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Imparting commercial antimicrobial dressings with low-adherence to burn wounds

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ABSTRACT

The objective of our study was to decrease the wound adherence of commercial silver based wound dressings by depositing a non-adherent layer. Our hypothesis was that this non-adherent layer will lower the dressing's adherence to burn wounds without compromising the antimicrobial activity or increasing the cytotoxicity.

A polyacrylamide (PAM) hydrogel layer was grafted on two commercial silver antimicrobial dressings (silver nanocrystal dressing (NC) and silver plated dressing (SP)) using a proprietary technique. The grafted PAM served as the non-adherent layer. Dressing adherence was measured with a previously published *in vitro* gelatin model using an Instron mechanical force testing instrument. The dressings were challenged with two clinically retrieved bacterial strains (Methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug resistant (MDR) *Pseudomonas aeruginosa*) with both a disk diffusion test, and a suspension antibacterial test. The cytotoxicity of samples to human neonatal fibroblast cells was evaluated with 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyltetrazolium bromide (MTT) assay.

Both untreated dressings showed high peeling energy: $2070 \pm 453\ J/m^2$ (NC) and $669 \pm 68\ J/m^2$ (SP), that decreased to $158 \pm 119\ J/m^2$ (NC) and $155 \pm 138\ J/m^2$ (SP) with the PAM deposition. Addition of the PAM caused no significant difference in zone of inhibition (ZOI) (disk diffusion test) or antibacterial kinetics (suspension test) against both bacteria ($p > 0.05$, $n = 6$) in either dressing. Survival of fibroblasts was improved by the PAM grafting from $48 \pm 5\%$ to $60 \pm 3\%$ viable cells in the case of NC and from $55 \pm 8\%$ to $61 \pm 4\%$ viable cells in SP ($p < 0.05$, $n = 12$).

It was concluded that PAM as a non-adherent layer significantly decreases the adherence of these two commercial antimicrobial dressings in an *in vitro* gelatin model while preserving their antimicrobial efficacy, and reducing their cytotoxicity.

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1. Introduction

According to data published by World Health Organization (WHO), approximately 270,000 people died in 2012 due to burns [1]. Bacterial infection in wounds is a significant factor jeopardizing healing and can lead to patient's' death [2]. Human skin is a protective barrier against microorganisms. With injury, pathogens can easily find their way to the underlying tissue [3]. Necrotic tissue in the wound bed can also act as a medium for the growth of microorganisms [4]. After injury, wounds are prone to infection from existing skin flora, such as *Staphylococcus aureus* [2]. Furthermore, the hospital environment and health practitioner's hands are other possible sources of infection transmission [2].

After a burn the following steps can help reduce infection: cleansing the wound, and protecting the wound from outside environment [5,6]. A wound dressing can be used to provide protection for the wound from external pathogens. Recently, the use of topical wound dressings with antimicrobial activity has been increasing [7–9]. There are different types of antimicrobial agents used in burn dressings; silver, iodine, chlorhexidine and honey are examples [7]. The most commonly used agent is silver. Among the available dressings for burn wounds several impregnated with silver are: Acticoat Flex (Smith & Nephew Medical Limited, England) (referred to as NC), and Silverlon (Argentum Medical, LLC, United States) (referred to as SP).

Antimicrobial activity of a wound dressing is not the only criterion that makes a dressing favorable for clinical use [10]. Dressing adherence to the wound bed is also a challenge. Exudate from the wound can penetrate into a dressing's structure and cause adherence to the wound after drying [11]. Furthermore, the protein structure of exudates can chemically bond to the dressing (mostly hydrogen bonding) [11]. Dressing adherence results in pain and trauma during removal and can lead to delay in wound's healing [12].

According to a survey by Hollinworth and Collier [13], 81% of clinical practitioners mentioned the highest level of pain was experienced during dressing removal.

Fibroblast cells are common cells in connective tissue and are mostly known for their role in wound healing [14–16]. When the tissue is injured, these cells start to migrate and deposit collagen in the damaged site, making the healing process easier [16]. Since the viability of fibroblast cells are of great importance in the healing process, cytotoxicity of the wound dressing on these cells are especially worthy of note. Ideally burn dressings should not compromise the healing process [17].

Among available materials for dressings, hydrogels are non-adherent to cells and tissues [18]. They are biocompatible three dimensional cross-linked networks [12,19]. Hydrogels have been previously used as a substrate for loading and releasing antimicrobial drugs [20–23]. Furthermore, their promising properties such as ability to absorb and hold water within their structure, makes them flexible and compatible with skin [12,19].

PAM hydrogel network has been used in our research group for modifying wound dressings [24,25]. PAM is a nontoxic polymer with its swelling ability independent of pH [26].

In a previous work done in our research group, polyacrylamide hydrogel was used as a low-adherent coating for poly(ethylene terephthalate) (PET) dressing [24]. Moreover, antimicrobial agents such as silver nanoparticles and N-chloramine were loaded into the hydrogel matrix, resulting in an antimicrobial dressing with low adherence to the wound bed [24].

The current study was designed to investigate the effect of PAM hydrogel deposition on the adherence property of commercially available silver based burn wound dressings. We hypothesized that deposition of a PAM hydrogel layer on the surface of commercially existing silver based wound dressings can reduce adherence to the wound without compromising antimicrobial activity.

2. Materials and methods

Pieces of 6 cm × 14 cm commercially available burn wound dressings, NC and SP were grafted with a cross-linked PAM layer. Community-associated (CA)-MRSA #40065 and multi-drug resistant (MDR) *Pseudomonas aeruginosa* #73104 were used as the model microorganism to challenge all the biocides. Both were clinical strains obtained from the CANWARD (Canadian Ward Surveillance) study assessing antimicrobial resistance in Canadian hospitals, www.canr.ca. ATCC-PCS-201 neonatal human dermal fibroblast was purchased from Cedarlane Corporation, Canada.

2.1. *Peeling force test*

The Instron 5956 machine (Instron, MA/United States) was used for peeling force testing. Treated and untreated dressings (3 cm × 14 cm) were first immersed in deionized (DI) water. NC and SP (treated and untreated) samples absorbed water up to 5 ± 0.1 and 3 ± 0.1 times their weight respectively. Samples were then spread on a clean surface and poly-tetrafluoroethylene (PTFE) frames with a 60 mm × 15 mm opening were placed over them.

To simulate wound exudate adherence to the dressing, a 40 wt% gelatin type A (purchased from Fisher Scientific, Ottawa, ON/Canada) was prepared with 70 °C DI water and poured into the PTFE molds. The gelatin/dressing modules were subsequently placed in an incubator at 32 °C (temperature of human skin) and 75% humidity (mimicking a moist wound environment) for 24 h. Our *in vitro* gelatin model was based on a simulation model by Andrews and Kamyab [11]. Gelatin in its viscose form can penetrate through the porous dressing and adhere to the wound dressing's fibers after solidification. This is similar to the action of proteinaceous exudate.

The peeling force test was done by peeling the dressing off samples at a constant rate of 100 (mm/min) with 180° peeling angle. The peeling test was done in triplicate and the average load needed to remove the dressings was recorded.

2.2. *Disk diffusion test*

Unless specified, the disk samples for this antibacterial test were cut after the deposition of PAM hydrogel layer. To