

Investigation of synthesis of PVP hydrogel by irradiation

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Background: A dressing often covers the wound to accelerate its healing. Hydrocolloid-type dressing to give better conditions for healing has been developed consisting of gelatin, pectin, water and hydrophilic polymer which promote healing. In recent years, much attention has been focused on the research and development of polymer hydrogels as biomaterials, such as contact lenses, wound dressing and drug-delivery systems. **Materials and Methods:** Hydrogels, as wound dressing were prepared with composite poly (N-vinyl-2-pyrolidone) (PVP) with several additives such as agar and polyethylenglycol (PEG) and by electron-beam. Electron beam was applied as a tool for initiation of crosslinking and sterilization of these materials. The effects of irradiation dose at the range of 10-40 KGy and various concentration of components on the characterizes of hydrogel such as gel content, degree of swelling (DS), equilibrium water content (EWC) and dehydration properties, transparency and microbial test were investigated. **Results:** After irradiation, the achieved gel content of hydrogels was obtained higher than 25%. Gels' degree of swelling with different concentrations was changed from 35 to 20 at the range of irradiation dose of 10-40 KGy. Also, at the same range of irradiation and concentration, EWC of gels was found to be 98 to 94 %. The dehydration results did not show variation with the tested parameters. **Conclusion:** Results showed that hydrogels membrane with composition PVP (10% w/w), agar and PEG (1-3%w/w) at the dose of 25 KGy had the amount of gel content 80-85%. Their DS and EWC were respectively obtained 30% and 96.5%. They were elastic, transparent, flexible, sterile and impermeable for bacteria. They absorbed a high capacity of water, attached to healthy skin, and they were easy to remove. It was concluded that the network was solely composed of crosslinked PVP plasticized by other compounds. *Iran. J. Radiat. Res., 2007; 5 (3): 131-136*

Keywords: Hydrogel, biomaterial, radiation polymerization, electron beams, wound dressing.

INTRODUCTION

In recent years, hydrogels with network structure which are consisting of more than 90% of water have been prepared. They have

the capability of swelling in water without being solved. They have found a wide range of biomedical applications including, healing variety of wound burn, foreign debris, surgical wound and open traumatic wound with infection.

Hydrogels as wound burn dressing have many interesting properties such as: immediate pain control, easy replacement, transparency to allow healing follow up, absorb and prevent loss of body fluids, barrier against bacteria, good adhesion, good handling, oxygen permeability, soft and elastic, but mechanically strong enough.

They are synthesized by chemical and physical methods. The chemical method involving synthesis of polymer molecules have reactive groups and react with suitable crosslinking agents ⁽¹⁾. When using this method for the formation of hydrogels for biomedical use, all of the necessary steps should be taken to ensure all of the monomers have been reacted.

If there are the undesired compounds such as unreacted monomers and toxic substances, it has to be washed out in a separate step. The inclusion of this step in the synthesis process can complicate the technology to be employed and may lead to a significant increase in production costs.

Ionizing radiation has been since long recognized as a very suitable tool for the formation of hydrogels. The advantages of ionizing radiation are easy process control, possibility of joining hydrogel formation and sterilization in one technological step, no

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need to add any initiators, crosslinkers, no waste and relatively low running costs.

Hydrogels based on PVP to be used as wound burn dressing were invented by Rossiak *et al.* ⁽²⁾. Radiation production of hydrogel wound dressings (HWDS) started first in Poland at the Technical University of Lodz in 1992. PVP based dressings obtained by e-beam irradiation, were commercialized under the registered trade marks KIK-gel and AQUA-gel ⁽³⁾.

Hydrogels of natural polymers, especially polysaccharides, have been used recently as biomaterial due to of their unique advantages such as lack of toxicity, biocompatibility, biodegradability, and abundance ^(4, 5). Blends of synthetic and natural polymers represent a new class of materials with better mechanical properties and biocompatibility than those of the single components. Therefore, the most recent research has focused on synthetic natural polymer blend materials such as cellulose diacetate/PVP ⁽⁶⁾, chitosan/PVP ⁽⁷⁾, agar/ poly (N-isopropyl acrylamide) ⁽⁸⁾, and agar/PVP/PEG ⁽⁹⁾.

