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Research Article

Synthesis and characterization of porous *co*-polymeric hydrogels of 2-hydroxyethyl methacrylate and N-vinylpyrrolidone via high internal phase emulsion

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ABSTRACT

Polymerized High Internal Phase Emulsion (Poly HIPEs) have attracted considerable attention in many fields focused on biomaterial applications. Porous hydrogel with controlled morphology was successfully prepared by *co*-polymerization of 2-hydroxyethyl methacrylate (HEMA) and N-vinylpyrrolidone (NVP) in the presence of N, N-methylene bisacrylamide (MBA as cross-linker) in high internal phase emulsions (HIPEs). The *co*-polymerization was based on the free-radical polymerization method by employing two immiscible liquids in the poly HIPE method. The void and window sizes in the poly (HEMA-*co*-NVP) were tailored by adjusting surfactant, cross linker and initiator concentration. The characterization of the poly HIPE-based *co*-polymer was done by Fourier transforms infrared spectroscopy (FT-IR), scanning electron microscopy (SEM), and thermogravimetric analysis (TGA). The highest water absorption value of synthetic porous hydrogel synthesized in the HIPEs method was 8.9 g/g with average pores size of 2-5 µm, while its synthetic hydrogel with the same values of reactants and without HIPEs method was 1.2 g/g. These results show that the poly HIPE-based polymerization of *co*-polymers can be intended to raise their water uptake.

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1. Introduction

Highly interconnected porous materials can be produced by high internal phase emulsions (HIPEs) [1]. HIPEs are highly viscous and paste-like emulsions [2], which contain very concentrated dispersed systems [3]. In general, HIPEs have two distinct phases: the major, dispersed phase is usually referred to as the internal phase, and the minor, continuous phase is stated as the external phase [2-6]. The dispersed (internal) phase occupies more than 74 % of the total volume fraction [4]. By polymerization of monomers in the external phase, polymeric materials with a high degree of porosity and interconnectivity between pores could be achieved [7]. The final porosity in resulting polymers can be in the range of 70 to 90%, and the total pore volume rises to 10 cm^3/g [2]. As the morphology of these materials is highly porous and interconnected, [8] synthesis of these porous polymers (poly HIPEs) obtains a great deal of interest. In this regard, they can find suitable applications in catalyst, electrodes, filtration systems, ion exchange resins, and scaffold for tissue engineering [9-15]. Since these porous structures with their low bulk densities can quickly absorb large volumes of liquids through capillary action. Recent works on poly HIPEs with tunable and narrow void size distributions have led to the development of theoretical models for describing the relationships between the void size and the mechanical behavior [16]. However, the chemical and process versatility of poly HIPE systems leads to increasing the use of them as templates for permeable materials with tailorable properties and structures [20-26]. Two from of o/w and w/o HIPEs are used for the synthesis of poly HIPES in emulsion scaffolds. The instability of oil in water frameworks leads to less study on the preparation of hydrophilic poly HIPEs in contrast to that of hydrophobic systems [17]. Hydrophilic poly HIPEs can be produced by hydrophilic monomers. These monomers such as acrylamide [18], acrylic acid [19], HEMA [20], and N-isopropyl acrylamide [21] have been seen more in articles among others. Poly HEMA is a non-toxic hydrophilic polymer that is characteristic of very good biocompatibility and is spready used in biomedical fields for applications such as drug delivery, implants, and contact lenses [22-26]. In recent years, many new poly HIPE systems have been developed, which include non-aqueous emulsions such as oil-in-oil (o/o), oil-in-water (o/w), supercritical CO_2 in-water and ionic liquid-in-oil [27-29]. HIPE stabilization is essential for poly HIPE syntheses, which is achieved by HIPE stabilizers, which are often surfactants. Stabilizers could also be amphiphilic particles and gels. The improvement of HIPE stabilizing techniques has recently acquired much consideration for manipulating HIPE properties to change the porosity designs of HIPE. The porosity structures of Poly HIPEs include factors like the void size, void interconnectivity, hole geometry (polyhedral or spherical), and the size of the interconnecting hole. How the gaps or spaces between porous structures are linked can greatly affect how those objects are utilized, applied, or the characteristics of the resulting Poly HIPE.

