels was found for the formulation with the maximum concentration of acrylic acid with a minimum percentage of cross-linker i.e., 90% acrylic acid with 7.5% crosslinker concentration.

Equilibrium swelling ratio

The prepared hydrogels were investigated for the pH depended on equilibrium swelling studies. The equilibrium swelling degree of AAc containing hydrogels is mainly controlled by the charge of the ionic monomer, degree of ionization, crosslinking density, pKa of the ionizable group and structure of the polymer network. In the present studies, it was found that the swelling was greatly influenced by the concentration of AAc concentration in the formulation. As the concentration of AAc in the solution grew, the swelling increased as well. In the formulation with AAc concentration, it leads to the increase of the electrostatic repulsion force, which results in the expansion of the network of the hydrogels. Besides the concentration of the AAc, all the formulations swelled with an increase in the pH value of the medium. The maximum swelling was obtained with the formulation FH 15 which contains the maximum concentration of AAc with the minimum concentration of cross-linker and the higher pH value of the solution.

The graph obtained by plotting pH versus equilibrium swelling showed a sudden decrease at around pH 3. The reason may be because of the pKa value of AAc which is around 3-4. When the pH values are lower than the pKa value, the carboxylic groups of AAc completely collapsed which results in a decrease in swelling.

Table 2: Uniformity of contents data for Rosiglitazone hydrogels.

Sl. No	Formulation	Trial 1	Trial 2	Trial 3	Average % Mean ± SD(n = 3)
1	FH 1	99.36	99.35	99.31	99.34 ± 0.026
2	FH 2	99.1	99	99.16	99.09 ± 0.081
3	FH 3	99.75	99.79	99.69	99.74 ± 0.050
4	FH 4	99.07	99.04	99.04	99.05 ± 0.017
5	FH 5	99.09	99.1	99.11	99.10 ± 0.010
6	FH 6	99.41	99.44	99.45	99.43 ± 0.021
7	FH 7	99.78	99.82	99.76	99.79 ± 0.031
8	FH 8	99.91	99.87	99.89	99.89 ± 0.020
9	FH 9	99.65	99.6	99.63	99.63 ± 0.025
10	FH 10	99.57	99.54	99.53	99.55 ± 0.021
11	FH 11	99.46	99.5	99.48	99.48 ± 0.020
12	FH 12	99.61	99.64	99.63	99.63 ± 0.015
13	FH 13	99.96	99.94	99.93	99.94 ± 0.015
14	FH 14	99.79	99.82	99.8	99.80 ± 0.015
15	FH 15	99.93	99.98	99.94	99.95 ± 0.026

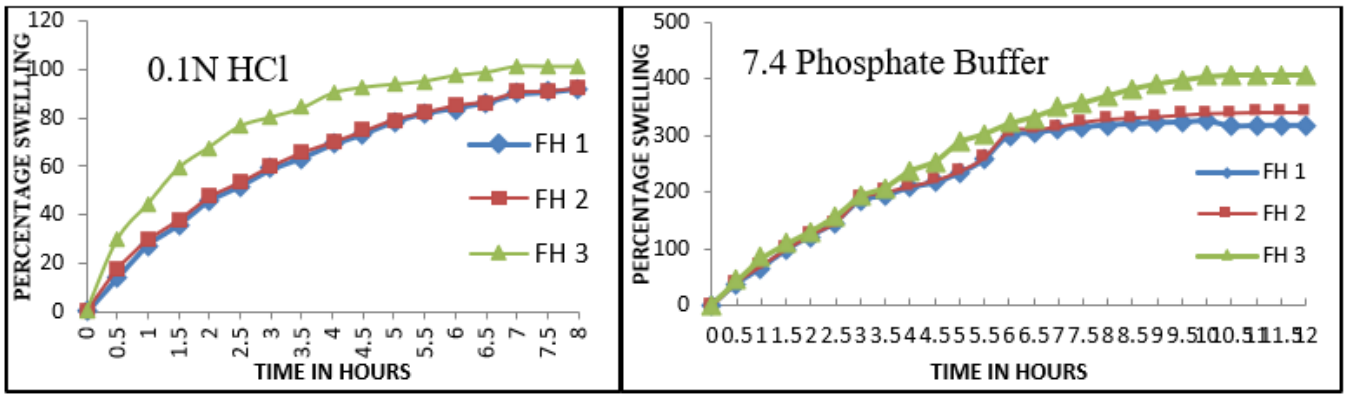

Figure 4: Effect of polymer ratio with 20% crosslinker on swelling in 0.1N HCl and pH 7.4 phosphate buffer.

In vitro Studies for Drug Release

The Influence of Polymer Concentration on the Release of Drug

The amount of medication released from the hydrogel *in vitro* was highly dependent on the concentrations of the polymer and cross-linker used. The AAc behaves as a pH-sensitive polymer for the hydrogel formulation. It shows a varying difference in the release pattern both in acidic and alkaline pH. For the first two hours in 0.1N HCl, the release was quite less in all cases ranging from as less as 6% to 36%. The reason behind the decreased release of the drug can be attributed to the fact that the swelling of the hydrogels in acidic pH is low. When the dissolution media was changed to the basic pH the release of the drug also increased and the reason again may be due to the increased swelling of the hydrogel in the buffer that is in pH 7.4 phosphate buffer.There were three ratios of polymer acrylic acid: PVP used i.e., 75:25, 80:20 and 90:10. For each ratio the crosslinker concentration were varied in five different percentages i.e. 20%, 15%, 12.5%, 10% and 7.5%.

According to the findings, acrylic acid, in conjunction with the cross-linker concentration, plays a significant impact in the drug release property of the compound. As the concentration of acrylic acid decreased, from 90% to 75% the drug release also decreased, or in other words the drug release increased as the concentration of acrylic acid increased and PVP concentration decreased. The optimums ratio of acrylic acid to PVP was found to be 90:10 where 90% was acrylic acid and 10% was PVP.

