# Effect of using high molecular weight crosslinker on the physical properties of super porous hydrogel composite

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## Abstract:

Superporous hydrogel composite is widely utilized and investigated as a gastro retentive drug delivery system. Materials used in Superporous hydrogel formulation have a profound effect on its properties', N-methylene bisacrylamide is the crosslinker of choice for the preparation of SPH.

The purpose of this study is to determine if using a new high molecular weight crosslinker such as polyethylene glycol diacrylate will affect the physical characteristics of SPH and drug release behavior. For the preparation of super porous hydrogel polyvinyl alcohol, acrylamide, polyethylene glycol diacrylate 700, N, N-Methylene bisacrylamide, sodium bicarbonate, and tween 20 were used. Trifluoperazine HCl was used as a model drug. The buoyancy, porosity, density, drug release, drug content, swelling ratio, and swelling time were studied and compared. All the physical characteristics and medication release profiles were impacted by changing the formulation parameters. The formula with the best physical qualities had 300 µl of acrylamide (40 percent w/v), 20 mg of polyvinyl alcohol, 200 µl of Tween 20 (v/v), 5 µl of polyethylene glycol diacrylate 700, 45 µl ammonium persulfate, 45 µl TEMED and 50 mg of sodium bicarbonate. Around 80% of the drug was released over the course of 12 hours according to zero order kinetics. By modifying the formulation parameters using polyethylene glycol diacrylate, Superporous hydrogel was successfully manufactured and has the best properties to be employed as a gastro retentive drug delivery system.

**Key words:** Superporous hydrogel composite (SPHC), polyethylene glycol diacrylate 700, high molecular weight crosslinker, polyvinyl alcohol, mechanical strength.

# تأثير استخدام الوزن الجزيئي العالي للروابط المتقاطعة على الخواص الفيزيائية لمركب هيدروجيل فائق المسام

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## الخلاصة:

يتم استخدام مركب هيدروجيل فائق المسام على نطاق واسع والتحقيق فيه كنظام لتوصيل الأدوية المعوية. المواد المستخدمة في تركيبة هيدروجيل فائقة المسام لها تأثير عميق على خصائصها. N، N- ميثيلين بيساكريلاميد هو الاختيار المتشابك لتحضير SPH. الغرض من هذه الدراسة هو تحديد ما إذا كان استخدام رابط متشابك جديد عالي الوزن الجزيئي مثل بولي إيثيلين جليكول دياكريلات سيؤثر على الخصائص الفيزيائية لـ SPH وسلوك إطلاق الدواء.

لتحضير كحول بولي فينيل هيدروجيل فائق المسام ، تم استخدام أكريلاميد ، بولي إيثيلين جلايكول دياكريلات ٧٠٠ ، N، N- ميثيلين بيساكريلاميد ، بيكربونات الصوديوم وتوين ٢٠. تم استخدام Trifluoperazine HCl كدواء نموذجي. تمت دراسة ومقارنة الطفو والمسامية والكثافة وإطلاق الدواء ومحتوى الدواء ونسبة الانتفاخ ووقت الانتفاخ.
تأثرت جميع الخصائص الفيزيائية وملف تعريف إطلاق الدواء من خلال تغيير معايير الصياغة. تحتوي الصيغة التي تتمتع بأفضل الصفات الفيزيائية على ٣٠٠ ميكرولتر من مادة الأكريلاميد (٤٠ بالمائة وزن / حجم)، و ٢٠ مجم من كحول البولي فينيل ، و ٢٠٠ ميكرولتر من توين ٢٠ (حجم / حجم) ، و ٥ ميكرولتر من بولي إيثيلين جليكول دياكريلات ٧٠٠ ، ٤٥ ميكرولتر من بيرسلفات الأمونيوم ، ٤٥ ميكرولتر من TEMED و ٥٠ مجم من بيكربونات الصوديوم. تم إطلاق حوالي ٨٠ ٪ من الدواء على مدار ١٢ ساعة وفقًا لحركية الترتيب الصفري. من خلال تعديل معاملات الصيغة باستخدام ثنائي أكريلات البولي إيثيلين جليكول، تم تصنيع هيدروجيل سوبيربوروس بنجاح وله أفضل الخصائص لاستخدامه كنظام لتوصيل الأدوية المعوية.

