ORIGINAL ARTICLE

Effects of Cross-linker Variation on Swelling Behavior of Hydrogels

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Abstract

Introduction: The main objective of this study is to find the effects of cross-linker variation on swelling behavior of hydrogels at different temperatures, that is, 30 min–120 min. Hydrogels are three-dimensional cross-linked structural arrangement of the polymeric materials with the ability to absorb huge amounts of water while maintaining their dimensional stability. **Materials and Methods:** A solution of 20% glutaraldehyde (GA) was prepared in 100 ml standard flask by dissolving 20.0 g GA in a standard flask (of capacity 100 ml) and make up the volume up to the mark using demineralized water (DMW). The gelatin-polyethylene glycol (PEG) composite hydrogels were prepared by simultaneous method, in which all the constituent component networks are polymerized concurrently. Different combinations of gelatin-PEG composite hydrogels were prepared with methylene blue (MB) dye in it. Swelling was studied with the help of the following equation: $I_s = \frac{W_d - W_s}{W_d} \times 100$ **Results and Discussion:** The observation showed that the decrease in the absorbance of MB release through the sample membrane may be due to the contraction of the microvoids formed between the polymeric chains. **Conclusion:** Based on our results which conclude that with increasing crosslinking agent from 5 ml to 15 ml, swelling ratio of the prepared sample decreased from 473.83 to 428.97 in DMW due to the decrease in the pore diameter of the sample. As a result, more and more solvent diffuses into the matrix and produce gel with increased swelling ratio.

Key words: Cross-linkers, dye, gelatin, glutaraldehyde, hydrogels, polyethylene glycol, spectrophotometer, swelling

INTRODUCTION

Hydrogels are three-dimensional cross-linked structural arrangement of the polymeric materials with the ability to absorb huge amounts of water while maintaining their dimensional stability.[1] Hydrogels on the basis of origins can be classified as natural or synthetic.[2] Hydrogel-forming natural polymers are proteins (collagen and gelatin) and polysaccharides (alginate and agarose). These hydrogels have low toxicity and good biocompatibility.[3] The synthetic polymers that form hydrogels are usually obtained through chemical polymerization methods by crosslinking the materials of desirable properties.[4] These hydrogels may have lower interfacial tension, soft and tissue like physical characters, greater permeability to undersized molecules, and release of entrapped molecules in a controlled manner.[4] These properties have made hydrogels a focus of exploration in different biomedical fields, for example, include wound dressings, super absorbents, drug delivery systems, and tissue engineering.[1] Many of the hydrogels are responsive to fluctuations in physical and chemical stimuli such as

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temperature, electric fields, solvent composition, light, pressure, sound and magnetic fields, pH, ions, and specific molecular recognition events.[5] Such hydrogels are called "smart hydrogels" and find applications in making actuators and valves, in the immobilization of enzymes and cells, in sensors, and in concentrating dilute solutions in bioseparation.[1] The properties of hydrogels such as swelling, mechanical, and biocompatible properties are important for its applications in engineering or other areas of biomedical fields.[2] These properties largely depend on the constituent materials and methods of preparations. Cross-linked networks of one type of hydrophilic monomer unit, for example, polyethylene glycol (PEG), polyvinyl alcohol, polyvinylpyrrolidone, polyacrylic acid, etc., were used to prepare homopolymer hydrogels. Two comonomer units are cross linked to produce the copolymer hydrogels. In this process, at least one of the monomer must be hydrophilic to make them swellable, for example, triblock poly(ethylene glycol)-poly(ε-caprolactone)-poly(ethylene glycol), copolymer of glycerol, and polyethylene oxide of different molecular weights.[6] The interpenetrating polymeric hydrogels are produced by the penetration of one cross-linked network into another linear polymer without any other chemical bonds between them. Due to the absence of restricting interpenetrating elastic network, interpenetrating networks (IPNs) can further adequately secure rapid kinetic response rates to temperature or pH, for example, entrapment of linear cationic polyallyl ammonium chloride in acrylamide/acrylic acid copolymer hydrogel.[4,5,7] IPNs are conventionally described as intimate mixture of two polymers, at least one of which is cross-linked or synthesized in the instantaneous presence of the other, for example, PEG diacrylate hydrogels modified with β-chitosan.[1,8] This process accomplished by immersing a pre-polymerized hydrogel into a solution of polymerization initiator and monomers. IPN method can overcome thermodynamic incompatibility. This happens due to the constant interlocking of network segments and restricted phase separation can be acquired. The stability of the bulk and surface morphology is ensured by the interlocked structure of the cross-linked IPN components.[2] The IPNs are relatively dense hydrogel with stiffer and tougher mechanical properties, controllable physical properties, and more efficient drug loading compared to conventional hydrogels. IPN pore sizes and surface chemistries can also be controlled to tune the drug release kinetics, interaction between the hydrogel and the surrounding tissues along with its mechanical properties.[9,10]