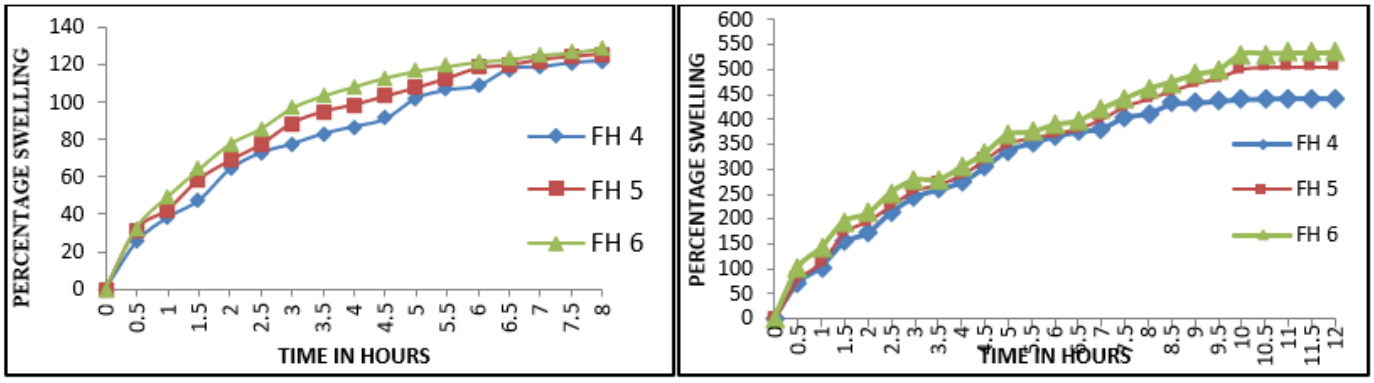

Figure 5: Effect of polymer ratio with 15% crosslinker on swelling in 0.1N HCl and pH 7.4 phosphate buffer.

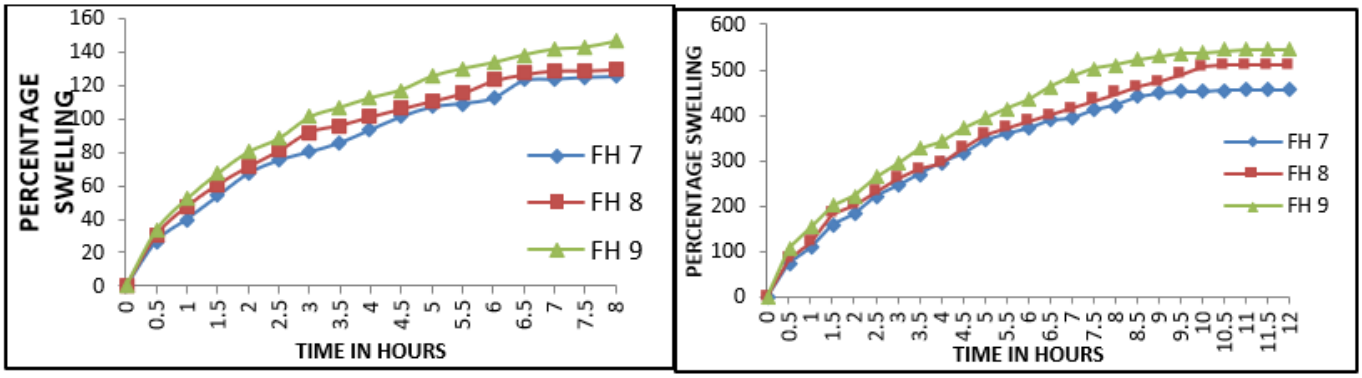

Figure 6: Effect of polymer ratio with 12.5% crosslinker on swelling in 0.1N HCl and pH 7.4 phosphate buffers.

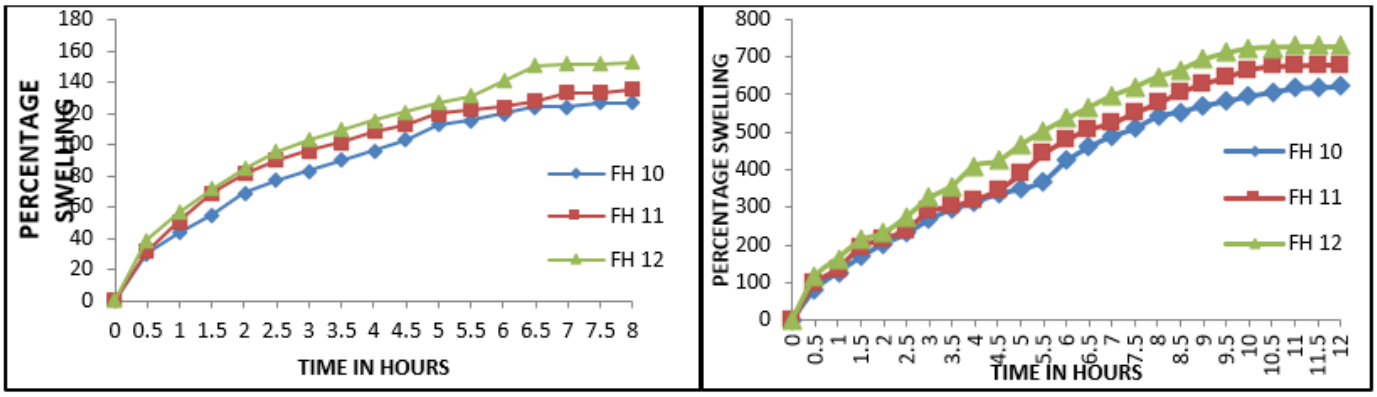

Figure 7: Effect of polymer ratio with 10% crosslinker on swelling in 0.1N HCl and pH 7.4 phosphate buffers.

Effect of N, N′ -methylene bisacrylamide Concentration in Drug Release

The amount of N, N′ -methylene bisacrylamide was decreased from 20% to 7.5% in formulations and its effect on drug release was studied with the varying concentration of the polymer ratio. The optimum drug release was found with a 7.5% crosslinker and a 90:10 polymer ratio.