**الكلمات المفتاحية:** مركب هيدروجيل فائق المسام(SPHC) ، بولي إيثيلين جلايكول دياكريلات ٧٠٠، رابط متشابك عالي الوزن الجزيئي، كحول بولي فينيل، قوة ميكانيكية

## Introduction

A gastrorotective drug delivery system (GRDDS) is a commonly employed and studied method for oral drug delivery that maintains the medication in the stomach for an extended period of time (1). It is particularly beneficial for medications with a narrow absorption window, those that are highly absorbed by the stomach, or those intended for local gastric impact (2). The floating system, mucoadhesive system, swellable, magnetic system, high-density sinking system, expandable, unfoldable system, and super porous hydrogel (SPH) are some of the various GRDDS that are being investigated, with SPH being of particular interest (3,4).

SPH is a three-dimensional hydrophilic non-soluble polymeric network that rapidly absorbs enormous quantities of water and expands to one hundred times their initial weight without dissolving(5). In addition to their biocompatibility, stability in the acidic environment of the stomach, and mechanical strength, their large size and buoyancy allow them to be employed as GRDDS. Either synthetic polymers, such as polyacrylamide, poly (acrylic acid), polyvinyl alcohol (PVA), and polyvinyl pyrrolidone (PVP), or natural polymers are exploited extensively (such as chitosan, carboxymethyl cellulose, gelatin, and alginate). One of the types of SPH is SPH composite (6,7). SPHC need to have specific physical requirements to be used as GRDDS. High mechanical strength, short floatation lag time, long flotation time, higher swelling ratio with low density are among the most important criteria to be available. These criteria are highly affected by the type and amount of polymers, and crosslinkers used, as well as the formulation conditions. For example, long floatation lag time or long time to swell will help to eliminate the dosage form quickly from the stomach without sustained effect. On the other hand, low mechanical strength will cause a deformation and rupture of the hydrogel due to peristaltic movement of the stomach and uncontrolled drug release will be achieved (8,9).

**N, N-methylene bisacrylamide (MBA)** is a small molecular weight molecule (MWt. 154.17 Dalton) crosslinker with two acrylate groups for crosslinking function. It is the crosslinker of choice for the preparation of SPHC and used for the preparation of different types of hydrogels. Polyethylene glycol diacrylate 700 (PEGDA) is high molecular weight crosslinker (MWt 700) with high water absorption capacity due to the long chain of PEG in its structure. It is widely used for the synthesis of hydrogel contact lenses and hydrogels for different applications.

Using crosslinker with high molecular weight such as PEGDA 700 for SPHC formulation may enhance the physical properties of the hydrogel and produce an optimized GRDDS (10).

Triflouperazine HCl (TRFP) will be used as a model drug in this research because it is readily absorbed from GIT with a low dose. It is white to pale yellow, crystalline powder, practically odorless, and has a bitter taste. Melting point is 242°, with decomposition. Freely soluble in water; soluble in alcohol; sparingly soluble in chloroform; insoluble in ether and in benzene. It has a log p of 5.03 (11). It is considered as zwitterion compound with two pKa values, $pKa_1 = 3.9$ and $pKa_2 = 8.1$ , so the solubility is minimum at the range of pH in which the zwitterion is the predominant species (11). The aim of the research is to formulate SPH using PEGDA as crosslinker with TRFP as a model drug and study the effect of changing the type of crosslinker from MBA to PEGDA and formulation variables on the physical characteristics and drug release kinetics. To our knowledge no SPHC was previously prepared using PEGDA 700 as crosslinker.

## Experimental Work Materials

Triflouperazine HCl (TRFP) (AV global corporation-India), N,N-methylene bisacrylamide (MBA) (CDH-India), polyvinyl alcohol (PVA) (Panreac-Spain), acrylamide (CDH-India), tween 20 (Alpha chemical-India), polyethylene glycol diacrylate (PEGDA, ammonium persulphate (APS) (THOMAS BAKER-India), tetramethyl ethylenediamine (TEMED) (HIMEDIA-India), sodium bicarbonate ( HIMEDIA -India )