In this research agar was used as natural polymer. Polysaccharides have a variety of properties, including the ability to stabilize viscous suspensions, to form film layers and to turn into gels. Also, PEG as plasticizer, can be used to improve the mechanical properties of hydrogel. These kinds of hydrogels exhibited properties which were different from the original polymers.

In the study we investigated the synthesis of PVP based wound dressing by using PVP, agar and low molecular weight PEG by electron-beam irradiation. Preliminary laboratory tests of the hydrogels including gel content, degree of swelling, equilibrium water content, dehydration and microbiological test were examined to evaluate the usefulness of hydrogels as a wound dressing hydrogel.

MATERIALS AND METHODS

Materials and instruments

PVP molecular weight (MW=1.84×10⁵ g/mol), agar (MW=5.90×10⁵ g/mol), PEG

(MW=4.40×10² g/mol) and culture mediums: nutrient agar and nutrient broth were supplied by Merck and Sigma chemical companies.

Electron-beam accelerator (Rodotron) model TT200, IBA Belgium (10 MeV, 6 mA, dose rate: 8.96±0.01 KGy/s), and STA instrument (simultaneous thermal analyzer) model: PL England were used.

Preparation of hydrogels

Various combinations of mixtures with concentrations of PVP (6, 8, 10, 16% w/w), agar (1, 2, 3% w/w) and PEG (1, 2, 3% w/w) solutions were prepared in 100 ml of deionized water at high temperature and samples were stirred. Then the hot mixtures were poured into molds, sealed, and finally irradiated at room temperature by e-beam with doses of 10-40 KGy. The product was a fully sterile permanent hydrogel in a form of a transparent sheet, of 3-4 mm.

Gel content

Gel content of the hydrogels was measured by extraction in hot distilled water of 60°C until they reached a constant weight. The gel content was defined as equation (1): where *wd* is the dried gel weight after extraction, and *wi* is the initial weight of the polymer.

$$\text{Gel}(\%) = \frac{wd}{wi} \times 100 \quad (1)$$

Degree of swelling

Degree of swelling could be described as water absorptivity (equation (2)) of the hydrogels. The gel samples were immersed in distilled water for 48h at room temperature. After weighting the mass of swollen gels, they were dried to the constant weight at 60°C. The degree of swelling (DS) was defined as equation (2): where *ws* is the weight of the swollen gels and *wd* is the dried gel weight.

$$DS = \frac{ws - wd}{wd} \quad (2)$$

Equilibrium water content (EWC)

The sample was immersed in water with the proportional of the mass of constant the

mass of water about 1:500, at room temperature. Swelling continued to reach a constant weight of the gel. Before weighting the sample, any surface water was removed with filter paper. The swelled gel was slowly dried to get to constant weight at 60°C. EWC was calculated as equation (3);

$$EWC = \frac{ws - wd}{wd} \times 100\% \quad (3)$$

Dehydration

The dehydration behavior was followed by measuring the difference of mass when the sample was isothermally (310k) (or 37°C simple body temperature) dried in a STA, within a synthetic air atmosphere.

Microbiological

A microbiological test was conducted to investigate the resistance of the membrane against bacteria penetration. The sterile membrane (with a dose of 25 KGy) was used with a thickness of 1.4 mm. The testing procedure was as follow: one side of the surface of the sterile membrane was put on a sterile Petri dish which contained plate count agar medium (nutrient agar/broth). The water suspension of *Bacillus* was spread onto the opposite surface of the membrane. Incubation in aerobic condition was carried out at a temperature of 30°C for 10 days. The progress of bacteria penetration was observed day by day.

RESULTS

The variation of the gel content of hydrogels with the dose, as well as the contents of PVP, agar and PEG are shown in figures 1, 2, 3. The gel content and crosslinking density of PVP/agar/PEG hydrogels increased with the increasing of the dose and the content of PVP. But the increase of agar and PEG concentration didn't have any effect on the results.

