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ScienceDirect
Nuclear Instruments and Methods in Physics Research B 255 (2007) 343–349
NIM B
Beam Interactions with Materials & Atoms
www.elsevier.com/locate/nimb

Role of natural polysaccharides in radiation formation of PVA–hydrogel wound dressing

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Received 5 October 2006; received in revised form 16 November 2006
Available online 16 January 2007

Abstract

Radiation processed PVA–polysaccharides hydrogels have been observed to be suitable for producing transparent, flexible, mechanically strong, biocompatible, effective and economical hydrogel dressings. The dressings were formed in single stage irradiation process achieving gel formation and sterilization at 25–30 kGy gamma radiation dose. No synthetic plasticizers and additives were used. Different formulations containing poly-vinylalcohol (PVA) and polysaccharides selected from combinations of agar and carrageenan were used to make the dressings. The selected polysaccharides themselves form thermo-reversible gels and degrade on irradiation. Using concentration of polysaccharides as low as 0.5–2% resulted in increase of tensile strength from 45 g/cm^2 to 411 g/cm^2, elongation from 30% to 410% and water uptake from 25% to 157% with respect to PVA gel without polysaccharides. Besides improving mechanical strength, agar contributes more to elongation and carrageenan to mechanical strength of the gel dressing. PVA formulations containing the polysaccharides show significantly different pre-gel viscosities behaviour. Increasing the concentration of agar in the formulation to about 2% converts the sheet gel to paste gel useful for filling wound cavities. The results indicate that pre irradiation network structure of the formulation plays an important role in determining mechanical properties of the irradiated gel dressing. Formulations containing 7–9% PVA, 0.5–1.5% carrageenan and 0.5–1% agar gave highly effective usable hydrogel dressings. Scanning electron micrographs show highly porous structure of the gel. Clinical trials of wound dressing on human patients established safety and efficacy of the dressing. The dressing has been observed to be useful in treating burns, non-healing ulcers of diabetes, leprosy and other external wounds. The dressings are now being marketed in India under different brand names.

Keywords: Hydrogel; Radiation processing; Wound dressing; Poly(vinyl alcohol); Agar; Carrageenan

1. Introduction

Use of hydrogels (hydrogel dressing) on burns and topical ulcers is getting world wide recognition as an effective treatment. Several types of hydrogels are now commercially available. There is a large number of burns and diabetic ulcer cases in India. Imported hydrogels are prohibitively expensive. The need was felt to develop advanced indigenous product to cater to the requirements using local and economical ingredients. Natural polysaccharides like agar and carrageenan find several applications in food and pharmaceutical industries. Their gelling characteristics could be used to achieve the desired properties in PVA based hydrogel dressings for biocompatibility as well as industrial adaptability for large scale manufacture [1,2]. Hydrogel matrix, which is a three-dimensional structure, is generally made up of hydrophilic polymers like poly(vinyl alcohol), poly(vinyl pyrrolidone), poly(acrylic acid), etc. and holds significant amount of water in its porous structure. The desirable properties in a hydrogel dressings are function of basic polymer structure, ingredients and the production process. Synthetic and natural polymers along with other chemical ingredients are used for

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doi:10.1016/j.nimb.2006.11.101