## Super porous hydrogel composite preparation

Gas blowing technique was used to create TRFP loaded SPHC. Acrylamide (AM) was used as the monomer, high molecular weight poly (ethylene glycol) diacrylate (PEGDA) systems (700 Da) were utilized as the crosslinker, and poly vinyl alcohol (PVA) was used as the composite agent. Tween 20 was used as a foam stabilizing agent, while ammonium persulfate (APS) and tetramethyl ethylenediamine (TEMED) were used as a polymerization initiator combination. As a gas-producing or foaming agent, sodium bicarbonate was utilized. F1MBA was also prepared using N,N-methylene bisacrylamide for comparison. First, the 20 mg of PVA was weighed and placed in a glass test tube (10 ml in volume). Then, stock solutions of AM (40 percent w/v) and APS (20 percent w/v) were produced in distill water, and 300 µl of the AM stock solution was added to the PVA, followed by 200 µl of tween 20 (v/v) and different amounts of PEGDA. At 50°C, the mixture was sonicated for 5 minutes. After sonication, 3 mg of TRFP was weighed and placed in the test tube, followed by 45 µl of the APS (20 percent v/v) stock solution and thorough mixing using a vortex mixer for a few seconds, then 45 µl of TEMED (20 percent v/v) was added. Immediately followed by the addition of APS 50 mg(w/w) of sodium bicarbonate was added, and the final formulation was allowed to stand for 15 min to complete the polymerization process. The SPHC was then withdrawn from the test tube using forceps and allowed to air-dry for 72 hours at room temperature (12).

The quantities in µl of crosslinker for each formulation are shown in Table 1.

**Table (1): The composition for the formulation of SPHC**

| Formula Component | F1 | F2 | F3 | F4 | F5 | F6 | F MBA |
|---|---|---|---|---|---|---|---|
| AM 40% (µl) | 300 | 300 | 300 | 300 | 300 | 300 | 300 |
| PVA (mg) | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| Tween 20(µl) | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| PEGDA 700 (µl) | 4 | 5 | 8 | 12 | 15 | 20 | --- |
| N,N-MethyleneBisAacrylamide(MBA) 1% (µl) | -- | -- | -- | -- | -- | -- | 40 |
| TRFP (mg) | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| APS 20% (µl) | 45 | 45 | 45 | 45 | 45 | 45 | 45 |

## Characterization of the prepared SPHC

### Porosity and density measurement

Density was measured using a solvent displacement technique. After weighing a dry sample of SPH ($W_{SPH}$), it was submerged in a predetermined volume of n-hexane in a graduated cylinder. The rise in the volume of n-hexane was utilized to compute the volume of SPHC ($V_{SPH}$). Equation 1 was used to calculate density (13) .

$$\text{Density} = W_{SPH} / V_{SPH} \quad .. (1)$$

To assess porosity, dry hydrogel was weighed (M1) and soaked in 25ml ethanol for 24 hours. The hydrogel was then extracted from the ethanol and excess fluid was blotted and weighed using filter paper and the weight was recorded as (M2). The porosity was calculated using equation 2: (13)

$$\text{Porosity} = (M_2 - M_1) / P\ V_{SPH} \ldots (2)$$

Where P = density of ethanol.

### Floating study

The dried hydrogel for each formula was placed in a beaker containing 100 ml of 0.1N HCl. The time it took for SPHC to float was referred to as the floating lag time, while the time it took for SPHC to remain buoyant was referred to as the total floating time (14) .

### Swelling ratio measurement

The swelling ratio was determined using the gravimetric technique (Qs). The dry SPHC was weighed ($W_d$), added to the swelling medium (0.1N Hcl), removed after a predetermined time, blotted with filter paper to remove excess fluid, and weighed again (Ws). The Qs was determined using equation 3 (15) :

$$Q_s = [(W_s - W_d) / W_d] *100 \ldots (3)$$

The period at which the swelling ratio remained constant and the weight of the hydrogel remained constant was regarded as the time at which the hydrogel attained its maximum volume (15).

### Mechanical strength study

The SPHC's mechanical strength was measured by adding weight to a swollen sample using (crush tester). The gram (gm) weight required to fracture the SPHC was reported as the mechanical strength (16) .

### Drug content determination

For each formulation, a sample of dry SPHC containing TRFP was added to 100 ml of 0.1N HCl (pH 1.2) in a volumetric flask and stirred with a magnetic stirrer for 24 hours. After measuring the absorbance with a UV spectrophotometer at the correct lambda max, the amount of TRFP in the tested formulation was then determined ($\lambda_{max}$= 255) (15,17) .

### In-vitro drug release

During the *in-vitro* drug release test for SPHC, the dissolution device (USP type II) was utilized in 900 ml of 0.1N HCl at 100 rpm paddle speed for 12 hours at 37.5°C.