The swelling behavior of the hydrated membranes as a function of dose with PVP,

agar and PEG concentration are shown in figures 4, 5 and 6.

Hydration properties of hydrogels membranes are shown in figures 7, 8 and 9. Along the increasing of dose, the EWC is

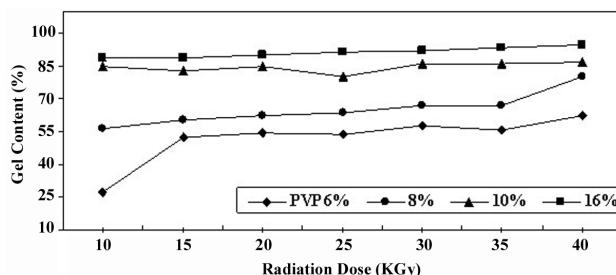


Figure 1. Gel content of hydrogels with different concentration of PVP (agar (1% w/w) and PEG (1%w/w)) vs. of radiation dose.

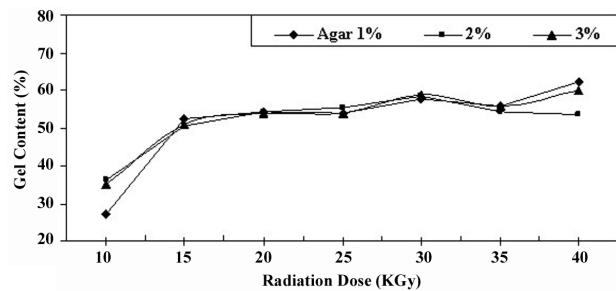


Figure 2. Gel content of hydrogels with different concentration of agar (PVP (6%w/w) and PEG (1.5%w/w)) vs. radiation dose.

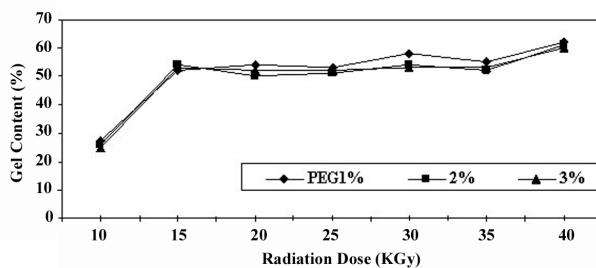


Figure 3. Gel content of hydrogels with different concentration of PEG (PVP (6% w/w) and agar (1.5%w/w)) vs. irradiation dose.

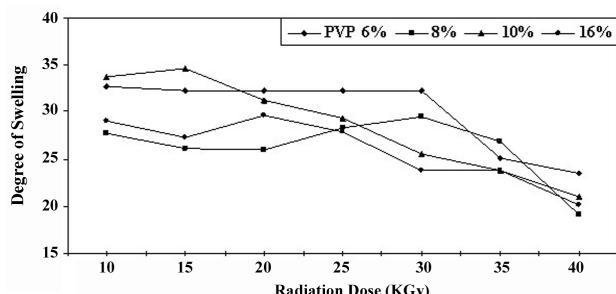


Figure 4. Degree of swelling of hydrogels with different concentration of PVP (agar (1%w/w) and PEG (1%w/w)) vs. radiation dose.

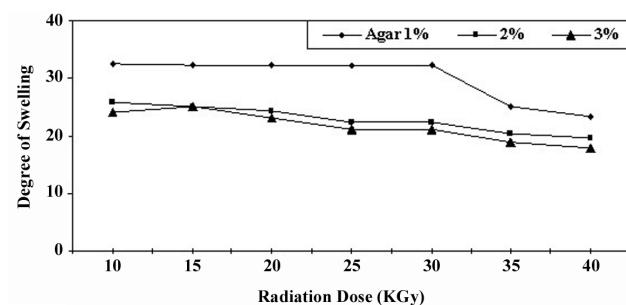


Figure 5. Degree of swelling of hydrogels with different concentration of agar (PVP (10%w/w) and PEG (1%w/w)) vs. radiation dose.