Diffusion Co-efficients

The swelling of the hydrogels took due to the diffusion of the dissolution medium into the polymeric network. The diffusion coefficients of all the formulations were calculated for both the acidic and the basic medium. It was found that the diffusion coefficients in the acidic medium were quite less than the basic medium.

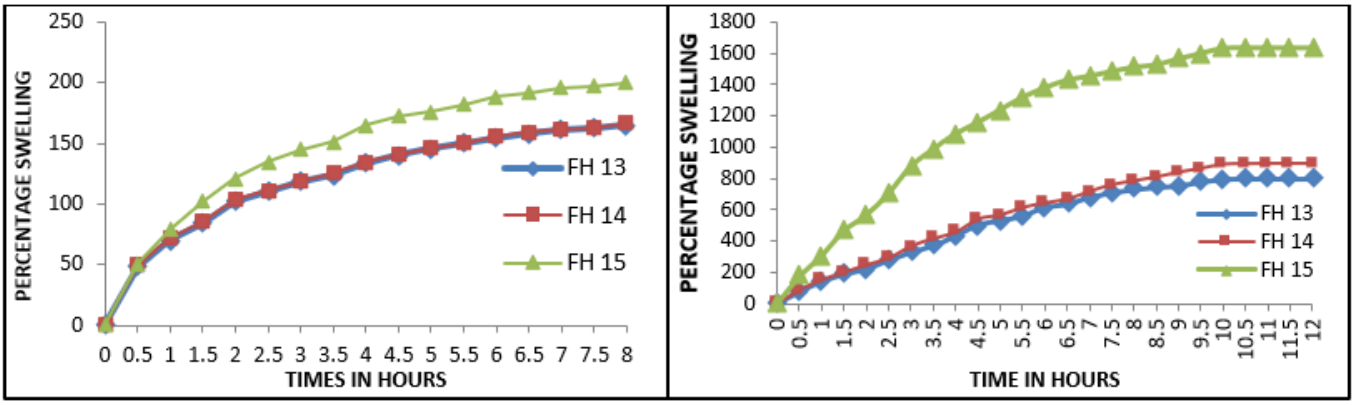

Figure 8: Effect of polymer ratio with 7.5% crosslinker on swelling in 0.1N HCl and pH 7.4 phosphate buffers.

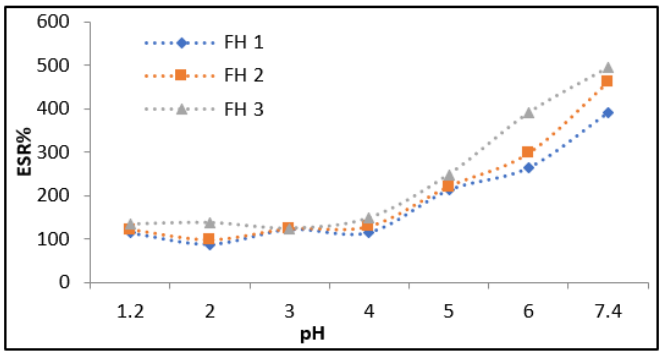

Figure 9: Effect of polymer ratio with 20% crosslinker on ESR.

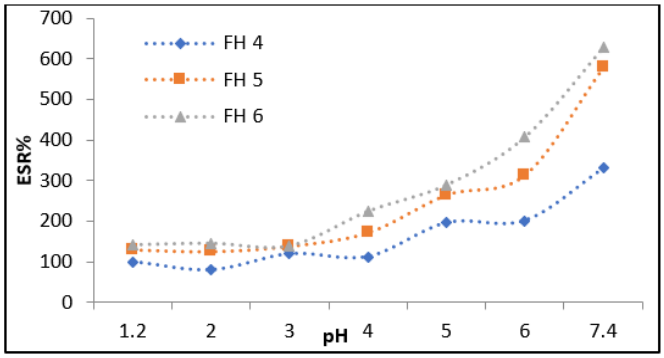

Figure 10: Effect of polymer ratio with 15% crosslinker on ESR.

The diffusion coefficients also depended on the polymeric concentration and the crosslinker concentration. Diffusion coefficients were high in the formulation where AAc concentration was high with a minimum concentration of crosslinker. The formulation FH 15 gave the maximum diffusion coefficients both in acidic and the basic medium.

Mathematical Model Fitting

When the results of *in vitro* drug release experiments were compared to those of *in vivo* drug release experiments in acidic and basic conditions, the results were fitted into various mathematical models, including Zero order, Higuchi, First order, and Peppas. It was found that with an increased concentration of crosslinker the release profile followed a diffusion-controlled release pattern (Higuchi model). As the concentration of the crosslinker decreased and AAc concentration increased the formulation showed Zero-order release profile. In the optimized formulation (FH 15) the 'R^2' value for zero-order was found to be 0.997 and the 'n' value for Peppas was found to be 0.9. The 'k' value for Peppas was found to be 0.106. From this, it can be concluded that the formulation (FH 15) showed a concentration-independent release pattern.

A value of 'n' between 0.5 and 1 indicate anomalous diffusion behaviour that is the time-dependent mechanism and it is called a non-Fickian mechanism, generally due to the swelling of the system in the solvent before the release takes place. In the present study the 'n' value for the optimized formulation FH 15 was found to be 0.9 thus the release mechanism was assumed to be anomalous diffusion systems

DSC Analysis

DSC thermograms of pure Rosiglitazone and formulation FH 15 were shown in Figures 19 and 20. In the case of pure Rosiglitazone, a sharp endothermic peak was observed, at 122°C, which corresponds to the melting process. Thermograms of formulation FH15 did not show any sharp peak in that region. The reason for the absence of the peak is due to the amorphous dispersion of the drug into hydrogels. There was no extra endothermic peak was observed which specified that the polymer did not interact with the drug.

