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Biocompatible Hydrogel Film of Polyethylene Oxide-Polyethylene Glycol Dimetacrylate for Wound Dressing Application

Haryanto[1*], Fani[2] and A Mahardian[3]

[1,2] Chemical Engineering Department, Faculty of Engineering, Universitas Muhammadiyah Purwokerto
[3] Pharmacy Department, Faculty of Pharmacy, Universitas Muhammadiyah Purwokerto, Purwokerto

*haryanto@ump.ac.id

Abstract. Hydrogel polymer is a new material which has a broad application for biomedical materials, pharmacy, drugs and agriculture. Hydrogel has ability to absorb and retain water which is very useful for medical applications. We developed polyethylene oxide-polyethylene glycol dimetacrylate using permanent crosslinking method via electron beam irradiation for wound dressing application. Various composition of pegdma/peo (0%, 5%, 10%, 15% and 20%) irradiated with electron beam to get the optimum composition for wound dressing application. The pegdma content in hydrogel film influenced the gel fraction, swelling ratio, mechanical properties and water vapor transmission rate. The results show that the increase in content of pegdma increased the tensile strength and gel fraction. The highest tensile strength (0, 65 MPa) and gel fraction (76%) reached at 20% pegdma/peo. In contrary 20% pegdma/peo hydrogel has the lowest swelling ratio (235%). Base on the results, 20% pegdma/peo hydrogel film is very potential for wound dressing application with high mechanical strength and ideal water vapor transmission rate.

1. Introduction

Wound healing is generally accelerated by various wound dressings. They often protect and cover the wound surface and also absorb the exudate in order to speed up its healing. Recently, hydrogel material especially hydrogel film has been used as a wound dressing material. Hydrogel dressing consists of insoluble polymers with a high water content making them an ideal dressing to facilitate autolytic debridement of necrosis and slough [1,2,3,4] Dressing should be easy to apply, be painless on removal, should create an optimal environment for wound healing, and should require fewer dressing changes, thereby reducing nursing time [2]. Therefore, the hydrogel having better mechanical strength is expected to be better for use as a dressing material. The hydrogel film can be formed by crosslinking of polymers such as polyvinyl alcohol, polyvinyl pyrolidone, polyacrilic acid, and poly (ethylene oxide) [5].

Among the water soluble polymers, polyethylene oxide shows the merit of its relatively low toxicity [6]. However, the pure PEO hydrogel has low mechanical strength and it is very fragile [7]. PEO is a

nonpolar, high-molecular-weight linear polymer of polyethylene oxide that has a large unfavorable free energy of interaction with proteins [8]. It is a biocompatible polymer that has been used as a component of a tissue sealant [9,10] and it has recently been used as a wound dressing [11,12]. PEGDMA is nontoxic, water soluble, which has polymerizable end groups. It already be used in medical application for various functions, among them are oral insulin delivery [13] and bone regeneration application [14]. However little research has been conducted on this material for wound dressing applications.

An electron beam is relatively simple for improvement or modification of polymeric materials through cross-linking, grafting, and degradation reactions [15]. Moreover, the radiation dose can be easily controlled and the experimental condition is straightforward for mass production of products. In addition, the product is free from unwanted chemical impurities such as residues from initiators, retarders, and/or accelerators for initiation and for manipulation of the crosslinking reaction in chemical crosslinking methods [12].

It is expected that co-crosslinking of PEO with PEGDMA with an e-beam irradiation can increase the mechanical and physical properties by increasing the crosslink density and the content of PEGDMA also expected can increase the water vapor transmission rate.

2. Materials and methods

2.1. Materials

Polyethylene oxide (PEO) and Poly (ethylene glycol) dimethacrylate (PEGDMA) were purchased from Sigma-Aldrich, St. Louis, USA.

2.2. Preparation of hydrogel films

Polyethylene oxide (PEO) (Mn $6x10^5$) and Poly (ethylene glycol) dimethacrylate (PEGDMA) (M_n 750) were used for preparation of the hydrogels. PEGDMA was purified by passing through Alumina coloumn to remove monomethyl ether hydroquinon inhibitor. Aqueous solution of PEGDMA/PEO (5 % w/w) was prepared by stirring the solution at room temperature for 24 hours. The composition of PEGDMA/PEO was changed from 0/100, 5/100, 10/100, 15/100, and 20/100 (w/w), respectively. The calculated amount of aqueous solution was poured into a petri dish to form dry PEO film with a thickness of 0.3 mm. The PEO solution was dried in the oven at 55 ^{0}C for 24 hours, and then remaining moisture was removed in a vacuum oven for 6 hours at the same temperature. Dry PEO films were sealed in an evacuated polyethylene bag, followed by irradiation at 300 kGy using an electron beam (EB).