making of hydrogels [3]. Some of the known methods of making hydrogel dressings using hydrophilic polymers include (i) physical method by repeated freezing and thawing (ii) chemical methods using chemicals like borax, boric acid, formaldehyde, glutaraldehyde, etc. and (iii) irradiation [3]. Work on formation of hydrogels of PVA by freeze–thaw method has been reported [4]. Some known hydrogels dressings use multi layer/laminates, foams dipped in gel like substance, jellies in collapsible tubes, gel pads, blends, etc. Most of the processes for manufacture of these hydrogels generally consist of distinct and separate steps of gel formation, cleaning of the gel and sterilization. Many of these formulations have number of synthetic chemical ingredients. Irradiation method is a cleaner process which does not require chemical initiators and crosslinkers. Hydrogels, being soft materials and containing large quantity of water, make their terminal sterilization practically difficult, using ethylene oxide and heat. Therefore, preservatives and antimicrobials are normally added in many of the available hydrogel dressings to keep them free from microbial contamination. The unique advantage of irradiation is that the process can be optimized to form and sterilize the gel dressing simultaneously. This results in reduction of steps in making of the dressing. A process developed and patented by Rosiak uses single step process wherein gel formation and sterilization takes place simultaneously [5]. The process involves the use of poly(vinyl pyrrolidone) as one of the major constituents along with agar-agar and plasticizers like polyethylene glycol, etc. Similar processes are being followed in Brazil, Syria, Philippines and Bangladesh to produce hydrogel dressings and studies on them have been reported [6–8]. However, PVA based hydrogels are preferable due to greater biocompatibility, economy and environmental friendly disposal. PVA can be disposed by incineration forming water and carbon dioxide and to some extent it is also bio-degradable. Unfortunately, PVA hydrogels have low mechanical strength and thermal stability. Therefore, different methods have been reported for increasing its strength, flexibility and heat stability [9,10]. These improvements require use of multistage processes, synthetic crosslinkers, plasticizers, humectants, etc. which are not desirable in hydrogel dressings. Hydrogel dressing made using only polysaccharides have also been reported [11]. The results of the studies carried out on radiation synthesis and development of PVA–polysaccharide based hydrogel dressing are described in this paper.

2. Materials and methods

2.1. Materials

PVA of average molecular weight 125,000 with 10–12% acetate content, natural polysaccharides agar-agar and carrageenan (kappa) were procured from M/s S.D. fine Chemicals and M/s Biosols India, respectively. These ingredients were used without any further purification.

Double distilled water was used for making aqueous solutions. Disposable plastic trays were used as containers for the gels. The trays were of $12\,\text{cm} \times 12\,\text{cm} \times 0.4$ dimensions.

Irradiation of samples were carried out in Gamma Chamber – GC-5000 (Supplied by BRIT, Mumbai, India) having a dose rate of 6.0 kGy/h and at ISOMED, gamma radiation sterilization facility for contract irradiation. The absorbed doses were measured using Ceric-Cerous sulphate dosimeters.

2.2. Gelation properties of natural polysaccharides

Gel softening temperatures of irradiated and non-irradiated agar and carrageenan gels were determined using thermomechanical analyzer, TMA-40 of Mettler Instruments. Gels were made by cooling, hot 1% aqueous solutions of non-irradiated and irradiated agar and carrageenan powder in quartz crucibles. For measurement, a constant force of 0.01 N was applied on the gels in quartz crucibles during heating between 35 °C and 150 °C at 10 °C/min in air. For differentiation of experimental results, quartz crucibles were filled to different depth with the polysaccharide solution.

2.3. Viscosity

Viscosity measurements were carried out using an Ubbelhode type viscometer at 26 ± 1 °C. PVA (8%) aqueous solution and PVA aqueous solution containing 0.2% of agar and carrageenan were autoclaved in 100 ml flask and then exposed to graded gamma radiation doses. Specific viscosity η_{sp} was measured as per Eq. (1):

$$[\eta_{sp}] = (t - t_0)/t_0, \tag{1}$$

where t_0 and t are the time of flow in viscometer for (i) 8% PVA aq. Solution (t_0) and its irradiated solution (t) (ii) 8% PVA aqueous solutions containing polysaccharide (t_0) and its irradiated solutions (t).

2.4. Preparation of hydrogel dressings

Hydrogel dressings (HD) used in the present study were produced by Varshney method [1] in the form of a sheet ($12\,\text{cm} \times 12\,\text{cm}$, 0.4 cm thick) by the process comprising the following steps:

(1) Preparation of aqueous solution of PVA, agar and carrageenan in distilled water.
(2) Heating the solution at 121 °C, 15 PSI for 15 minutes in autoclave.
(3) Pouring the hot solution in the trays and cooling to set the solution into gel, covering with polyester film and sealing in polyethylene bags.
(4) Gamma irradiation at 25–30 kGy.