XRD Analysis

The XRD analysis of pure drug Rosiglitazone, hydrogels without the drug and the formulation FH 15 are shown in Figures 21-23. X-ray diffraction pattern of the pure rosiglitazone shows characteristics peaks (2θ) at 4.640, 8.520, 13.890, 19.950, 24.50, 25.070 and 27.240. But the characteristic peaks of the pure drug were absent in the XRD patterns of formulation FH 15 which clearly indicated that the crystalline drug Rosiglitazone was distributed in molecular form into the hydrogel structure.

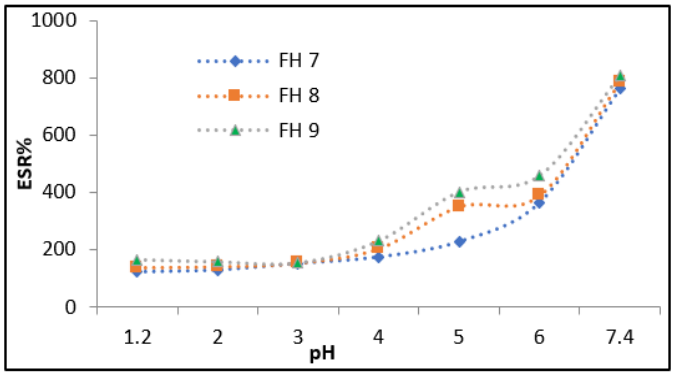

Figure 11: Effect of polymer ratio with 12.5% crosslinker on ESR.

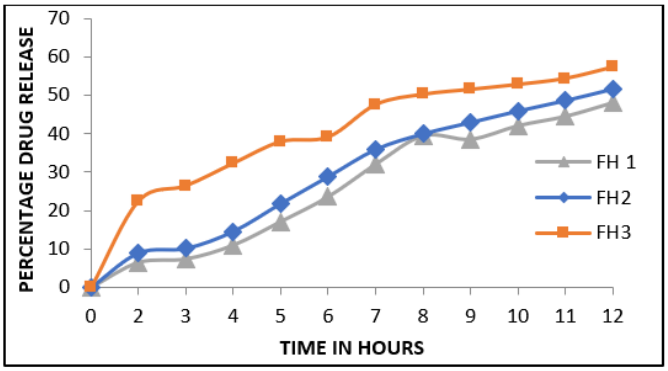

Figure 14: Effect of polymer on 20% crosslinker on drug release.

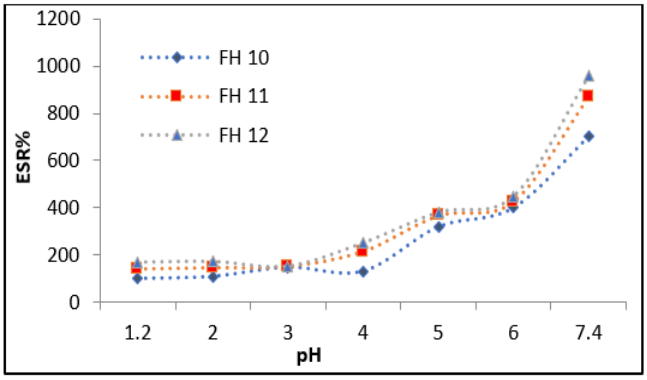

Figure 12: Effect of polymer ratio with 10% crosslinker on ESR.

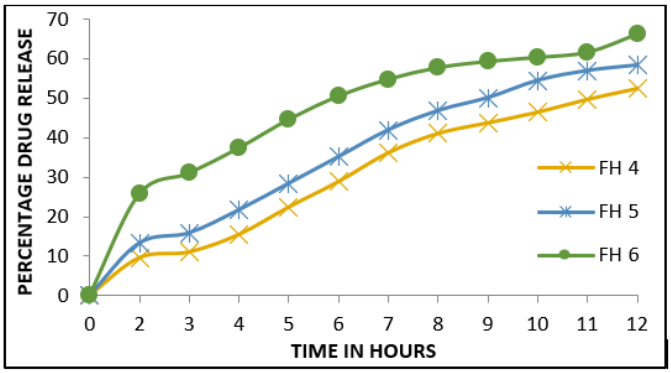

Figure 15: Effect of polymer on 15% crosslinker on drug release.

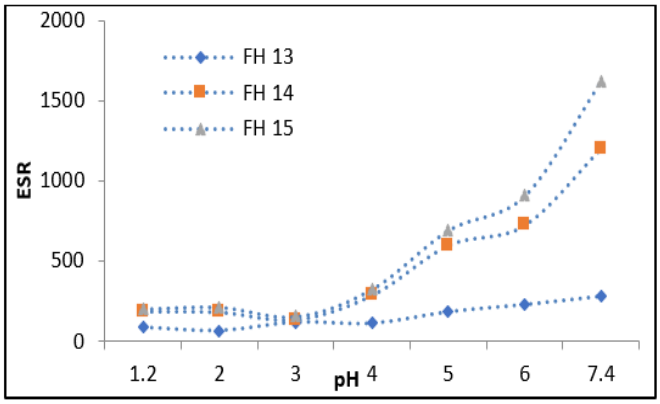

Figure 13: Effect of polymer ratio with 7.5% crosslinker on ESR.

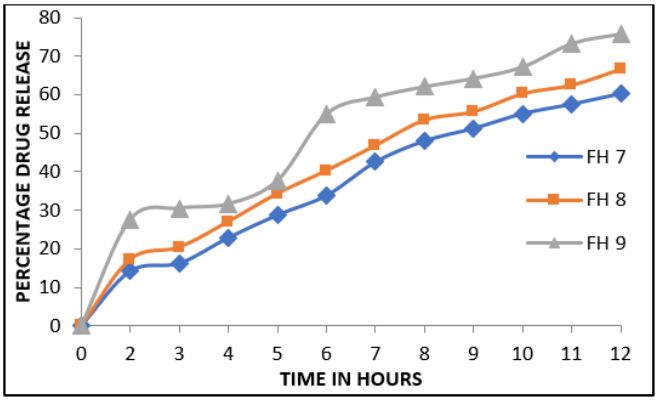

Figure 16: Effect of polymer on 12.5% crosslinker on drug release.