2.3. Characterization of the crosslinked hydrogel film

FTIR-C86199 (Perkin Elmer) was used to analyze the properties of the chemical functional group of the crosslinked hydrogel film. Samples were scanned at wavenumber range of 4000-500 cm^{-1} with resolution of 4 cm^{-1}.

2.4. Determination of gel fraction

Immediately after irradiation, the seal was opened and the weight of the dry PEO/PEGDMA film sample (2cm x 2cm) was measured accurately. After thatat, the crosslinked PEO film was placed in distilled water at 50 ^{0}C for 24 hours for removal of the soluble parts. The insoluble gel obtained was dried in the oven at 50 ^{0}C for 24 hours and then in a vacuum oven at 50 ^{0}C for 6 hours in order to obtain a constant dry weight. The gel fraction was determined from the weight ratio between the insoluble dry gel weight and the initial weight of the polymer,

$$\text{Gel fraction} = (Wc / Wo) \times 100\ [\%] \quad (1).$$

where Wc and Wo are the weight of insoluble dry gel and the initial weight of a dry film [16]

2.5. Determination of swelling ratio

The known weight of the crosslinked dry PEO film (2cm x 2cm) was soaked in distilled water at room temperature until the film reached the equilibrium weight. The weight of the swollen gel was measured at different swelling time intervals after removal of excessive surface water using filter papers. The procedure was repeated until there was no further weight increase. The swelling ratio (SR) was calculated using the following equation:

$$SR = (Wt/Wo) \times 100\ [\%] \quad (2).$$

where Wt and Wo are the weight of swollen gel at time t and that of the dry PEO film, respectively.

2.6. Mechanical pproperties

The tensile strength and tensile strain of crosslinked PEO/PEGDMA hydrogel films were measured using a tensile test machine (UTM Taiwan) with a constant extension rate of 10 mm/min, at room temperature.

2.7. Determination of water vapor transmission rate

The water vapor transmission rate was measured using JIS 1099A standard test methods.13, 14 A round piece of crosslinked dry PEO film was mounted on the mouth of a cup with a diameter of 7 cm containing 50 g $CaCl_2$ and placed in an incubator of 90% RH at 40 °C. The water vapor transmission rate (WVTR) was determined as follows:

$$WVTR = ((W_2-W_1)/S)\ [g\ m^{-2}h^{-1}] \quad (3).$$

Where W_1 and W_2 are the weight of the whole cup at the first and the second hours, respectively, and S is the transmitting area of the sample.

3. Results and discussion

3.1. FT-IR analysis

FTIR spectra of films with 100% PEO and 20% PEGDMA/PEO composition before and after irradiation were shown in Fig. 1. There were typical peaks for pure PEGDMA film at 1715 cm^{-1} and 1640 cm^{-1}. Compared with unirradiated films FTIR spectra (0 kGy), all irradiated films showed lower absorption band of C=O at 1715 cm^{-1}, with the increase of irradiation dose, the absorption peak decreased significantly, and at the same time the stretching vibration peak of C=C group at 1640 cm^{-1} was disappeared at all irradiation dose rates. Those evidences indicated that crosslinking between PEO and PEGDMA have been successfully carried out and increase with increasing irradiation dose.