Properties of hydrogels

The most important characteristic properties of the hydrogels that are needed to be evaluated before their applications are swelling behavior: One of the most important properties of hydrogels is its ability to absorb liquids (swelling thermodynamics) and the rate at which the hydrogels absorb the liquid (swelling kinetics).[6]

Types of hydrogels

Stimuli responsive hydrogels, pH responsive hydrogels, temperature responsive hydrogels, thermoreversible hydrogels, glucose responsive hydrogels, antigen-responsive hydrogels, light-sensitive system ion sensitive system, and magnetically responsive system.[2,6,7]

MATERIALS AND METHODS

Methylene blue (MB) (S. D Fine, India), PEG (Sigma-Aldrich Chemicals [USA]), glutaraldehyde (GA) (S. D Fine, India), hydrochloric acid (HCl) (S. D Fine, India), and gelatin (GE) (Fluka [Buchs, Switzerland]) were used. All reagents and chemicals used were of analytical grades.

Preparation of stock solutions

Preparation 1000 ppm of MB solution

The stock solution of MB of 1000 ppm was prepared by dissolving 0.1 g of MB dye in a 100 ml standard volumetric flask. The stock solution of the dye was kept in dark to protect it from any photochemical reactions.[11]

Preparation of 0.1 M HCl solution

The stock solution of 0.1 M HCl was prepared by dissolving 0.90 ml HCl in demineralized water (DMW) in a 100 ml standard flask.

Preparation of 20% GA solution

A solution of 20% GA was prepared in 100 ml standard flask by dissolving 20.0 g GA in a standard flask (of capacity 100 ml) and make up the volume up to the mark using DMW.

Preparation of gelatin-PEG composite hydrogels

The gelatin-PEG composite hydrogels were prepared by simultaneous method in which all the constituent component networks are polymerized concurrently. Different combinations of gelatin-PEG composite hydrogels were prepared with MB dye in it. To make them homogeneous, components were thoroughly mixed by stirring the solution during preparation.[8,11] The composition of the prepared samples is given in Table 1.

Swelling study

The maximum hydration capacity of the gelatin and PEG hydrogel was determined by weighing the dried sample (W_d) and then weighing the sample again after immersion in DMW at room temperature for 30 min.[6] The water absorption of the sample was calculated using the following equation:

Table 1: Weights of the chemicals taken in different formulations of hydrogels

Components	Samples prepared						
	SP1	SP2	SP3	SP4	SP5	SP6	SP7
Gelatin (g)	2.0	2.0	2.0	2.0	2.0	3.0	4.0
Polyethylene glycol (g)	0.5	0.5	0.5	0.5	1.5	0.5	2.5
Methylene blue (1000 ppm) (ml)	10.0	10.0	5.0	5.0	5.0	5.0	5.0
Glutaraldehyde (ml)	10.0	20.0	10.0	5.0	10	10	15.0

$$I_s = \frac{W_d - W_s}{W_d} \times 100$$

Where, I_s is the percentage swelling index.

RESULTS AND DISCUSSION

Effects of cross-linker variation on dye release

Tables 2 and 3 determine the membrane dye releasing property due to the variations of cross-linker (5 ml, 10 ml, and 15 ml) which shows the release behavior of MB from the membrane in the hydrogel compositions S.P-3, 4, and 7 in DMW and 0.1 M HCl, respectively.[3,12,13] The observation showed that the decrease in the absorbance of MB release through the sample membrane may be due to the contraction of the microvoids formed between the polymeric chain. Obtained experimental results illustrate that with increasing crosslinking agent from 5 ml to 15 ml, absorbance of the prepared sample decreased from 0.426 to 0.422 in DMW and 0.474 to 0.419 in 0.1 M HCl due to decrease in the pore diameter of the sample.[4,9,10]

Effects of cross-linker variation on swelling behavior

Table 2 determines the membrane swelling property due to the variation of cross-linker (5 ml, 10 ml, and 15 ml) in the hydrogel compositions S.P-3, 4, and 7 in DMW. The observation showed that the decrease in the swelling ratio of the sample membrane may be due to the contraction of the microvoids formed between the polymeric chains.[4,9,10] Obtained experimental result illustrates that with increasing crosslinking agent from 5 ml to 15 ml, swelling ratio of the prepared sample decreased from 473.83 to 428.97 [Table 2] in DMW due to the decrease in the pore diameter of the sample.