At predefined intervals, a 5 ml sample of the dissolution medium was removed and replaced with an equivalent volume of new medium solution. A UV spectrophotometer (Shimadzu, Japan) was utilized to measure the absorbance of each sample, and the percentage of drug release was computed (14).

**Drug release kinetics**

Zero order, first order, Higuchi, and Korsmeyer-Peppa plots were used to model the kinetics of drug release from SPHC. The *in vitro* release data were fitted into the equations in Table (2) for each model. After examining each formula's R2 regression coefficient, the release kinetic model with the highest $R^2$ value was chosen (18).

**Table (2): Mathematical model equations**

| Mathematical model | Equation | Interpretation of symbols |
|---|---|---|
| Zero Order model | $M_t = M_0 + K_0 t$ | $M_t$ = the amount of drug dissolved in time t.<br>$M_0$ = the initial amount of drug in solution which is often zero.<br>$K_0$ = the zero-order release constant. |
| First Order model | $\text{Log } M_t = \log M_0 - K_1 t/2.303$ | $M_t$ = the amount of drug released in time t.<br>$M_0$ = the initial amount of drug in the dosage form<br>$K_1$ = the first order release constant. |
| Higuchi Model | $M_t = K_H (t)^{0.5}$ | $M_t$ amount of drug release at time t,<br>$K_H$ = the Higuchi diffusion constant |
| Korsmeyer-Peppas Model | $q = M_t / M_\infty = k_{KP} . t^n$ | $q = M_t/M_\infty$ is the fraction of drug released at time t<br>$k_{KP}$ is the release rate constant,<br>n is the diffusion exponent, which indicates the type of drug transport mechanism through the polymer |

The type of drug release mechanism was determined using the Korsmeyer-Peppas model's diffusion exponent value (n). Fickian diffusion occurs if (n) is less than 0.5, anomalous (non-Fickian) diffusion if (n) is between 0.5 and 1, Case-II transport (erosion) if (n) equals 1, and Super case-II transport if (n) is greater than 1.

**Fourier transform infrared spectroscopy**

Fourier transform Infrared spectroscopy FTIR was utilized to assess the probability of chemical bond formation between the medication and the constituents of the formula during polymerization. Examining the pure drug, the formula without the drug, and the formula with the drug. Using Bruker FTIR (Shimadzu, Japan) and Attenuated Total Reflectance (ATR) technology, the samples were examined. Utilizing FTIR spectral scanning between 400 cm-1 and 4000 cm-1 (19–22) .

**Scanning electron microscopy (SEM)**

The SEM investigation was conducted using a scanning electron microscope (SEM Tescan vega lll czech). Prior to study, the SPHC sample was adhered to an aluminum stub with double-sided adhesive tape and rendered electrically conductive with a thin layer of gold (about 20 nm) deposited under vacuum. The surface of the sample was

scanned with an electron beam of high intensity, typically between 0.5 kV and 40 kV, to form a picture in a raster scan pattern. SEM generates high-resolution images of sample surface properties (23).

**Statistical analysis**

The 2018 version of the Statistical Analysis System- SAS application was used to determine the effect of various factors on study parameters. In this study, a T-test or Least Significant Difference –LSD test (Analysis of Variation-ANOVA) was performed to compare means significantly.
In this study, the outcomes were provided as mean ±SD of three values for each experiment (19) .
Significant 0.05 (P≤0.05).

## Results and Discussion

**Appearance of SPHC prepared**

Free radical polymerization was the method used for the hydrogel synthesis. Formulation using PEGDA were successfully prepared and had similar appearance as formula using MBA. All formulations were evaluated and the results can be seen in Table 3 and will be discussed below.

**Effect of crosslinker type on the properties of the SPH**

As previously mentioned, MBA is typically used as crosslinker and F1MBA was prepared and compared with F1 which was prepared with PEGDA and the results are demonstrated in table 3. As noticed, when using PEGDA mechanical strength and density were significantly ($p \leq 0.05$) increased in F1 compared with F1MBA which is probably due to the large molecular weight and polymeric nature of the molecule. Also floating lag time and swelling ratio were significantly ($p \leq 0.05$) higher because PEGDA is water loving molecule and has the tendency to absorb large amount of water through hydrogen bonding (24). Floatation lag time was significantly ($p \leq 0.05$) lower in F1 compared to F1MBA formula. The long chains of PEGDA will provide larger spaces within the polymeric matrix which will allow water to diffuse quickly and easily into the hydrogel providing a shorter floating lag time. Similar results were reported by Kaşgöz et al when compared the use of MBA and PEGDA 400 for the preparation of acrylamide-maleic acid hydrogels. They reported that when PEGDA 400 was used the swelling rate, gel capacity and diffusion coefficient of the hydrogels prepared were improved (25).