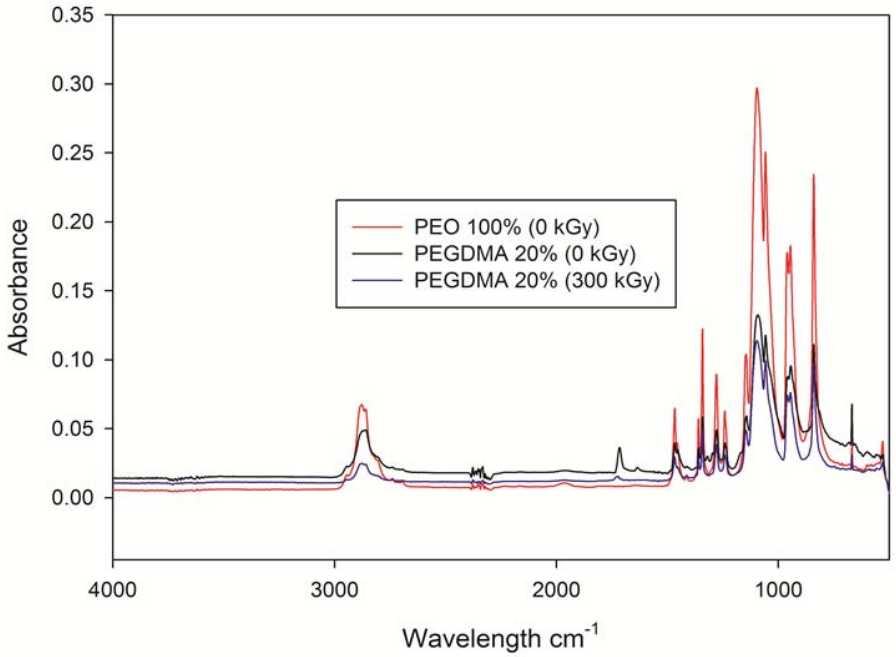


Figure 1. FTIR spectra of hydrogel 20% PEGDMA/PEO films before and after irradiation.

Effect of PEGDMA content on gel fraction, swelling properties, mechanical properties and water vapor transmission rate.

3.1.1. The gel fraction and swelling properties of PEO/PEGDMA hydrogel. A small amount of PEGDMA was added to the PEO in order to increase the mechanical strength of the e-beam crosslinked PEO. Fig. 2a shows the gel fraction of PEO/PEGDMA hydrogel. The result showed that the gel fraction increased almost linearly with increasing the weight percentage of the PEGDMA in a mixture. The swelling ratio of PEO/PEGDMA hydrogel film with various compositions as a function of swelling time is shown in Fig. 2b. It shows that all of the hydrogel films absorb water very rapidly and reach an equilibrium weight within 5 minutes. The swelling ratio decreased with the increasing content of PEGDMA, and the equilibrium swelling ratio of the crosslinked hydrogel films decreased from 800% in the film without the presence of PEGDMA to 235% in that with 20% of PEGDMA. The result indicated that the higher content of PEGDMA can decrease the water absorption capacity of PEO/PEGDMA hydrogel due to the crosslinking of PEGDMA together with radicals in PEO backbones via radical polymerization. In addition, PEGDMA also enhanced the crosslinking reaction of the PEO/PEGDMA film owing to reduced viscosity, which can enhance the coupling reaction of radicals before the radical decays into an unreactive species.

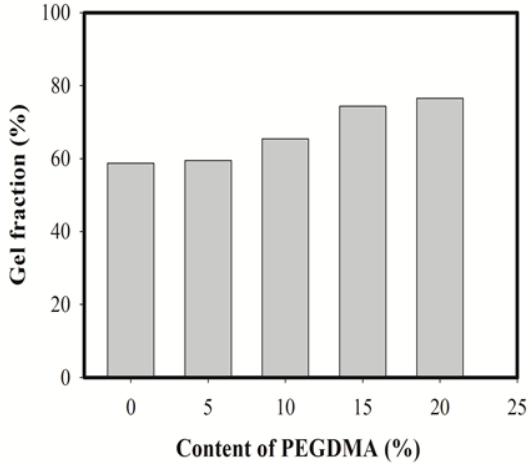


Fig. 2a.

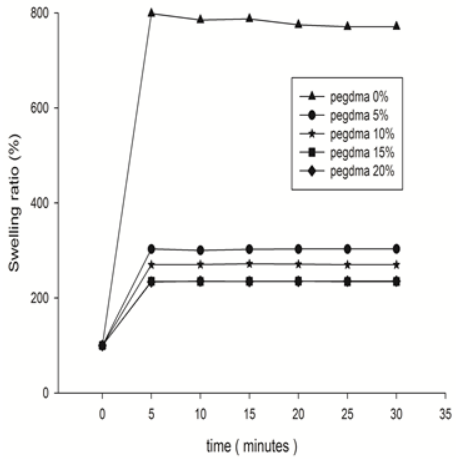


Fig. 2b.

Figure 2. Gel fraction and Swelling ratio of crosslinked PEGDMA/PEO hydrogel films.

3.1.2. Mechanical properties. The tensile strength of PEO/PEGDMA wet hydrogel film as a function of the PEGDMA content is shown in Fig. 3a. It can be seen that the tensile strength of PEO/PEGDMA hydrogel showed increased from 5 % to 20% of PEGDMA due to the increased crosslink density and reached the maximum value (0.65 MPa) with 20% of PEGDMA. Fig. 3b shows the percentage elongation of the PEGDMA/PEO films. The percentage elongation increased steadily with the increasing content of PEGDMA. The result indicates that Tensile strength and percentage elongation of the PEO/PEGDMA film are high enough for application as wound dressing.