Poly HIPEs can be arranged into open-cell structures and closed-cell structures according to the void interconnectivity. Closed-cell Poly HIPEs are utilized in applications where encapsulating is needed [30, 31], however, open-cell poly HIPEs are utilized in various applications including the ability to adsorb substance [9], controlled release [32-35], tissue engineering [36], and reaction supports [37]. Precise control of interconnection between holes for many applications can be accomplished through adjustment techniques, the nature of monomers, and internal phase content. HEMA is a biocompatible monomer commonly used in biomedical applications. Poly HIPE hydrogels synthesized with HEMA are often well-tolerated by the body, making them suitable for applications such as tissue engineering and drug delivery. It is our interest to report the synthesis of PHEMA/NVP hydrogel in HIPE method to make the best use of the beneficial properties of monomers, in biological application due to their higher water absorbency, porosity and mechanical strength of Poly HIPE NVP mixed with HEMA hydrogels.

In this work, the preparation of a cross-linked *co*-polymeric hydrogel based on HEMA and NVP monomers via a poly HIPE template (poly (HEMA-*co*-NVP)) is described. The preparation procedure was optimized by changing key factors such as the concentration of surfactant, monomers, and cross-linker in the stable ratio of volume fraction between the oil and aqua phase. The optimization value for each factor was based on the maximum water absorption which is an indirect indication of total porosity and size of pores.

2. Experimental sections

2.1 Materials

The following reagents were used for poly HIPE production: cyclohexane (99.5%, Merck), 2-hydroxyethyl methacrylate (HEMA, 97%, Aldrich), N-vinylpyrrolidone (NVP), *N*, *N'*-methylenebisacrylamide (MBA, 99%, Sigma-Aldrich), ammonium persulfate (APS, 98%, Sigma-Aldrich), *N*, *N*, *N'*, *N'*-tetramethylethylenediamine (TEMED, 99%, Merck), Triton X-100 (Sigma Aldrich), ethanol (99.5%, Merck), and distillate water. All materials were used as received.

2.2 Apparatus

2.2.1 Scanning electron microscopy

The porous morphologies of poly HIPE products were characterized by field emission scanning electron microscopy (FE-SEM), model MIRA3 TESCAN Company.

2.2.2 FT-IR

The conformation of porous monolith poly HIPE-based *co*-polymeric hydrogel (poly (HEMA-*co*-NVP)) was analyzed by Fourier transform infrared (FT-IR) spectrophotometry, which was determined by a Shimadzu IR Prestige-21 spectrometer in the wavelength number region of 400-4000 cm^{-1} using KBr pellets under hydraulic pressure of 750 kg/cm^{2}.

2.2.3 TGA

The thermal gravimetric analysis (TGD_9800, Japan) was used for the determination of the thermostability of poly HIPEs-based polymers.

2.3 Methods

2.3.1 Poly HIPE-based co-polymeric hydrogel synthesis

The monolithic materials were produced by the radical polymerization of O/W emulsions characterized by a large volume of internal phases. In a typical procedure, NVP (0.165 g -1.48 mmol) was dissolved in 2.6 mL distilled water to be completely resolved then HEMA (1.172 mL), MBA (0.04, 0.091, 0.126, 0.151 g - 0.259, 0.59, 0.81, 0.97 mmol) and APS (0.007, 0.015, 0.03, 0.06 g – 0.03, 0.06, 0.131, 0.26 mmol) as monomer, cross-linker and initiator respectively were added to the NVP solution. The mixture was stirred with a magnetic stirrer (Heidolph, Germany) at a speed of 400 rpm for 20 min to reach a clear solution. Triton X100 (0.7, 0.37, 1.1 mL) as surfactant was added slowly to the mixture with an increased speed of stirrer to 600 rpm to give a homogenized solution. 11 mL of cyclohexane (oil or internal phase) was added drop by drop to the mixture in consistent mixing speed at 400 rpm to form stable HIPEs. After the completion of the addition process, the stirring was continued for 20 min to get a homogenous concentrated emulsion. Subsequently, 200 µl of TMED was added into the emulsion with stirring speed of 600 rpm for 40 seconds and the resulting stable concentrated emulsion was transferred into a small tube and sealed. The tube was immersed in a 50 °C water bath and kept for 24 h to form a hydrogel product. The remaining initiator, emulsifier, and stabilizer were removed by Soxhlet extraction in distilled water and then ethanol over two successive nights. The poly HIPE was dried in a vacuum oven at 50 °C for 24 h (38-40).

