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Novel cellulose based materials for safe and efficient wound treatment

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ABSTRACT

The present study aims at achieving effects of improved hydrophilicity and microorganism inhibition, which are rarely simultaneously present in wound dressings. Viscose fibers in their non-woven form were modified using two different pathways. Effects of a two-step procedure, i.e. alkaline or oxygen plasma treatment followed by the attachment of silver chloride nanoparticles were compared to a one-step procedure, i.e. ammonium plasma treatment, which results in both desired material characteristics simultaneously.

The surface properties of untreated and differently modified cellulose samples were analyzed by X-ray photoelectron spectroscopy (XPS), scanning electron microscopy (SEM), in vitro silver release, and hydrophilicity measurements. The treatment effect on antimicrobial activity was determined by the AATCC 100-1999 standard test. In light of the introduced wound dressing preparation procedures and the desired wound dressing characteristics, the effectiveness of the used procedures was evaluated. Antimicrobial activity was proven against all Gram negative bacteria, while the Gram positive bacteria survive the as-prepared samples. Hydrophilicity was proven to be excellent using both preparation procedures. The mentioned results prove the potential of the used procedures and encourage future developments toward the clinical proof of concept.

1. Introduction

Successful wound treatment is not possible without assuring and maintaining proper hydrophilicity and an effective antimicrobial activity (Thomas, 2008). There are many known super-hydrophilic materials of synthetic origin (Chen & Chiang, 2010; Klode et al., 2011; Lalani & Liu, 2012), which can be used in wound treatment. Although their hydrophilic properties are excellent, they have several other drawbacks, ranging from their inability to be additionally functionalized to gain antimicrobial properties, their possible irritation on human skin and a higher production cost (Klode et al., 2011). Natural cellulose like cotton is rarely used as a wound dressing absorber due to rather low purity as well as relatively high production costs. Cellulosic fibers, i.e. viscose, in a form of woven or non-woven textiles are the most used wound dressing base materials. Although the sorption capacity as well as the wettability rate of viscose is much better than for many other similar materials (e.g. lyocell, modal), these properties are still not optimal and definitely below the capacities of alginate (Rowe, Sheskey, & Quinn, 2009).

Materials with a superior sorption capability combined with an efficient infection control, with minimized unwanted side effects are nowadays sought for the preparation of advanced, healing promoting wound dressings. In order to achieve both desired effects, several procedures are available that mostly combine different functionalization steps one after another. Improvement of cellulose absorption properties is mostly acquired by co-polimerisation (Hengstberger, Kaltenecker, & Oppermann, 1999), doping (Junping, Xin, Dequan, & Li, 2010), deposition (Hyde et al., 2011) and by chemical processes, e.g. alkaline treatment, bleaching (Durso, 1978; Fengel & Wegener, 1984; Freytag & Donzé, 1983; Lewin, 1984). Controlling bacterial or fungal growth on fabric can be achieved using biologically-active polymers (Breitwieser, Spirk, et al., in press; Chekmareva, 2002), by the inclusion of potential antimicrobial compounds, e.g. collagen (Hart, Silcock, & Gunnigle, 2002),

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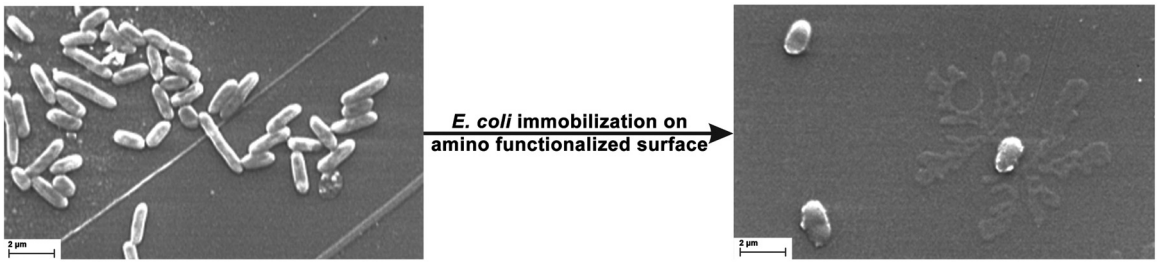

Fig. 1. Interaction of bacterial cells with surfaces with amino functional groups leads to their destruction (Reichel, 2012).

and chitosan (Baohua, Hu, & Meng, 2009; Jing, Zhang, Zhang, Zhao, & Yuan, 2009; Madhumathi et al., 2010; Watthanaphanit, Supaphol, Tamura, Tokura, & Rujiravanit, 2010; Wu et al., 2004), by binding drugs onto the polymer surface (Kontogiannopoulos, Assimopoulou, Tsivintzelis, Panayiotou, & Papageorgiou, 2011; Watanakunakorn & Glotzbecker, 1978) or by chemically modifying the polymer structure through introduction of various functional groups such as amino (Gilbert & Moore, 2005; Mikhaylova et al., 2011; Zemljic Fras, Persin, & Stenius, 2009), hydroxyl, carboxyl, aldehyde (Chekmareva, 2002; Hart, Silcock, & Gunnigle, 2002), and combinations of carboxyl and amino, epoxy, methoxy, thiol and sulphone. Amino groups are known to adsorb onto the bacterial cell wall, which provides the molecules bearing this functional groups to diffuse into the cell interior, where the disruption of the cytoplasmic membrane finally leads to the bacterial cell destruction (Reichel, 2012). Typical bacterial cell destruction due to the interaction with an amino functionalized surface is shown in Fig. 1.