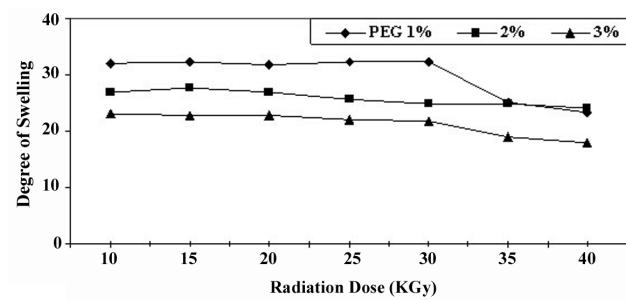


Figure 6. Degree of swelling of hydrogels with different concentration of PEG (PVP(10%w/w) and agar (1%w/w)) vs. radiation dose.

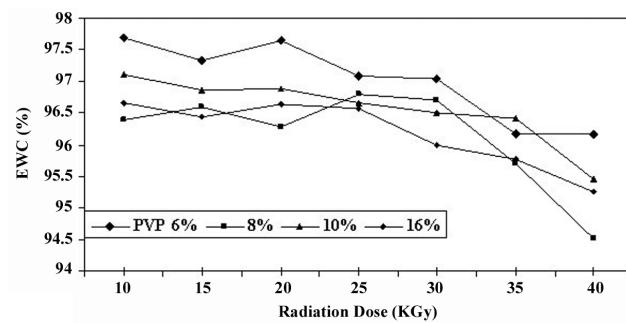


Figure 7. Equilibrium water content of hydrogels with different concentration of PVP (agar(1.5%w/w) and PEG(1.5%w/w)) vs. radiation dose.

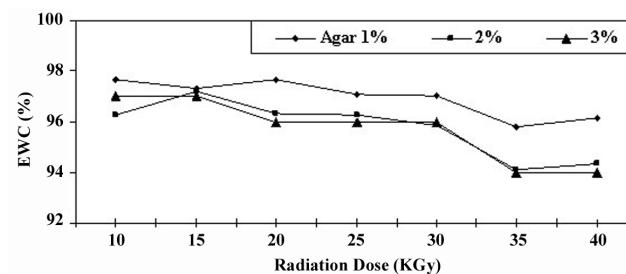


Figure 8. Equilibrium water content of hydrogels with different concentration of agar (PVP(10%w/w) and PEG(1.5%w/w)) vs. radiation dose.

slightly decreasing. Also, the addition of agar causes to decrease the EWC (figure 8). Figures 8 and 9 show exactly the same pattern as figure 7.

The relative weight (%) loss observed in thermo gravimetric curve from figure 10 shows that after 60 min at 37°C (as same as the body temperature) in order to simulate the use of the membrane on wounded skin, sample (PVP 10%w/w, PEG 1.5%w/w, agar 1.5%w/w at 25KGy) dehydrated about 92.6%. So it can be concluded the properties of hydration/dehydration were related to diffusion rather than to the capillarity of osmosis and to the chemical retention of water in the polymeric matrix.

Results of biological test showed that for samples at three irradiation doses (20, 25 and 30 KGy) related to the resistance of polymeric membrane as a barrier against bacteria penetration, hydrogels irradiated with more than 20 KGy could not be penetrated by bacteria for 10 days.

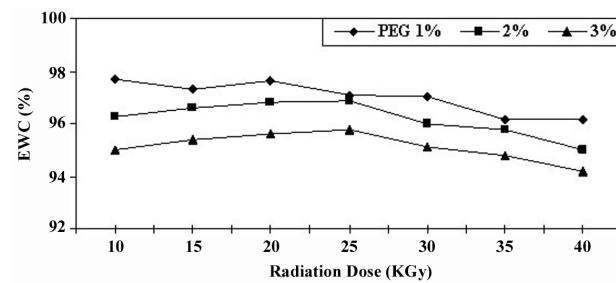


Figure 9. Equilibrium water content of hydrogels with different concentration of PEG (PVP(10%w/w) and agar (1.5%w/w)) vs. radiation dose.