2.3.2 Bulk synthesis

Using the values of sample C in Table 1, which demonstrated the highest water absorption, a bulk hydrogel polymer was prepared without using the HIPE method (without adding a dispersed phase and a surfactant). The resulting bulk polymer (hydrogel) was heated in a convection oven over 50 °C for 24 hours. The monolith was washed with distilled water and ethanol to remove unreacted reagents and then dried in a convection oven at 50 °C over a night.

Table 1. Composition of the aqueous and organic phase of emulsion with high internal phase and water absorption results (Ws x100).

Sample	Water phase						Oil phase	Ws(X100)
	NVP(g)	HEMA(mL)	MBA(g)	APS(g)	Triton X100(mL)	Water(mL)	Cyclohexane(mL)	
A	0.165	1.172	0.041	0.031	0.7	2.6	11.3	450 ±05
B	0.165	1.172	0.091	0.031	0.7	2.6	11.3	600 ±08
C	0.165	1.172	0.126	0.031	0.7	2.6	11.3	890 ±15
D	0.165	1.172	0.151	0.031	0.7	2.6	11.3	710 ±09
E	0.165	1.172	0.126	0.061	0.7	2.6	11.3	407 ±04
F	0.165	1.172	0.126	0.016	0.7	2.6	11.3	300 ±02
G	0.165	1.172	0.126	0.007	0.7	2.6	11.3	_
H	0.165	1.172	0.126	0.031	0.4	2.6	11.3	370 ±05
I	0.165	1.172	0.126	0.031	1.1	2.6	11.3	410 ±04

2.4 Water Uptake Studies

The poly HIPE samples were washed and dried then they were broken into pieces of approximately the same sizes. To every sample (around 30 mg), 5 mL of distilled water was added to the closed container and kept at room temperature. Excess water was removed with filter paper before the weight of the samples was recorded after 1 h, 2h, and 24 h. Triplicate analysis was done in all samples. The error rate was small and about one and a half percent. The water uptake percentage (WU) was calculated as follows based on W_s (swelled weight) and W_d (dried weight)

$$W_S \ (x100) = ((W_s - W_d)/W_d) \ x100$$

3. Result and discussion

Co-polymerization and crosslinking of HEMA and NVP substrates were done in an emulsion medium, using APS as a free radical initiator, TEMED as a *co*-initiator, and MBA as a crosslinking agent. The proposed route for this *co*-polymerization process is illustrated in **Fig. 1**. The oxidation reaction produced sulfate anion radicals from APS, and then they attack the unsaturated bond of HEMA or NVP monomers to initiate the co-polymerization process. As a result of being a cross-linking agent in the reaction mixture, a three-dimensional network result.

3.1 Characterization of Poly HIPE-based co-polymeric hydrogel

3.1.1 The FT-IR spectra

FT-IR spectrum of (HEMA) is shown in **Fig. 2**. There are 3250 cm^{-1} (OH stretch), 2960 cm^{-1} (CH alkyl stretch), 1719 cm^{-1} (C=O stretch), and 1171 cm^{-1} (C-O stretch) bands related to different functionality of HEMA. The spectrum of the NVP shows characteristic peaks at 3396 cm^{-1} (OH stretch), 2970 cm^{-1} (CH alkyl stretch), 1706 cm^{-1} (C=O stretch) 1629 (N-H bending), and 1423 cm^{-1} (C-N stretching) bands. Also, the FT-IR spectra of poly HIPE-based poly (HEMA-*co*-NVP) show characteristic peaks at 3385 cm^{-1} (O–H stretching), 2942 cm^{-1} (aliphatic stretches), 1658 cm^{-1}1 and 1724 cm^{-1} (C=O stretching of NVP and HEMA), respectively. These peaks indicate the formation of the copolymer. Compared to the IR spectrum of

HEMA, poly (HEMA-*co*-NVP) showed a new peak at around 1665 cm^{-1}, corresponding to the carbonyl stretching banding of NVP [38]. As reported before, with increasing NVP content [39], this characteristic absorption band was strengthened, which further confirmed the presence of NVP in the final structure of resulted in poly HIPE-based copolymer hydrogel.