Also, diffractograms of both the formulation FH 15 and placebo formulation were almost identical, indicating the amorphous dispersion of the drug after entrapment into polymeric hydrogels.

SEM Analysis

The swelling of the hydrogel is greatly influenced by the pH of the media. Thus the surface morphology of the hydrogels swelled in different pH i.e. 0.1N HCl and pH 7.4 were studied. It was found that the hydrogel swollen in pH 7.4 contains a porous surface compared to that of hydrogel swollen in 0.1 N HCl. The reason behind the more porous surface may be due to the pH-sensitive swelling of the AAc. The porous surface of hydrogels, in basic pH, is also signified the release of more amount of drugs in basic media than in the acidic medium.

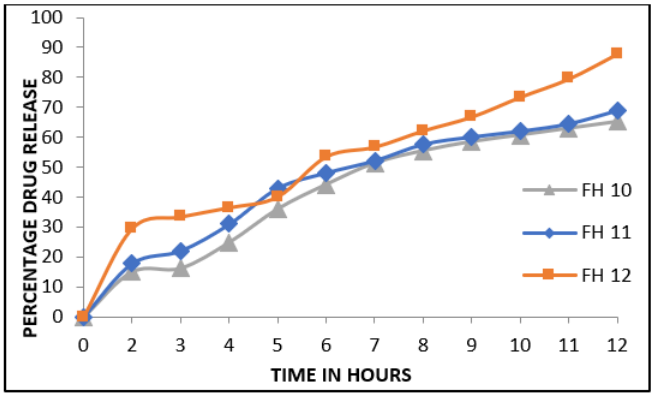

Figure 17: Effect of polymer on 10% crosslinker on drug release.

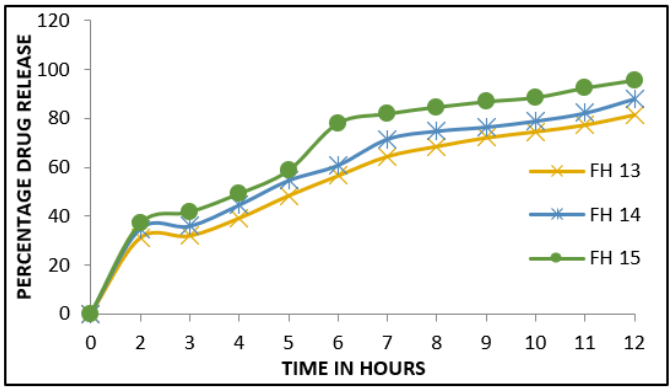

Figure 18: Effect of polymer on 7.5% crosslinker on drug release.

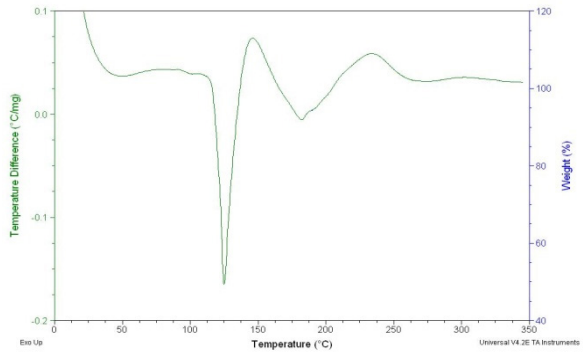

Figure 19: DSC of Pure Rosiglitazone.

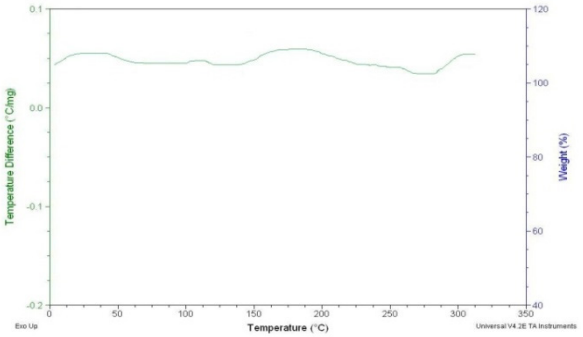

Figure 20: DSC of best formulation FH 15.

Stability Studies

The most effective formulation, FH 15, was subjected to stability testing in accordance with ICH recommendations. It was carried out under an accelerated environment for 90 days at 40°C and 75 per cent relative humidity, as well as under real-time settings at 25°C and 60 per cent relative humidity and 30°C and 65 per cent relative humidity. Every 30 days, the percentage of drug content was determined, as well as the percentage of drug release. The data collected revealed that there was no significant change in the percentage of drug content or the percentage drug release profile as a result of the procedure.

Rosiglitazone hydrogels were found to be effective *in vitro* and in a variety of other characterisation parameters, leading to the conclusion that they might be used for administration. Drug integrity and stability in the hydrogels were maintained throughout storage, with no major chemical interactions occurring between the drug and excipients during storage.

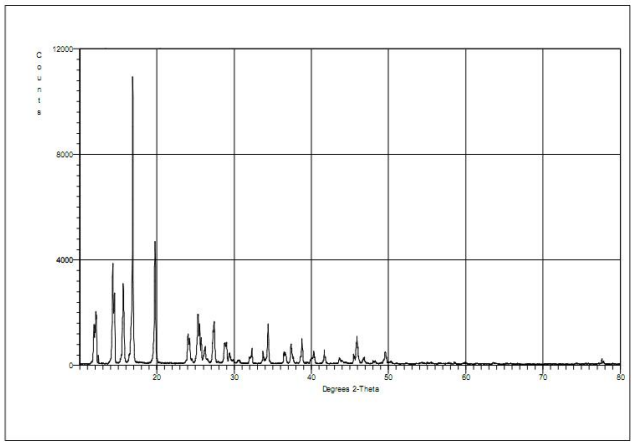

Figure 21: XRD of pure Rosiglitazone.