**Table (3): Physical characterization results of the prepared SPHC.**

| Formula no. | Density g/cm$^3$ | Swelling Time (hr.) | Swelling Ratio | Porosity | Mechanical Strength (g) | Floating lag time (min.) | Floating Time (hr.) | Drug Content (%) |
|---|---|---|---|---|---|---|---|---|
| F1 | 0.93± 0.015 | 11 | 3.8±0.21 | 0.33± 0.025 | 558±2.8 | 12±1 | 24 | 103.1% |
| F1MBA | 0.844± 0.005 | 8 | 2.1±0.13 | 0.37± 0.058 | 443±3.5 | 28±1.7 | 24 | 96% |
| F2 | 0.93± 0.015 | 10 | 4.3±0.31 | 0.31± 0.015 | 575±5 | 13±1 | 24 | 101.5% |
| F3 | 0.94± 0.015 | 8 | 3.4±0.83 | 0.29± 0.05 | 610±4.04 | 15±0 | 24 | 96.8% |
| F4 | 0.98± 0.01 | 8 | 3.1±0.46 | 0.26± 0.01 | 764±5 | 15±0 | 24 | 95.2% |
| F5 | 1.05± | 7 | 3.1±0.51 | 0.23± | 756±7.3 | 27±2.5 | 24 | 83.8% |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0.008 | | | 0.025 | | | | |
| F6 | 1.02± 0.09 | 7 | 3.1±0.08 | 0.15± 0.025 | 760±3.77 | 27±2.5 | 24 | 84.6% |

As noticed in figure 1 the release of the drug from F1 was significantly slower ($p \leq 0.05$) compared to F1MBA. The retard in release probably due to the higher mechanical strength and lower porosity of F1 compared to the formula F1MBA which was more porous and weaker than F1 which enable the acidic media diffuse faster and let the drug release within shorter time (16). Similar results were observed when vildagliptin was prepared as SPHC. they noticed that with reducing porosities of the hydrogels prepared the release of the drug was delayed due to less opening in the polymeric matrix of the hydrogel (26). Using PEGDA as crosslinker revealed optimized properties compared to MBA.

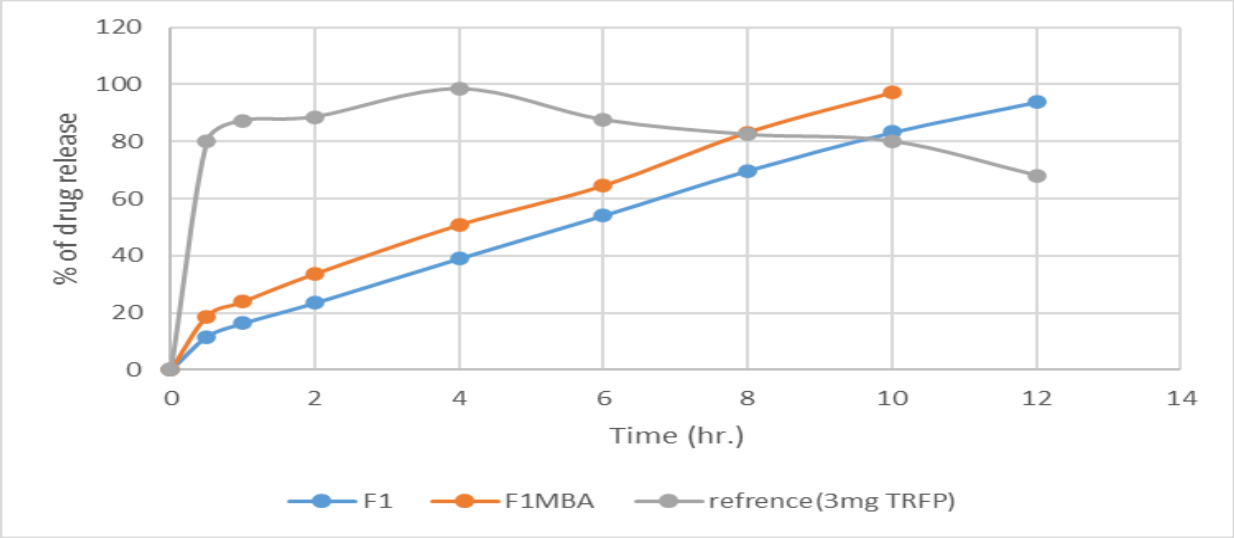


**Figure (1): Effect of different type of cross linker (MBA 1%) on the release profile of model drug for formulas F1MBA with F1 that contain (PEGDA) as crosslinker**