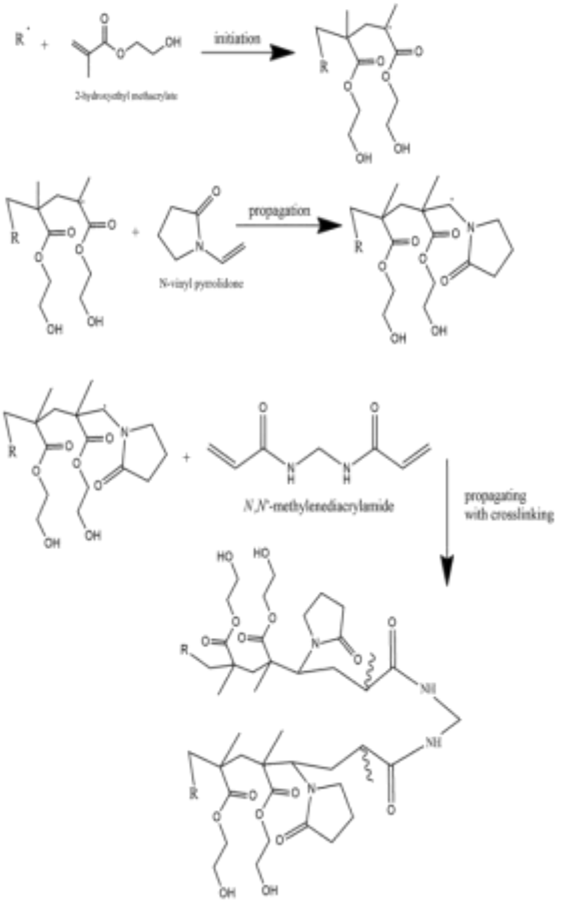

Fig. 1. Synthetic route for preparation of poly (HEMA-*co*-NVP).

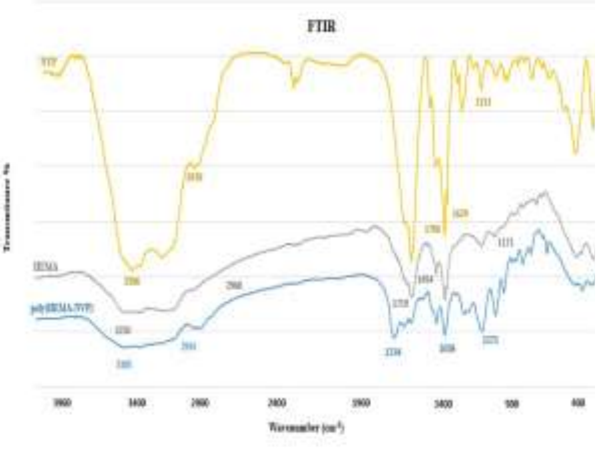

Fig. 2. FT-IR spectra of poly (HEMA-*co*-NVP) hydrogel, HEMA, and NVP.

3.1.2 Scanning electron microscopy images

To evaluate the structure and morphology of optimized poly HIPE-based poly (HEMA-*co*-NVP) hydrogel, it was washed in Soxhlet with ethanol and distilled water for two consecutive nights and then dried in vacuum oven to remove the solvent, then for SEM was used. Arranged samples were placed into an SEM test chamber and shot at various magnification rates. The results show the size and shape of HIPE holes in **Fig. 3. (a, b, c, d).** The presence of holes and roughness of the surface in the synthesized final poly HIPEs show a high porosity in the structure of the resulting sample. The visible large pores (holes) on the porous integrated surface of the optimized poly HIPE samples are caused by the connection of smaller droplets of the dispersed phase to each other and the creation of larger droplets (Ostwald ripening phenomenon). By removing the droplets of the dispersed phase, cavities or pores are created. Windows (holes in the wall structure that surround the holes) are the reason for connecting the holes.

The spongy structure of optimized poly HIPE-based hydrogel is a strong reason for the high-water absorption of this polymer which absorbs around 9 times its weight. The average sizes of pores were about 2–5 µm. Homogeneous interconnected porous channels and mutual network structure are also observed that there is no break in the morphological structure that disturbs its integrity. This situation has also been evaluated by water absorption test.