CONCLUSION

In the present work, an antidiabetic drug Rosiglitazone was tried to deliver in the form of hydrogels for 12 hr as a controlled drug delivery system. The polymers used were namely acrylic acid and polyvinylpyrrolidone along with cross-linker MBA and initiator PPS. The concentration of the polymer and the cross-linker was varied to obtain an optimized formulation. Among the different formulations (FH1 to FH 15), the formulation FH 15 was selected as the best formulation based on the polymer-crosslinker combination. Formulation FH 15 contained Acrylic acid 90%, polyvinylpyrrolidone 10% and methylene bisacrylamide 7.5% and 5% potassium persulphate. It showed a maximum of 99.95%

Table 3: Diffusion coefficients of the formulations both in acidic and basic medium.

Formulation	Diffusion co-efficient in 0.1 N HCl cm^2/s	Diffusion co-efficient in pH 7.4 Buffer cm^2/s
FH 1	7.479×10^{-09}	5.355×10^{-07}
FH 2	7.397×10^{-09}	4.979×10^{-07}
FH 3	7.737×10^{-09}	6.766×10^{-07}
FH 4	6.766×10^{-09}	2.694×10^{-07}
FH 5	6.750×10^{-09}	2.839×10^{-07}
FH 6	6.320×10^{-09}	1.759×10^{-07}
FH 7	6.634×10^{-09}	2.486×10^{-07}
FH 8	6.6166×10^{-09}	2.605×10^{-07}
FH 9	6.420×10^{-09}	1.634×10^{-07}
FH 10	7.574×10^{-09}	4.466×10^{-07}
FH 11	7.774×10^{-09}	3.888×10^{-07}
FH 12	7.555×10^{-09}	3.049×10^{-07}
FH 13	8.326×10^{-09}	8.549×10^{-07}
FH 14	8.335×10^{-09}	8.415×10^{-07}
FH 15	7.224×10^{-09}	6.353×10^{-07}

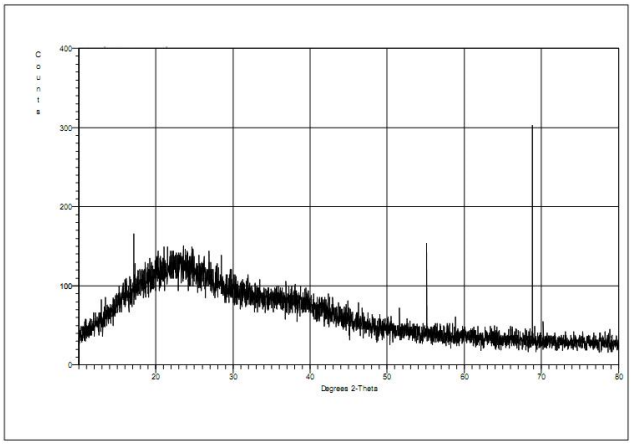

Figure 22: XRD of hydrogel without Rosiglitazone.

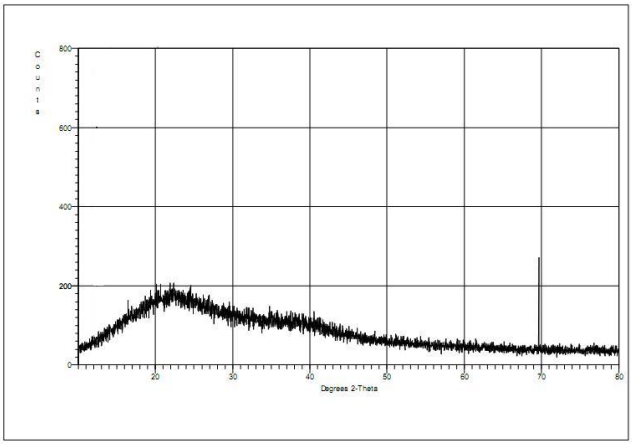

Figure 23: XRD of formulation FH 15.

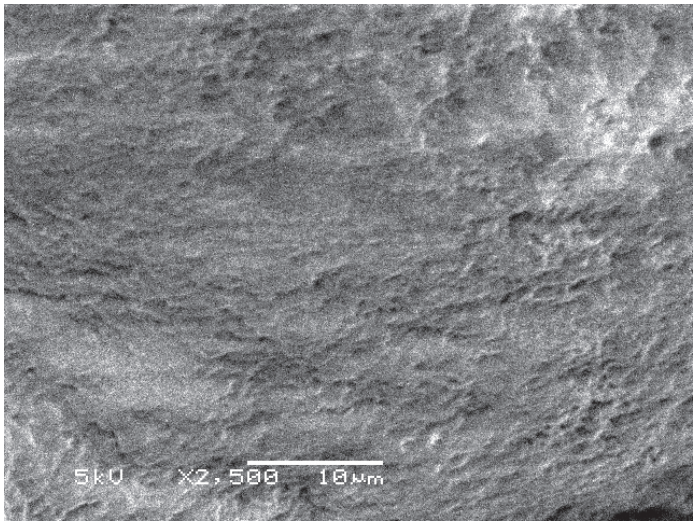

Figure 24: SEM of Rosiglitazone hydrogels swollen in 0.1 N HCl.

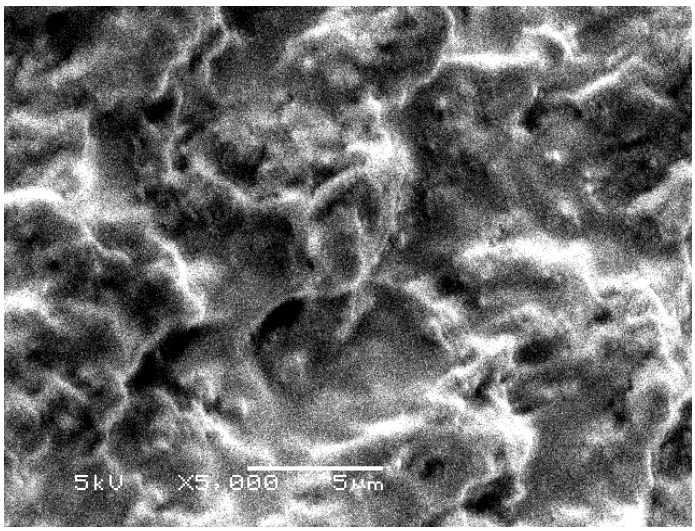

Figure 25: SEM of Rosiglitazone hydrogels swollen in pH 7.4 phosphate buffer.

of drug content, optimum percentage swelling in acidic and basic medium and maximum *in vitro* drug release of 95.60% in a controlled delivery manner at the end of 12 hr. The formulation also showed the maximum diffusion coefficients in both the acidic and the basic medium. The drug release was found to be more in alkaline media than acid media.

