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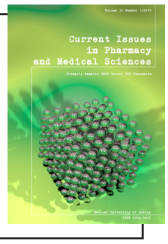

Medical textiles with silver/nanosilver and their potential application for the prevention and control of healthcare-associated infections – mini-review

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ABSTRACT

Healthcare-associated infections (HAI), especially those in hospitalized patients, can be regarded as an important public health problem worldwide. In this article we presented an overview on the use of antimicrobial textiles, including those with silver/nanosilver, as a new approach to countering HAI by reducing the potential risk of the pathogen transmission between patients and healthcare workers. The strong antimicrobial *in vitro* activity of these engineered textiles was confirmed *in vitro* against several HAI-associated pathogens, including multiresistant strains belonging to alert pathogens. However, according to literature data, the sole use of antimicrobial clothing by healthcare workers appears to not be sufficient for the prevention and control of HAI. Further comprehensive and controlled studies are needed to assess the real-time efficacy of the antimicrobial textiles in healthcare settings. Moreover, there is a need to control the silver use not only for medical applications, but also for non-medical purposes due to a possibility for the emergence and spread of silver resistance among microorganisms, especially Gram-negative bacteria.

INTRODUCTION

Healthcare-associated infections (HAI), especially hospital (nosocomial) infections, can be regarded as an important public health problem worldwide. These infections have a massive impact on morbidity and mortality, and come with a substantial cost and burden on healthcare institutions. According to the European Center for Disease Prevention and Control (ECDC), approximately 4 million patients are estimated to acquire HAI in the *European Union* each year and approximately 37,000 deaths result directly from these infections. A large proportion of these are due to the life-threatening infections caused by the most common multidrug-resistant bacteria, i.e. *Staphylococcus aureus*, *Enterobacteriaceae, Pseudomonas aeruginosa* for which the number of directly attributable deaths is currently estimated at 25,000 [1].

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HAI are due to the interaction of three factor groups: (i) patient-associated factors, (ii) healthcare-associated factors and (iii) environmental factors. There are three basic principles for the prevention and control of HAI: (i) remove sources of infection by treating infections and practising appropriate decontamination procedures, (ii) prevent transmission by way of good hand hygiene, aseptic procedures and appropriate isolation, (iii) enhance immunity with good nutrition and appropriate antibiotic prophylaxis or vaccination. New approaches to combatting HAI have been introduced recently, including antimicrobial medical textiles. These serve as horizontal approaches that reduce the potential risk of a broad range of infections as they are not pathogen-specific [2].

Transmission of microorganisms, including HAI-associated pathogens, involves three elements: a source, a susceptible host and a mode of transmission. In the healthcare setting, the movement of pathogens between the patient, healthcare providers and the environment, is known as the transmission or the epidemiologic triangle. Strategies to decrease the pathogen`s movement in the transmission triangle can be generally focused on the patient (*e.g*. antimicrobial-impregnated clothing), the environment (*e.g*. antimicrobial surfaces or textiles), or the healthcare workers, including doctors, nurses, laboratory personnel and technical professionals (*e.g.* antimicrobial-impregnated clothing) [3,4].

TEXTILES WITH SILVER/NANOSILVER AND THEIR ANTIMICROBIAL PROPERTIES – PROS AND CONS

Textiles impregnated/coated with silver/nanosilver take an important place among those with antibacterial and/or antifungal properties. These engineered textiles have multiple medical and non-medical applications [5-8].

Silver has been used for centuries for certain supposed beneficial effects, often for hygienic purposes and more recently as antimicrobial agents. The antimicrobial activity of silver ions is due to the targeting macromolecules such as proteins and DNA or RNA. Sulfhydryl groups from cysteine (Cys) residues, being a ligand for metal and/or cofactors, is the main molecular bulls-eye for silver ions in several metalloproteins, including those involved in cell respiration and energy conservation. The effect results in enzyme inactivation and disturbance of vital cell processes. Apart from sulfur, silver has a high affinity to phosphorus as well. Silver ions binds to the bases of nucleic acids, forming complexes with DNA or RNA, followed by gene mutations and/or inhibition of replication. What is more, silver ions may cause morphological and structural changes of the cell envelope, i.e. the cell wall and cell membrane, together with the enhancement of their permeability – which leads to cell lysis. Silver can be also regarded as an agent predisposing to oxidative stress in bacterial cells. Due to these reasons, silver can be regarded as an important biocidal agent with a wide spectrum of activity against both Gram-positive and Gram-negative bacteria, as well as fungi [9].