**Effect of changing crosslinker percentage on the properties of SPH**

Since PEGDA was successfully used as crosslinker, the effect of increasing the concentration of crosslinker was studied and the results are presented in table 3 and figure 2. Results showed that the increase in crosslinker amount led to significant ($p \leq 0.05$) increase in mechanical strength with a significant decrease in porosity ($p \leq 0.05$) because of diminishing of network space (pores) and stronger bonds are formed between the monomers and crosslinker which reduces the size and number of interconnecting pores in the hydrogel matrix. Also, at higher amount of PEGDA the cross linking density increases and the networks of the polymers become more rigid, and the two polymer chains will attach more strongly to each other (27). The diminishing of network space (pores) observed with higher crosslinker percentage allows less water to enter the hydrogel thus significantly ($p \leq 0.05$) prolonging floating lag time.

It was noticed that swelling ratio increased significantly from ($p \leq 0.05$) F1 to F2 then reduced and remain constant in F3-F6 in spite of increasing PEGDA concentration. A possible explanation is that the stretching of the polymer matrix reached maximum value and with increasing density the free volume that can be occupied by water molecules was reduced.

Similar results were reported with increasing crosslinker concentration of baclofen SPHC. when crosslinker amount increased from 1% to 2.5% the swelling ratio increased from 18.4-37.5 while increasing the percentage to 3.5% reduced the swelling ratio to 33.3 (28).
The results obtained is consistent with previously reported data by Kumar et al. They reported that increase MBA concentration in metformin SPHC from 1% to 2.5% (w/v) resulted in an increase in swelling ratio and mechanical strength (29).

The percent of drug release for all formulas was significantly ($p \leq 0.05$) decreased when the crosslinker amount increased. Crosslinker obstructs drug dissolution and diffusion of dissolution media by increasing mechanical strength and reducing porosity of the interconnected chains of the SPHC (16). Similar results were previously observed when SPHC of vildagliptin was prepared. The release of the drug was reduced with increasing crosslinker percentage (26).

