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Research paper

Physico-mechanical properties of wound dressing material and its biomedical application

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ABSTRACT

A bioadhesive wound dressing material, based on gelatin, was prepared by solution casting, and its properties were evaluated. The tensile strength (TS) and percentage elongation at break (Eb) of the membranes were found to be 12.7 MPa and 40.4%, respectively. The buffer uptake and water uptake of the prepared membranes were found to be 298 and 312%, respectively, after 8 min. A scanning electron micrograph of the membrane revealed its uniform porosity, which is an essential criterion to be an ideal wound dressing. From microbial sensitivity analysis, it was found that the membrane had a significant resistance against infection. The wound-healing characteristics of the membrane were evaluated using a rat (*Rattus norvegicus*) model. Full-thickness wounds were created on the ventral side of the *Rattus norvegicus* and were dressed with the membrane; eco-plast was used as a control. The wound healing and bioadhesion were monitored at 3-day intervals by real-time imaging. The results revealed that the prepared membrane was more effective in healing the wound than conventional wound dressing.

1. Introduction

Wound healing is a dynamic process, and the performance requirements of the dressing can change as healing progresses. However, it is widely accepted that a warm, moist environment encourages rapid healing, and most modern wound care products are designed to provide these conditions (Winter, 1962; Barnett and Irving, 1991). Wound care often is labor intensive, requiring frequent attention by skilled professionals. Severe wounds (injury or burning) take millions of lives each year all around the world. Severe wounds damage the epithelium or even the endothelium of skin, which is the primary defense barrier of the body (Loke et al., 2000). People die due to severe infection and most likely due to dehydration (Hinrichs et al., 1992; Khil et al., 2003). Conventional wound dressing materials do not provide notable infection resistance. They also lack any water-retaining property to minimize the dehydration. But an ideal wound dressing material should control the wetness and humidity, provide bacterial resistance, and enhance the activities of the growth factors. It should have permeability for oxygen and carbon dioxide, and be able to absorb the wound exudate, and enhance the healing.

Biomaterials have taken part in the development of novel treatments over the last 30 years. The incorporation of natural materials such as gelatin, pectin, starch, cellulose, alginate, chitin, collagen, polyamino acids, hyaluronates, and dextran into synthetic wound dressings has been shown

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to enhance the healing process (Cardona et al., 1996; Grzybowski et al., 1997; Suzuki et al., 1998). The structures of these materials, primarily composed of sugar and/or amino acid residues, are analogs of protein and growth factor structures in the human body that may be more relevant for stimulating the appropriate physiological responses required for cellular regeneration and tissue restructuring in wounds. The development of biopolymers modified with stimulus molecules has added new dimensions in wound dressing for its fulfillment of the requirements to be a perfect wound dresser. An improved dressing can enhance both the rapidity of healing and the quality of the outcome, including reducing infection, pain, and scarring. An improved dressing also can reduce costs, by improving the rate of wound healing and thereby reducing the duration of treatment, and by allowing for less frequent and simpler attention by medical professionals. Improved methods for monitoring wound healing can facilitate better choice of treatment, and reduce costs by allowing for less frequent attention by medical professionals.

Gelatin is a well-characterized protein fragment obtained by partial degradation of water-insoluble collagen fiber, and it has been widely used in the biomedical field, because of its merits, including its biological origin, biodegradability, hydrogel properties, and commercial availability at a relatively low cost. It is also a biocompatible and very low antigenic material. Gelatin has also been used in medicine as a plasma extender wound dressing, an adhesive, and in absorbent pads for surgical use (Choi and Regenstein, 2000). Recently, gelatin has been demonstrated to exhibit activation of microphage (Klose et al., 1952; Wainewright, 1977) and high-hemostatic effects (Montero et al., 1999). Consequently, it has been used in a wide variety of wound dressings and as a biomaterial in tissue engineering (Gennadios et al., 1994).