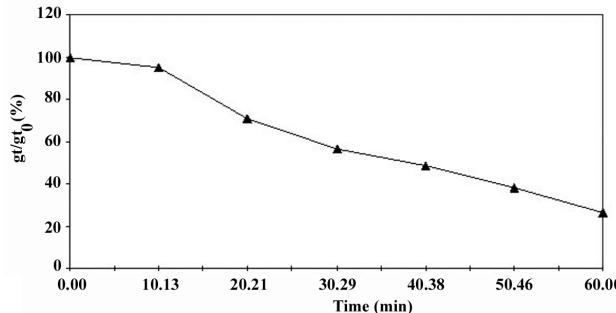


Figure 10. Dehydration of hydrogel (PVP (10%w/w), agar 1%w/w, PEG 1%w/w) at 25 KGy vs. time (gt=hydrogel weight at time t, g0= hydrogel weight at t0).

DISCUSSION

The obtained results showed that the main network of hydrogels consisted of PVP molecules, and only PVP molecules underwent through crosslinking. These results also proved that other materials didn't take part in the structural network by crosslinking. The effect of polysaccharide in PVP hydrogels could improve fluidity of gel before irradiation. Moreover, the addition of PEG as plasticizer could improve the physical properties of hydrogel membranes. According to these results, a dose of 25 KGy could be quite sufficient to cause simultaneously the reaction of crosslinking in such system with sterilization of hydrogels. In addition, Rosiak reported the dose of 25 KGy to be quite sufficient to cause the reaction of crosslinking in such system⁽¹⁰⁾. Lugao *et al.*⁽⁸⁾ have shown that the network was solely composed of crosslinked PVP plasticized by other compounds. They found out that PEG under radiation has a tendency to crosslink and to degrade at the same time; however, PEG in such low concentration at low dose could probably be degraded only. Therefore, the non-crosslinked components were acting as radical sink and this trapping effect could be used to fit the dose /properties relationship.

According to the swelling behavior of the hydrated membranes, the formation of gel explained the fact that by applying radiation, crosslinking network between polymer materials were formed. The degree of swelling was inversely proportional to the gel content and crosslinking density due to resistance increase in water to penetrate the network.

Hydration properties of hydrogels membranes show the resistance of network to water penetration. The rate was approximately the same for all PVP concentrations. In previous works on the hydration properties of hydrogel membranes^(8, 9); it was shown that along with increasing the dose, the amount of hydration and the degree of swelling were decreasing. The kinetic of water absorption

in membranes was reported by Hilmy and Darwis in 1993⁽⁹⁾. They showed that increasing immersion time would increase the amount of water absorption markedly up to a constant level.

It can be concluded by the relative weight (%) loss that the residual mass directly has been dependant on the concentration of solid material in the sample. Similar experiments were done with membranes prepared by gamma irradiation to study the dose rate effect and no difference was found between studied samples⁽⁸⁾.

The results of the biological test regarding to the resistance of polymeric membrane, as a barrier against bacteria penetration, showed that the membrane with various thicknesses could not be penetrated by bacteria up to 7 days of observation. After being incubated for 2 days at ambient environment, *flavus* grows on the membrane surfaces. So, even in tropical environment, they would not be penetrable for microorganism⁽⁸⁾.

Based on the obtained result, it could be said that hydrogel with composition of PVP (10%w/w), agar, PEG (1-3%w/w) which was irradiated at 25 KGy could be convenient to be used as a wound dressing. The hydrogel contained 80-85%w/w gel. The amounts of DS and EWC respectively were obtained 30 and 96.5%. They show some properties that could meet the requirements of an ideal wound dressing. The polymer membrane had properties such as: prevention against bacteria infection; absorption of a significant amount of water (DS over 30 and EWC over 90%); transparent, soft and be pleasant in touch and painless on removal.

The result showed that only aqueous solution PVP and agar didn't gelatinize well and the main network of polymer consists of only PVP molecules before irradiation. Addition of agar and PEG could improve the mechanical properties of hydrogel. Measurement of mechanical properties such as textile strength, elongation at break, etc. would be valuable for clinical usefulness of this wound dressing.

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