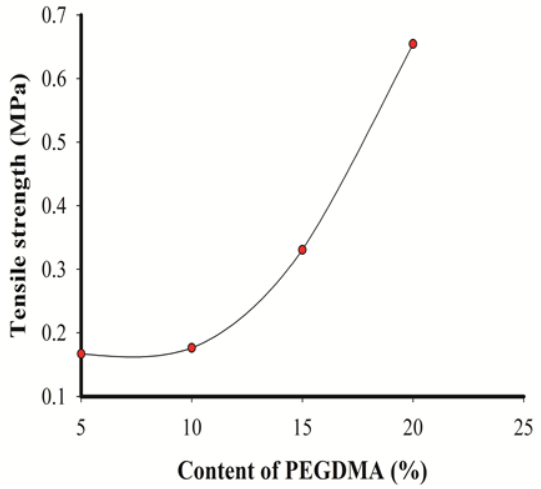


Fig. 3a.

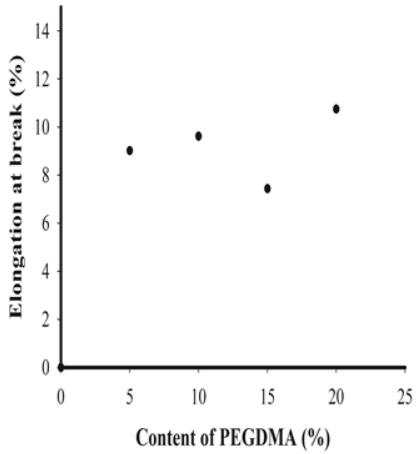
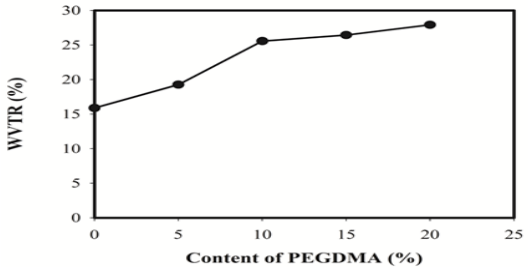


Fig. 3b.

Figure 3. Mechanical Properties of crosslinked PEGDMA/PEO hydrogel films.

3.1.3. Water Vapor Transmission Rate (WVTR). The effect of the content of PEGDMA on the WVTR of the hydrogel is shown in Fig. 4. The figure shows that the WVTR value is almost constant for all compositions of PEGDMA because most of the matrix is PEO. The average WVTR was 25 g m^{-2} h^{-1} for 5 – 20 % of PEGDMA, however, that of pure PEO was somewhat lower, 15.89 g m^{-2} h^{-1}. When the value of WVTR is too high, the wound can dry rapidly, resulting in scars. In addition, if the value is too low to

accumulate exudates, the healing process can be retarded, resulting in increased risk of bacterial growth [17] Use of an ideal dressing is known to control evaporation of water from a wound at an optimal rate. The rate for normal skin is 8.5 g m^{-2} h^{-1}, while that for injured skin can range from 11.6 g m^{-2} h^{-1}. Therefore, the ideal wound dressing should have a WVTR similar or greater than 11.6 g m^{-2} h^{-1}. The WVTR of the PEO/PEGDA hydrogel was close to the ideal value for wound dressing.



Figue 4. Water vapor transmission rate of pegdma/peo hydrogel film

4. Conclusion

The PEO/PEGDMA hydrogel film prepared by e-beam irradiation at 300 kGy was nontoxic and biocompatible with high mechanical strength. The PEO/PEGDMA hydrogel contained no toxic ingredients due to the absence of any organic inhibitor, accelerator, and inorganic catalyst. Moreover, it can accelerate wound healing process after surgery. Results of *in vitro* study implied that the test material (PEO/PEGDMA) has very promising wound dressing materials. In addition, the increasing content of pegdma in PEO/PEGDMA hydrogel film was able to increase the mechanical properties and the water vapor transmission rate. These findings were considered direct evidence that PEO/PEGDMA hydrogel film definitely influenced by the content of PEGDMA, the results confirmed that PEO/PEGDMA hydrogel film has a great potential for future use in wound dressing application.

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