There is no mass diffusion limitation due to the matrix pore size, which is larger than the size of biological molecules (proteins and drugs), or organic compounds, as a result of this structure, it can easily allow them to pass through.

The SEM images of grafted polymer are in **Fig. 3(e, f, g)**. This polymer is synthesized with optimized figures and only synthesized in the aqua phase.

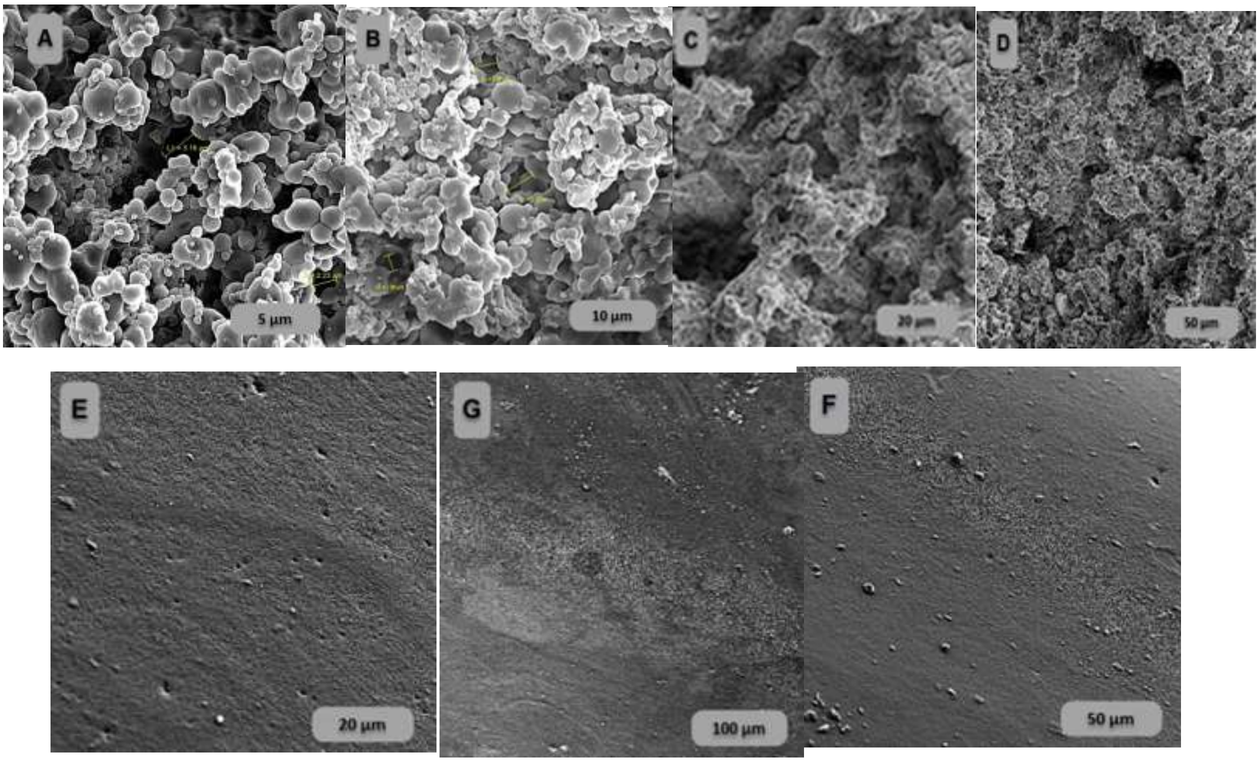

Fig. 3. SEM of optimized Poly HIPE-based hydrogel with porous structures from lower magnification to higher (a, b, c, d) compared to smooth bulk polymer hydrogel structure (e, f, g).

The smooth surface of the polymer showed the low amount of water absorption.

3.1.3 TGA thermograms analyzer

TGA and DTG analysis was accomplished to investigate the thermal stability of poly HIPE-based poly (HEMA-*co*-NVP) hydrogel. Examining the thermogram of poly (HEMA-*co*-NVP) hydrogel in **Fig. 4**, at first, an insignificant weight loss is seen at 150 °C, which is related to the removal of moisture content. Then Followed by three thermal degradations were seen around the temperatures 410, 450, and 580 °C. The main mass loss was the second thermal degradation which is ascribed to decomposition of polymer network. The first degradation started at 410 °C and the mass loss was about 10 %, which it continued with a steep slope to reach nearly 500 °C and all remaining mass was about 55%. In the first two steps, the polymer degradation could be initiated through chain ends having olefin and saturated aliphatic groups, respectively, which leads to evaporation of CO and CO_2 [41]**.** The total remaining weight percent was 36.5% at almost nearly 600 °C, which results in producing of sodium carbonate**.** the lack of pores and interconnected structures (It absorbs almost its weight).