Physically the hydrogels were flexible and creamy white initially but after drying for 4 hr it becomes fragile and yellowish in colour. The FTIR study clearly reveals that there was no drug-polymer interaction in the formulation. From the XRD it was found the drug was distributed in a molecular state in the formulation. The SEM study of the formulation FH15 showed the formation

Table 4: Effect of polymer on 20%, 15%, 12.5%, 10% and 7.5% cross linker on drug release [Average % release Mean ± SD (*n*=3)].

Time in Hrs	20% Cross linker on drug release			15% Cross linker on drug release			12.5% Cross linker on drug release			10% Cross linker on drug release			7.5% Cross linker on drug release		
	FH 1	FH2	FH3	FH 4	FH 5	FH 6	FH 7	FH 8	FH 9	FH 10	FH 11	FH 12	FH 13	FH 14	FH 15
0	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
2	6.4 ± 0.10	8.95 ± 0.20	22.47 ± 0.30	9.56 ± 0.20	13.25 ± 0.19	25.69 ± 0.10	14.17 ± 0.19	17.25 ± 0.10	27.70 ± 0.10	15.09 ± 0.19	17.86 ± 0.30	29.54 ± 0.10	31.0 ± 0.25	34.76 ± 0.14	36.92 ± 0.25
3	7.3 ± 0.19	10.13 ± 0.19	26.4 ± 0.10	11.02 ± 0.20	15.82 ± 0.10	31.00 ± 0.25	16.18 ± 0.10	20.37 ± 0.20	30.54 ± 0.19	16.27 ± 0.20	22.09 ± 0.25	33.49 ± 0.19	31.98 ± 0.30	35.94 ± 0.35	41.70 ± 0.30
4	11.00 ± 0.30	14.57 ± 0.30	32.28 ± 0.19	15.47 ± 0.25	21.66 ± 0.20	37.38 ± 0.35	22.86 ± 0.20	27.05 ± 0.10	31.67 ± 0.30	24.89 ± 0.30	31.00 ± 0.36	36.57 ± 0.30	39.20 ± 0.10	44.56 ± 0.30	49.23 ± 0.19
5	17.14 ± 0.20	21.83 ± 0.19	37.89 ± 0.10	22.44 ± 0.15	28.38 ± 0.10	44.62 ± 0.19	28.74 ± 0.20	34.33 ± 0.19	37.80 ± 0.16	36.05 ± 0.19	43.02 ± 0.30	40.22 ± 0.10	48.41 ± 0.30	54.61 ± 0.31	58.74 ± 0.20
6	23.59 ± 0.19	28.85 ± 0.30	39.09 ± 0.10	28.91 ± 0.40	35.13 ± 0.25	50.53 ± 0.10	33.83 ± 0.22	40.26 ± 0.10	55.07 ± 0.35	44.23 ± 0.10	48.17 ± 0.19	53.61 ± 0.35	56.57 ± 0.19	60.84 ± 0.19	78.03 ± 0.15
7	32.02 ± 0.19	35.91 ± 0.35	47.52 ± 0.20	36.24 ± 0.19	41.93 ± 0.23	54.82 ± 0.29	42.55 ± 0.19	46.78 ± 0.20	59.40 ± 0.19	51.35 ± 0.35	52.24 ± 0.19	56.81 ± 0.17	64.49 ± 0.16	71.54 ± 0.20	81.89 ± 0.26
8	39.39 ± 0.19	39.96 ± 0.10	50.17 ± 0.30	41.12 ± 0.19	46.82 ± 0.35	57.75 ± 0.32	48.00 ± 0.10	53.35 ± 0.30	62.09 ± 0.10	55.45 ± 0.26	57.72 ± 0.20	62.25 ± 0.25	68.58 ± 0.24	74.82 ± 0.19	84.66 ± 0.10
9	38.48 ± 0.20	42.92 ± 0.19	51.45 ± 0.03	43.81 ± 0.10	50.08 ± 0.19	59.33 ± 0.25	51.26 ± 0.19	5.51 ± 0.20	64.25 ± 0.10	58.47 ± 0.19	60.18 ± 0.31	66.89 ± 0.10	72.14 ± 0.25	76.45 ± 0.19	86.89 ± 0.10
10	42.01 ± 0.20	45.90 ± 0.20	52.74 ± 0.40	46.52 ± 0.25	54.46 ± 0.10	60.36 ± 0.20	55.09 ± 0.10	60.18 ± 0.34	67.24 ± 0.19	60.68 ± 0.25	62.10 ± 0.26	73.50 ± 0.10	74.61 ± 0.35	78.92 ± 0.30	88.58 ± 0.19
11	44.44 ± 0.20	48.62 ± 0.10	54.31 ± 0.10	49.79 ± 0.30	56.93 ± 0.40	61.67 ± 0.35	57.56 ± 0.18	62.38 ± 0.10	73.31 ± 0.30	62.89 ± 0.10	64.59 ± 0.25	79.60 ± 0.30	77.37 ± 0.10	82.24 ± 0.19	92.50 ± 0.15
12	48.00 ± 0.30	51.63 ± 0.40	57.27 ± 0.10	52.53 ± 0.30	58.30 ± 0.19	66.30 ± 0.10	60.31 ± 0.10	66.54 ± 0.19	75.80 ± 0.25	65.12 ± 0.10	69.03 ± 0.19	87.95 ± 0.19	81.53 ± 0.20	88.08 ± 0.20	95.60 ± 0.20

Table 5: Mathematical Model Fitting of obtained Drug Release Data.