One of the drawbacks of gelatin for tissue engineering applications is its solubility in aqueous media; therefore, gelatin-containing structures for long-term biomedical applications need to be crosslinked (Venien and Levieux, 2005). In this experiment, polyethylene glycol (PEG) was used as a crosslinker to modify the gelatin membrane as well as to increase the adhesiveness of the membrane. PEGs are water-soluble synthetic polymers, with general formula $HO–(CH_2CH_2O)_n–H$; they are non-toxic, biodegradable, biocompatible, and also non-antigenic (USFDA, 2006). PEGs are widely used in various applications including pharmaceuticals and biotech industries. They are also used as co-solvents, lubricants and stabilizers, bases in topical products, precipitants and crystallization agents for proteins, and as chemical agents for pegylation of proteins. The incorporation of PEG with gelatin has the aim of developing a material which would have good mechanical properties, be thermally stable in the human body, and have good swelling property and effective water absorption capacity; the most important thing is to develop a biocompatible material without any side-effect to the applied natural system. In this research, the design of a wound dressing material based on gelatin was studied. Preliminary laboratory tests as well as preclinical animal study of the produced membranes were conducted for the identification of their usability in wound dressing applications.

2. Materials and methods

2.1. Materials

Type-B gelatin (partial alkaline hydrolysis) was procured from E. Merck, Germany. The molecular weight was 10,000 g/mol. Polyethylene glycol (PEG) was obtained from BDH, England. Injectable ciprofloxacin was purchased from Square Pharmaceutical Ltd., Dhaka, Bangladesh. Rats (*Rattus norvegicus*) were purchased from the Animal Resource Department, ICDDR-B, Mohakhali, Dhaka, Bangladesh.

2.2. Methods

2.2.1. Preparation of gelatin-based membrane

Gelatin granules (10 g) were dissolved in deionized water (100 ml) with continuous stirring at 60 °C to make a viscous solution (the final volume was 50 ml). The solution was autoclaved for 15 min at 121 °C for sterilization. Then the solution was cast at room temperature. The films (membrane) were formed after 48 h of casting. The membranes of gelatin were collected, and then subjected to further drying in vacuum desiccators for 2 days. Then the membranes were stored in desiccators prior to testing. The membranes of gelatin/PEG were also prepared by solution casting. Different percentages of PEG (5–50% w/v) were added to the gelatin solution. The thickness of the membrane was 0.5 ± 0.1 mm.

2.2.2. Antibiotic incorporation and in vitro drug release studies

An antibiotic agent (ciprofloxacin) was incorporated into the gelatin/PEG membrane. Sterile injectable ciprofloxacin was used as the antibiotic agent because of its effectiveness as an antibiotic against air-borne bacteria as well as enterobacteriaceae (Mason et al., 1995; Jeff et al., 2002). Three different doses (0.05%, 0.1%, and 0.2% w/v) of ciprofloxacin-containing membranes were prepared by adding ciprofloxacin solution to the gelatin/PEG solutions during casting of the membrane. A drug release study of the membrane was performed by placing small disks of both antibiotic-added gelatin/PEG membrane and control (gelatin/PEG) membrane on a bacterial lawn. Antibiotic sensitivity (a zone of inhibition) was observed after overnight incubation at 37 °C and compared with that from blank gelatin membrane.

2.2.3. Measurement of pH

The pH of the gelatin/PEG solution was determined using a digital pH meter (Philip, PW-9409, UK) with an efficiency level of ± 0.3.

2.2.4. Mechanical properties

The mechanical properties, namely the tensile strength (TS) and percentage elongation at break (Eb), of the membranes were determined by using a Universal Testing Machine (INSTRON, model 1011, UK) with cross-head speed of 10 mm/min and gauge length of 20 mm. The load capacity was 500 N and the efficiency was within ±1%. The mechanical tests on gelatin-containing PEG membranes were performed at 65% relative humidity and at room temperature to enable identical moisture content.