3.2 Optimization of effective factors in water absorbency

3.2.1 The impact of crosslinker concentration

Fig. 5, shows the impact of MBA concentrations on the water absorbency of synthesized poly HIPE. Increasing the mass ratio percent of crosslinkers to monomers leads to a substantial increase in water absorbency. Normally, according to the research water absorption is expected to be decreased with increasing crosslinking ratio [42, 43]. Surprisingly, here, the water absorption is more rapid and more significant with the increasing amount of crosslinker from 0.024 mol/L to 0.075 mol/L to reach the top of 890 %, then it declined with a steep slope to 710 %. This result is inconsistent with the claims of Silverstein [44].

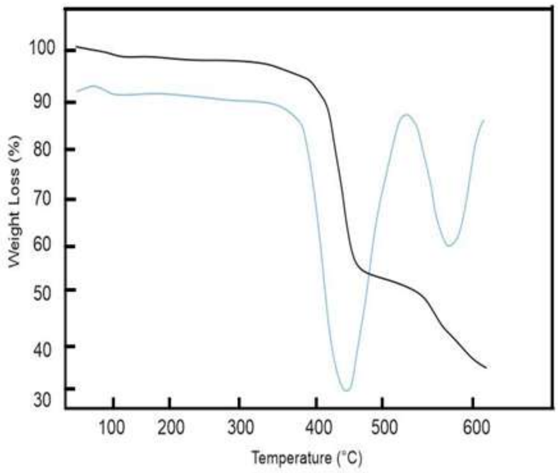

Fig. 4. TGA and DTG thermograms of poly (HEMA-*co*-NVP) hydrogel.

There are two absorption mechanisms in the poly HIPEs, absorption within the interaction with the hydrophilic polymer through hydrophilic monomers in the walls of the HIPE structure and absorption within capillary action through the porous poly HIPE structure. MBA is more hydrophilic than HEMA with two strongly hydrogen-bonding amide groups [43,44]. As a result, the polymer molecule becomes more hydrophilic and has a considerable tendency to absorb water with increasing amounts of MBA. But there is a narrow synthesis window (MBA content), raising the percent of cross-linker from the optimized amount leads to separating, agglomerating, and forming a heterogeneous poly HIPE wall structure. Therefore, the final product is too brittle to determine its absorbency.

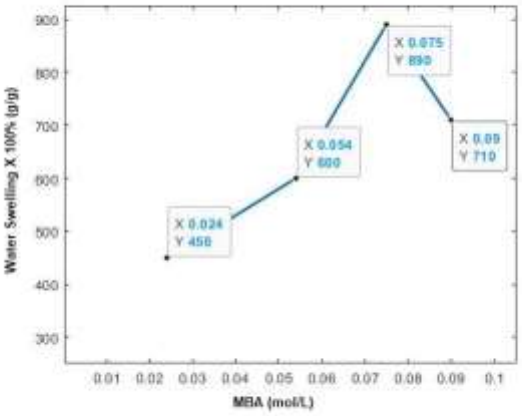

Fig. 5. The impact of cross-linker concentration on water absorbency of the hydrogel.

3.2.2 The impact of initiator concentration

The swelling ratios of the ploy HIPE-based poly (HEMA-*co*-NVP) hydrogel for various initiator concentrations are displayed in **Fig. 6**. As indicated by this figure, with increasing the APS concentration from 0.0025 up to 0.05 mol/L, water absorbency is increased from 300 to 890 g/g and then is decreased substantially to 470 g/g with a further increase in the concentration of initiator from 0.05 to 0.1 mol/L. The increasing initiator concentration, increased polymerization reaction, and consequently higher water absorbency. However, APS concentrations higher than the optimum value (0.05) resulted in low-swelling absorbent. It could be attributed to an increase in terminating step reactions, which, thus, becomes the growth of crosslinking density in reaction. Chen et al. [46] mention this possible phenomenon as ‘‘self-crosslinking.’’ A resulting decline in water absorbency is normal due to crosslinking keeping the network from spreading to its highest degree. Also, a decline in molecular weight (MW) of resulting poly HIPE leads to decreasing swelling value. Therefore, there is an inverse relationship between MW and initiator concentration [16].