Formulation	Zero order		First order		Higuchi		Peppas			Diffusion (D X 10^{-13} CM^2/S)
	R^2	K	R^2	K	R^2	K	K	N	R^2	
FH 1	0.975	0.344	0.994	-0.027	0.996	0.651	0.040	1.1	0.972	1.01
FH 2	0.970	0.344	0.992	-0.028	0.996	0.651	0.048	1.0	0.976	1.02
FH 3	0.970	0.379	0.994	-0.033	0.996	0.589	0.059	1.0	0.978	1.49
FH 4	0.961	0.347	0.990	-0.029	0.993	0.643	0.067	0.9	0.982	1.26
FH 5	0.959	0.345	0.989	-0.029	0.993	0.647	0.081	0.8	0.990	1.25
FH 6	0.992	0.437	0.975	-0.043	0.988	0.515	0.085	0.9	0.990	1.85
FH 7	0.975	0.395	0.993	-0.034	0.993	0.566	0.057	1.0	0.993	1.56
FH 8	0.954	0.392	0.986	-0.034	0.989	0.564	0.069	0.9	0.998	1.59
FH 9	0.995	0.494	0.977	-0.051	0.991	0.456	0.070	1.0	0.999	2.34
FH 10	0.931	0.398	0.980	-0.037	0.976	0.546	0.071	1.0	0.989	1.71
FH 11	0.955	0.408	0.986	-0.040	0.989	0.544	0.095	0.8	0.996	1.75
FH 12	0.988	0.497	0.946	-0.062	0.979	0.451	0.135	0.7	0.991	2.36
FH 13	0.995	0.540	0.927	-0.063	0.969	0.411	0.077	0.9	0.989	2.70
FH 14	0.994	0.549	0.917	-0.068	0.967	0.405	0.093	0.9	0.993	2.78
FH 15	0.997	0.583	0.902	-0.082	0.974	0.383	0.106	0.9	0.994	3.15

R^2 = regression coefficient, n = time exponent, K = release rate constant.

Table 6: Percentage Drug content of FH 15 during stability study.

Time in Days	% Drug content		
	25°C/60% RH	30°C/65% RH	40°C/75% RH
0	99.6 ± 0.30	99.8 ± 0.30	99.6 ± 0.30
30	96.0 ± 0.25	96.5 ± 0.29	95.7 ± 0.31
60	97.2 ± 0.32	96.8 ± 0.25	97.5 ± 0.22
90	97.9 ± 0.27	96.7 ± 0.25	96.1 ± 0.30

Table 7: Percentage Drug release of FH 15 during stability study.

Time in Days	Average % drug release at 12 hr, Mean ± SD (*n*=3)		
	25°C/60% RH	30°C/65% RH	40°C/75% RH
0	96.03 ± 1.05	96.03 ± 1.05	96.03 ± 1.05
30	96.00 ± 0.05	95.88 ± 0.09	95.76 ± 0.21
60	95.75 ± 0.22	95.70 ± 0.12	95.62 ± 0.28
90	95.69 ± 0.29	95.64 ± 0.48	95.60 ± 0.27

of pores on both pH 1.2 and pH 7.4 buffer, but the pores were found more in hydrogels swelled in pH 7.4 buffer. In the stability study, the formulation FH15 showed very negligible changes in percentage drug content and in percentage drug release profile for periods of 90 days. Based on the various characterizations and the *in vitro* dissolution profile, it was concluded that Rosiglitazone could be formulated as a hydrogel and administered in the form of the capsule through the oral route and as a controlled drug delivery system.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AAc: Acrylic acid; **PVP:** Polyvinylpyrrolidone; **MBA:** N,N/-methylene bisacrylamide; **PPS:** Potassium persulphate; **cm:** Centimeter; **°C:** Degree Centigrade; **DSC:** Differential Scanning Calorimetry; **FT-IR:** Fourier Transform Infrared; **GIT:** Gastro Intestinal Tract; **λ_{max}:** Lambda Maximum; **µg:** Microgram; **µm:** Micrometer; **mg:** Milligram; **mL:** Milliliter; **nm:** Nanometer; **RH:** Relative Humidity; **rpm:** Rotation per minute; **SEM:** Scanning Electron Microscopy; **SD:** Standard Deviation; **UV:** Ultraviolet; **XRD:** X-ray Diffraction; **N:** Number of trial; **°F:** Fahrenheit; **W/V:** Weight in Volume; **W/W:** Weight in Weight.

SUMMARY

The aim of the present study was to formulate hydrogels of Rosiglitazone using AAc and PVP as a polymer, N, N′ -Methylene bisacrylamide as crosslinking agents and potassium persulphate as an initiator for the polymerization process. Solubility was found to be 0.834 mg/mL in phosphate buffer pH 7.4. The melting point of Rosiglitazone was found to be 120-121°C. The FTIR, DSC and XRD studies reveal that there was no drug-polymer interaction. The crosslinker concentration was varied within the polymer ratio to check the effect of the crosslinker on different polymer ratios. All the hydrogels formulations were evaluated for their *in vitro* evaluation parameters like percentage drug content, percentage swelling, ESR and *in vitro* release studies. From all the prepared formulations, the best formulation was selected considering all the *in vitro* parameters with DSC, XRD and SEM analysis and subjected to long term and accelerated stability studies. Drug content uniformity study showed the drug was uniformly distributed in the formulations. Results of swelling studies indicated that formulated hydrogels swell more in basic media (pH 7.4) than in acidic media (pH 1.2). The stability studies of best formulation FH 15 for 90 days at 25°C with 60% RH, 30°C with 65% RH, and 40°C with 75% RH for percentage drug content and percentage drug release performed every 30 days and results showed insignificant change in drug content and drug release profile. Based on the *in vitro* characterization and various other characterization parameters, it was concluded that Rosiglitazone could be administered in the form of hydrogels. During storage, the drug remained unchanged and stable in the hydrogels, and there was no substantial chemical interaction between the drug and the excipients in the formulation.

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