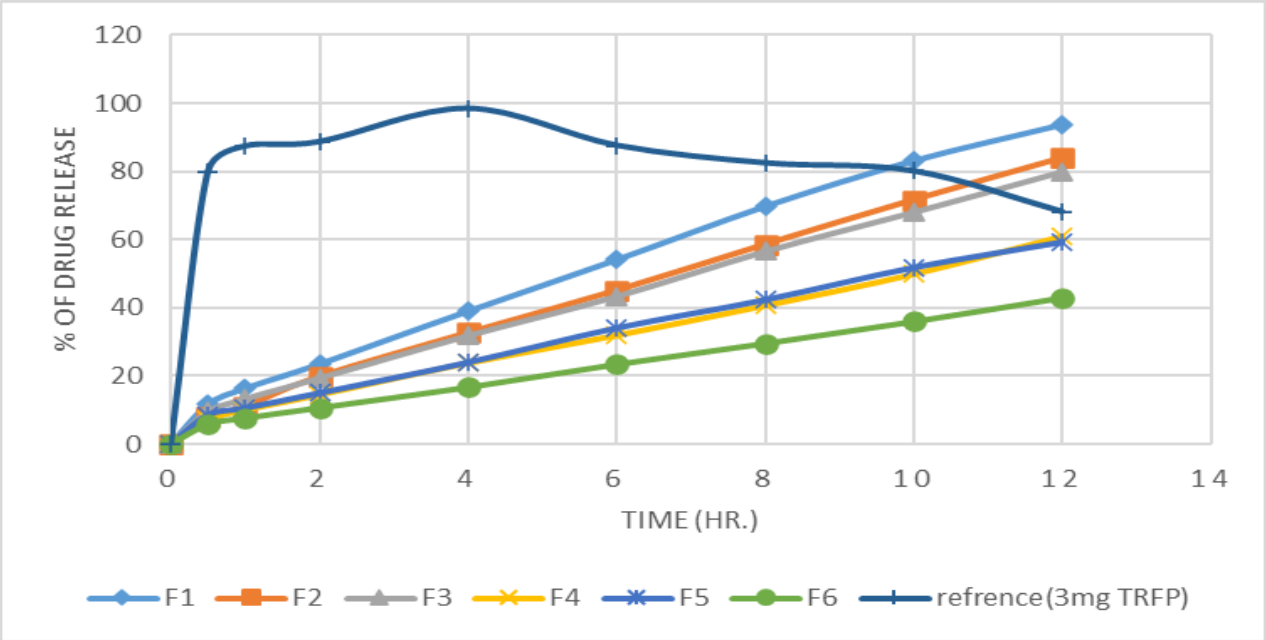


**Figure (2): Effect Of different amount Of Cross Linker (PEGDA) On The Release Profile Of model Drug For Formulas F1-F6**

**Mathematical model of drug release**

All formulations, with the exception of F5 and F1MBA, followed zero order kinetics, as seen in table 4 which means that a constant amount of the drug is released with time regardless of the amount of drug left in the hydrogel. Formula using MBA (F1MBA) followed Higuchi kinetics which means the drug release followed Fickian diffusion while F5 followed first order kinetics which means the release of the drug is dependent on the concentration of the drug remain in the dosage form.

**Table (4): mathematical models correlation coefficient values**

| Formulas | Zero order | | First order | | Higuchi | | Korsmeyer-peppas | | |
|---|---|---|---|---|---|---|---|---|---|
| | $K_0(hr^{-1})$ | $R^2$ | $K_1(hr^{-1})$ | $R^2$ | $K_H (hr.)^{1/2}$ | $R^2$ | $K_{KP} (hr.)^{-n}$ | $R^2$ | n |
| **F1** | 7.5799 | 0.9909 | 0.209 | 0.92 | 0.5466 | 0.9737 | 29.23 | 0.9904 | 1.4659 |
| **F2** | 6.7678 | 0.9963 | 0.140 | 0.9531 | 0.5432 | 0.9728 | 20.51 | 0.9948 | 1.312 |
| **F3** | 6.3308 | 0.994 | 0.122 | 0.9628 | 0.5028 | 0.9809 | 28.44 | 0.9892 | 1.454 |
| **F4** | 4.7165 | 0.9935 | 0.070 | 0.9776 | 0.4332 | 0.9844 | 29.08 | 0.9882 | 1.4637 |
| **F5** | 4.6766 | 0.9909 | 0.069 | 0.9918 | 0.4201 | 0.9828 | 34.96 | 0.9789 | 1.5436 |
| **F6** | 3.3248 | 0.9923 | 0.042 | 0.9933 | 0.3555 | 0.9874 | 34.59 | 0.9808 | 1.539 |
| **F1MBA** | 8.8698 | 0.9748 | 0.301 | 0.859 | 0.573 | 0.9811 | 59.84 | 0.9857 | 1.777 |

**Selection and further examination of the optimum formula with FTIR**

For a SPHC to work as an ideal GRDDS the gel should quickly swell to a large size and float for a long period in the stomach. Also, it should have a mechanical strength to withstand the peristaltic movement of the stomach and slow the release of the drug for a once daily application (30). A balance between physical properties is required for optimum GRDDS. Based on the above criteria physical properties of all formulations were compared, and F2 was determined to be the best formulation due to its low floating lag time (13 min), time to reach maximum swelling (10 hr.), high swelling ratio (4.3), mechanical strength of 575 g, and 80 percent of the drug release within 12 hours follow zero order release profile. Similar pattern was used to choose optimum formulation when carvedilol SPH was prepared (12).

Since the drug was present during the polymerization process, it was important to determine whether the drug was impacted by the process. To do this, Bruker FTIR (Shimadzu, Japan) using Attenuated Total Reflectance (ATR) technology was employed. We looked at the FTIR spectra of the pure drug, PVA, PEGDA, Acrylamide, the drug-containing formula, and the drug-free formula. Figure 3 illustrates how the drug's peaks may be seen in the SPHC spectrum, proving that the drug and the polymers don't have any chemical incompatibilities (14).