Effects of gelatin on swelling ratio

Tables 3 and 4 determine the swelling behavior of compositions containing varying amount of gelatin (2 g, 3 g, and 4 g) at fixed GA and PEG in the hydrogel compositions S.P-3, 6, and 7 in DMW and 0.1 M HCl, respectively. According to the experimental result, we conclude that with increasing gelatin composition from 2 g to 4 g, swelling ratio of the prepared sample also increased. This is due to the hydrophilic nature of gelatin that the interaction between the solvent and gelatin increased which result into swollen hydrogel.[12]

Table 2: Swelling ratio comparison in sample-3, 4, and 7 in demineralized water (GA variation)

Time taken (minutes)	Sample-4 (5 ml GA)	Sample-3 (10 ml GA)	Sample-7 (15 ml GA)
30	356.07477	241.1215	167.28972
60	411.21495	372.8972	295.3271
90	450.46729	421.49533	390.65421
120	473.83178	452.33645	428.97196

GA: Glutaraldehyde

Table 3: Swelling ratio comparison in sample-3, 6, and 7 in demineralized water (Ge variation)

Time taken (minutes)	Sample-3 (2 g Ge)	Sample-6 (3 g Ge)	Sample-7 (4 g Ge)
30	295.33	392.52	513.08
60	378.50	500.00	593.46
90	477.57	658.88	718.69
120	543.93	749.53	796.26

Table 4: Swelling ratio comparison in sample-3, 6, and 7 in 0.1 M HCl (Ge variation)

Time taken (minutes)	Sample-3 (2 g Ge)	Sample-6 (3 g Ge)	Sample-7 (4 g Ge)
30	294.39	379.44	420.56
60	379.30	426.17	483.18
90	476.96	514.02	552.34
120	544.33	596.26	616.82

Effects of PEG on swelling behavior

Tables 5 and 6 determine the swelling behavior of the compositions containing varying amount of PEG (0.5 g, 1.5 g, and 2.5 g) with fixed amount of GA and gelatin in hydrogel compositions S.P-3, 5, and 7 in DMW and 0.1 M HCl, respectively.[5,8] The observation showed that with increasing PEG compositions from 0.5 g to 2.5 g, swelling

Table 5: Swelling ratio comparison in sample-3, 5, and 7 in demineralized water (PEG variation)

Time taken (minutes)	Sample-3 (0.5 g PEG)	Sample-5 (1.5 g PEG)	Sample-7 (2.5 g PEG)
30	294.91	614.02	783.18
60	376.98	912.15	1033.64
90	476.86	1061.68	1228.04
120	542.99	1116.82	1331.78

PEG: Polyethylene glycol

Table 6: Swelling ratio comparison in sample-3, 5, and 7 in 0.1 M HCl (PEG variation)

Time taken (minutes)	Sample-3 (0.5 g PEG)	Sample-5 (1.5 g PEG)	Sample-7 (2.5 g PEG)
30	296.18	551.40	687.85
60	377.41	658.88	808.41
90	478.21	661.68	821.50
120	544.13	707.48	943.93

PEG: Polyethylene glycol

ratio of the prepared sample also increased.[12] This may be due to the hydrophilic nature of PEG that the increased in the PEG amount suggested its increased interaction with the nearby solvent which causes swelling of the microvoids. As a result, more and more solvent diffuses into the matrix and produce gel with increased swelling ratio.

CONCLUSION

Based on our results which conclude that with increasing crosslinking agent from 5 ml to 15 ml, swelling ratio of the prepared sample decreased from 473.83 to 428.97 in DMW due to the decrease in the pore diameter of the sample. Increasing gelatin composition from 2 g to 4 g, swelling ratio of the prepared sample also increased, due to the hydrophilic nature of gelatin that the interaction between the solvent and gelatin increased which result into swollen hydrogel. Increasing PEG compositions from 0.5 g to 2.5 g, swelling ratio of the prepared sample also increased, due to the hydrophilic nature of PEG that the increased in the PEG amount suggested its increased interaction with the nearby solvent which causes swelling of the microvoids. As a result, more and more solvent diffuses into the matrix and produces gel with increased swelling ratio. Due to their high biocompatibility and water absorption capacity, they have been used in dental materials, wound dressing, implants, drug delivery, injectable polymeric systems, agriculture, sanitary pads as well as transdermal systems, ophthalmic applications, hybrid-type organs, etc.

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CONFLICTS OF INTEREST

No conflicts of interest.

CONTRIBUTION OF AUTHORS

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