Many heavy metal cations (i.e. Hg^{2+}, Pb^{2+}) have antimicrobial activity, but are very toxic. Other metal ions such as e.g. cooper (Cady, Behnke, & Strickland, 2011; Esteban-Cubillo, Pecharromán, Aguilar, & Moya, 2006), and zinc (Lee & Huang, 1995) have been identified as acting destructively toward microbes, but were not found safe for patients, unless prepared in specific forms (Fraser, Cuttle, Kempf, & Kimble, 2004; Percival, Bowler, & Russell, 2005) and the environment.

Many different products with high antimicrobial activities are commercially available for quite a long time (Kuroyanagi et al., 1994; Robb & Nathan, 1981). Among these, is silver certainly one of the most important antimicrobial agents used in wound treatment (Corum et al., 2011). Silvers broad-spectrum antimicrobial activity is still not fully understood, but is believed to be connected with the silvers ability to interact and denaturize various biological macromolecules by interacting with their thiol-, carboxyl, phosphate-, and imidazole-functional groups (the so-called oligodynamic effect). For example, these interactions are the cause of interferences in the respiratory chain in the cytochromes of some bacteria; additionally can silver ions interfere with components of the microbial electron transport system, bind DNA, and inhibit DNA replication (Lansdown, 2002; Lok et al., 2006). While both mentioned cases encourage further use of silver based products, is the lack of specificity of such interactions also the reason for citocompatibility issues (Eid & Azzazy, 2012; Kokura et al., 2010; Liu, Sonshine, Shervani, & Hurt, 2010; Seetharaman et al., 2011). In recent years several different research groups pointed out that the silver release from wound dressings can have cytotoxic effects on the healthy tissue (AshaRani, Low Kah Mun, Hande, & Valiyaveettil, 2008; Kim, Yang, & Ryu, 2010; Lina et al., 2010). Due to this, novel approaches were developed, which can either lead to a safe silver binding, meaning that the antimicrobial activity is preserved, while the silver stays bound to the wound dressing over the course of its application (Breitwieser, Moghaddam, et al., in press; Eid & Azzazy, 2012) or rely on the use of new antimicrobial agents that act specifically only on desired pathogens (Infante et al., 2004; Malmsten, 2011).

In this study we prepared two different procedures to maximize the efficacy of achievement desired wound dressing characteristics. The developed procedures were used for the preparation of cellulose-based wound dressing materials and were compared regarding the desired dressing surface characteristics—optimal hydrophilicity and a safe, efficient antimicrobial activity. The two-step procedure consists of a pre-treatment, i.e. alkaline or oxygen plasma treatment for improving absorption properties, which is followed by a sol–gel procedure for the attachment of antimicrobial silver chloride nanoparticles. The applied sol–gel method was chosen due to its capability to effectively attach silver chloride nanoparticles onto cellulose materials, as shown in our previous study (Pivec et al., 2012). A similar formulation was also used by other researchers (Tomsic et al., 2009) with the same emphasis–improvement of the potential to be used in the development of future wound dressings. The second used pathway was a one-step procedure, introducing plasma treatment using ammonium gas to simultaneously obtain improved sorption and antimicrobial properties.

Elemental surface chemical composition was obtained by X-ray photoelectron spectroscopy, while the sample morphology was investigated using scanning electron microscopy (SEM). Silver release from materials was monitored using the Franz static diffusion cell, while its concentration was determined using atomic absorbance spectrometry (AAS). Improved viscose non-woven hydrophilic properties were characterized by water up take monitoring, while antimicrobial properties were determined by AATCC 100-1999 standard test (American Association of Textile and Colorists, 1999).

2. Experimental

2.1. Materials

A cellulose material, as regenerated cellulose fibers (CV) in its non-woven form was used, as produced by KEMEX, The Netherlands. The surface mass of the fabrics was 175 g/m^2 (SIST ISO 3801) and the thickness under normal conditions was about 1.7 mm (SIST EN ISO 5084). The untreated sample is noted as U.

2.2. Preparation procedures

2.2.1. Two-step pathway

1.STEP-a: Alkaline treatment

Viscose non-woven was impregnated using an alkaline solution (53 g/L of NaOH; ratio 1:10; pH = 13.1). The treatment was performed for 5 min at room temperature.

After treatment, the samples were rinsed with distilled water until the conductivity of the rinsing water reached a conductivity of 3 μS/cm. The samples in a stretch form were dried in an oven