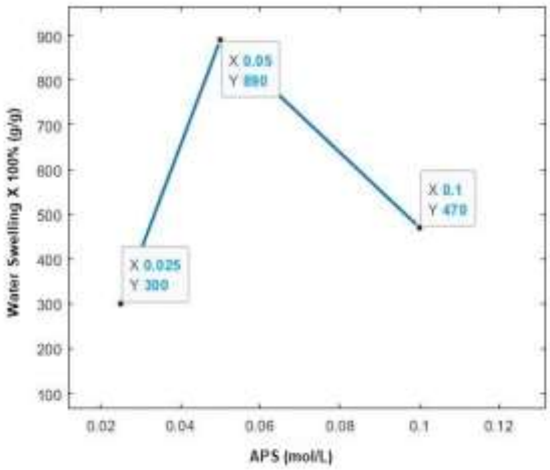

Fig. 6. The impact of initiator concentration on water absorbency of a hydrogel.

3.2.3 The impact of surfactant

In the synthesis of porous structure, the percent of surfactant is necessary to produce a stable emulsion by the end of the polymerization process. If the separation of two immiscible phases happens, in the middle of the polymerization process the resulting poly HIPE is not especially applicable because of limited voids. Early work on poly HIPEs pointed out that a closed-cell structure was manufactured at a surfactant concentration below 5% of the external phase while a highly interconnected open-cell structure was produced at a higher surfactant concentration (more than 7%) [47]. Enhancing the surfactant concentration lessens the droplet size and, thus, lessens the thickness of the envelope of the external phase surrounding the droplets. As the film thickness decreases, the number of voids and interconnecting structures increased. So, has a direct significant effect on increasing absorption value. Here, the lower amount of surfactants leads to an unstable emulsion in the polymerization process and the higher amount produces a viscous emulsion which is hard to process in the mixing stage. Also, a viscous environment impedes polymerization to continue. In Figure 7 the best results were achieved when the triton X100 was 700 µlit (18 % water phase) with increasing the value to 1100 g/g (30% water phase) the water absorption was decreased more than twice to reach 410 g/g **(Fig. 7).**

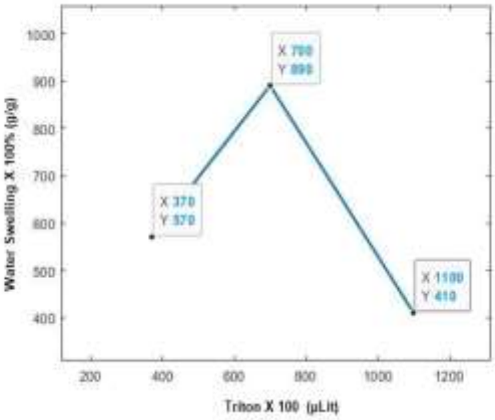

Fig. 7. The impact of surfactant concentration on water absorbency of a hydrogel.

4 Conclusion

In this research, crosslinking, and *co*-polymerization of HEMA and NVP substrates were done in an emulsion medium, through a free radical initiator to obtain the corresponding hydrogel. Poly HEMA is used for its good characteristics like hydrophilic, biocompatibility, availability, inexpensive, biocompatibility, and biodegradability. Different concentrations of initiator, surfactant, and cross-linker were used to prepare the mentioned porous polymer with high water absorption. According to the results, the highest water absorption value of porous hydrogel synthesized in the HIPEs method was 8.9 g/g, while its block polymer with the same reactants values without the HIPEs method was 1.2 g/g. Results showed that changes in cross-linker concentration and surfactant have a greater effect on water absorption, using cross-linker more than the optimal level leads to the instability of the emulsion reaching steward ripening, and finally the resulted poly HIPEs with a very fragile structure is created. As a result, there is a narrow-controlled range for the cross-linker and surfactant concentration in the final optimized polymer.

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