Silver particles having at least one dimension that is less than 100 nm and containing 20-15,000 silver atoms are termed ‘nanosilver particles’ or ‘nanosilver’. Nanosilver particles (nanosilver) are increasingly used in a variety of products, primarily for their strong antimicrobial properties. It is supposed that in aqueous solutions, nanosilver releases the silver ions responsible for its antimicrobial activity. However, comparative studies on the antimicrobial effect of silver salts such as nitrate, citrate and chloride have revealed that nanosilver have stronger activity than silver ions themselves. This can be explained by the fact that nanosilver possesses extremely large surface area which allows better contact with microbial cells [10].

The increasing use of silver/nanosilver textiles may result in the growing problem of microbial resistance analogous to that observed for antibiotics. However, it should be noted that due to the pleiotropic molecular basis of antimicrobial silver/nanosilver effect, the development or selection of resistance appeared to be limited. In recent literature data [6], two types of silver resistance in Gram-negative bacteria have been described – endogenous resistance based on mutations, and exogenous resistance associated with horizontal transfer of resistance genes. Mechanisms of both endo- and exogenous resistance involve the limitation of silver accumulation in the periplasm, including silver efflux. Gram-negative bacteria can also develop resistance to nanosilver after repeated exposure, but this resistance could evolve without any genetic changes [11,12]. It should be stressed that several important nosocomial pathogens, including multiresistant strains belong to Gram-negative bacteria, in particular, the carbapenemases-producing *Enterobacteriacae* [1]. Due to these observations, there is a need to monitor the emergence and spread of silver- and nanosilver-resistant isolates, especially among Gram-negative bacteria, in order to preserve silver’s utility for various applications.

There are several studies showing the significant antibacterial and antifungal inhibitory effect *in vitro* of silver/nanosilver containing textiles. In the experiments, the microbial growth reduction reached almost 100% after 24h-incubation. These textiles were also revealed to possess inhibitory effect against several pathogenic bacterial and fungal species, including resistant/multi-resistant strains [13-15].

The wide range of applications of silver/nanosilver holds potential risk for human health. Thus, in order to define the health-risk assessment of silver/nanosilver textiles, it is important to quantify and to characterize the silver species released from a textile, as well as to determine and to characterize the silver species penetrating into the skin. Bianco *et al*. [16] applying the *in vitro* model of skin sample preparation, found that the use of commercially available, nanosilver-containing textiles leads to the release of silver and to its penetration into the skin, followed by the formation of aggregates in the epidermis and dermis. It is supposed that these aggregates may slow down systemic absorption of silver, being simultaneously a reservoir of silver with prolonged release and being responsible for its local effects. However, the presence of silver within the skin makes it systematically available, allowing for the distribution throughout the organism, especially in case of the damaged skin. This may lead to toxic effects. In addition, nanosilver was shown to induce the production of proinflammatory cytokines such as interleukin-6 and interleukin-10 and to influence selenium metabolism, leading to the decreased incorporation of selenium into selenoproteins, *e.g.* glutathione peroxidase or thioredoxin reductase. The mentioned enzymes play a vital role in the defense against oxidative stress.

On comparing the toxicity of silver and nanosilver, it should be noted that the toxic effects of nanosilver are dependent not only on the dose, but also on the particle size. Indeed, smaller nanosilver particles (10 and 20 nm) are more toxic than that the larger ones (40, 60, and 100 nm). Moreover, the evaluation of safety of the nanosilver-containing products requires a comprehensive approach – including ascertaining the influence of nanosilver on the human body, together with its biotransformation in the organism and in the environment [10].

Despite these limitations, textiles with silver/nanosilver impregnation, due to their strong antimicrobial activity, as well as the relatively low risk of biological toxicity and environmental toxicity, possess a wide spectrum of applications, including that for medical purposes. These engineered textiles can be regarded as a new approach to reducing surficial microbial contamination [2,3,5-8].