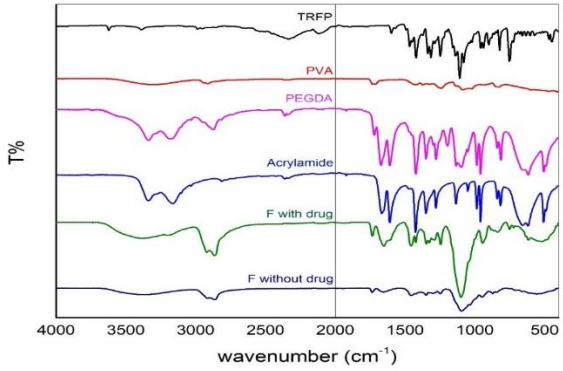


**Figure (3): ATR-FTIR of (a)TRFP (b)PVA (c)PEGDA (d)Acrylamide (e)formula with drug (f) formula without drug**

**Scanning electron microscopy (SEM)**

Pore size and shape of the prepared hydrogels were examined for F1 using SEM at different magnification and the results can be seen in Figure 4. The images confirmed the presence of pores in the hydrogel structure.

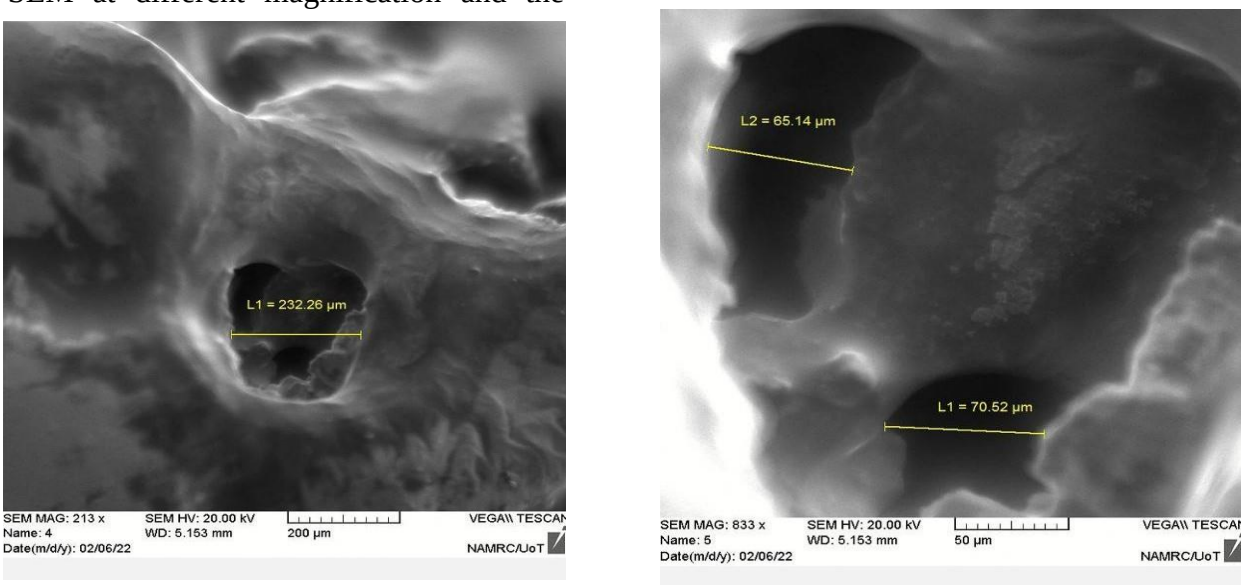


**Figure 4: Scanning electron microscopy (SEM) for F1 at different magnification powers**

## Conclusions

PEGDA was successfully used as crosslinker for the preparation of SPHC and hydrogels prepared had optimized properties compared to hydrogel prepared using MBA. When increasing the amount of PEGDA the physical parameters, such as swelling ratio, floating lag time, density, and floating duration, were affected. Formula 2 containing 300 µl of AM (40 percent w/v), 20 mg PVA, 200 µl of Tween 20 (v/v), 5 µl PEGDA v/v, 3 mg (w/w) of TRFP, 45 µl of APS (20 percent w/v), 45 µl of TEMED (20 percent v/v), and 50 mg of sodium bicarbonate was selected as the optimal formulation due to its optimal physical properties and sustained drug release through zero order kinetics. Using PEGDA provides an opportunity to enhance the properties of SHP as GRDDS.

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