THE PRACTICAL USE OF ANTIMICROBIAL TEXTILES IN HEALTHCARE SETTINGS

Medical textiles can be regarded as an important reservoir of potential and opportunistic pathogens involved in HAI, hence, contributing to their transmission. Microorganisms colonizing the patient skin, nasal cavity and the anus/ genitalia areas, as well as that present in the body fluids, secretions and/or excreta often contaminate these items. Textiles may, hence, be regarded as a good substrate for growth of microorganisms under appropriate moisture and temperature conditions [4]. Antimicrobial textiles have, therefore, attracted a great deal of interest in recent years due to their antimicrobial properties and thus the potential for reducing the transmission of HAI-associated pathogens. Medical textiles include protective cloths, mattresses, bed cloths, wound dressings or bandages, etc. [2,3,5-8].

However, little literature data are available concerning the effect of antimicrobial silvered/nanosilvered medical textiles in hospital settings in the aspect of the reduction of the prevalence of HAI-associated pathogens, and thus the reduction of HAI incidence. Of note, most articles were focused on their use in the hospital staff clothes to reduce their bacterial contamination and transmission [17-20].

Openshaw *et al*. [17] undertook an experiment in which hospital patient textiles were laundered by way of a novel silver-based procedure. In this study, two samples were collected from each textile: upper and lower areas on centerline of bottom fitted sheets and areas corresponding to chest and suprapubic area of gowns. According to the data obtained, the treatment resulted in a significant decrease in microbial contamination as compared to conventional treatment (*e.g*. from 83% to 48%). Herein, the textiles sampled post-patient use had decreased contamination in terms of total aerobic bacteria count, as well as in the prevalence of *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA). However, while statistically significant reduction was observed in case of total aerobic bacteria and *S. aureus*, the low prevalence of MRSA was a limitation to drawing a statistically significant conclusion in this case.

Groß *et al*. [18] performed a study in emergency medical settings in order to test whether the wearing of silver-impregnated clothes by emergency service workers would reduce microbial contamination. The experiment had a duration of one week. They found no significant differences in the extent of microbial contamination between conventional and the silver-impregnated clothes. These authors concluded that a larger sample size should be considered in order to verify this results.

Similar studies were performed by Condó *et al*. [19]. They evaluated the microbial contamination of hospital staff uniforms made from silver-containing textiles in a comparison to conventional uniforms; these uniforms were used by doctors, nurses and allied health assistants working in different hospital wards (pediatrics, surgery and long-term care unit). Evaluation of the contamination was carried out comparing the number of colony forming units (CFU) recovered at the beginning and at the end of the work shift in terms of the prevalence of bacterial species from *Micrococcaceae*, *Enterococcaceae*, *Enterobacteriaceae* and *Pseudomonadaceae* families. For each uniform, six samplings were performed (three at the beginning and three at the end of the work shift) choosing as contact points three areas frequently in contact with hands and at risk of contamination: right pocket, left pocket and small pocket. In this experiment, the increase in the total viable counts from beginning to end of the work shift was slightly lower for experimental than traditional uniforms, but this difference was not statistically significant. The authors concluded that despite the not entirely encouraging results, the use of silver as a antimicrobial agent has potential in countering HAI through the breakdown of hospital pathogen transmission routes.

In the data obtained during the Antimicrobial Scrub Contamination and Transmission (ASCOT) trial [20], antimicrobial-impregnated scrubs, including silver-containing cloths, were not effective at reducing bacterial contamination as compared to traditional cloths measured as the sum of colony-forming units (CFU) of bacteria identified on nurse scrubs from each clothing location. These studies enrolled nurses from medical and surgery intensive care units of the university hospital, and samples for microbiological analysis were collected during 3 consecutive 12-hour shifts in the intensive care unit. The obtained results confirmed that the clothing of healthcare providers regularly becomes contaminated with important HAI-associated pathogens and, as a result, can act as their reservoir or route for transmission. The authors proposed that future studies of antimicrobial-impregnated textiles should be focused on textiles that have frequent and long-term contact with patients, such as bed linens and gowns.

CONCLUSION

The presented overview on antimicrobial textiles, including those with silver/ nanosilver, that used by healthcare workers, reveals that this strategy alone appears to be not sufficient for the prevention and control of HAI. This is despite the strong antimicrobial *in vitro* activity of these engineered textiles. However, further comprehensive and controlled studies are needed to assess the real efficacy of such antimicrobial textiles in healthcare settings. It must be underlined that the silver used for medical applications should be controlled to avoid its overuse, while the silver used for non-medical purposes should be restricted in order to prevent the emergence and spread of silver resistance among microorganisms, especially Gram-negative bacteria.

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