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Percutaneous penetration of silver from a silver containing garment in healthy volunteers and patients with atopic dermatitis

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HIGHLIGHTS

- Silver is increasingly used in functionalized products for consumers and medicinal products.
- Dermal absorption of silver after wearing a silver containing garment did not exceed the current reference dose.
- Dermal absorption of silver in healthy volunteers and patients with atopic dermatitis did not significantly differ from each other.
- Dermal exposure to silver containing textile did not lead to increased levels of IL-1 cytokines in the stratum corneum.

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ABSTRACT

Human data on dermal absorption of silver under "in use" scenario are scarce which hampers health risk assessment. The main objective of the present study was to determine percutaneous penetration of silver after dermal exposure to silver containing garment in healthy individuals and atopic dermatitis (AD) patients. Next to assess pro-inflammatory effect of silver in the skin. Healthy subjects ($n = 15$) and patients with AD ($n = 15$) wore a sleeve containing 3.6% (w/w) silver on their lower arms for 8 h during 5 consecutive days. The percutaneous penetration parameters were deduced from the silver concentration-depth profiles in the stratum corneum (SC) collected by adhesive tapes. Furthermore, silver was measured in urine samples collected before and after exposure. Inflammatory response was assessed by measuring IL-1α and IL-1RA in the exposed and non-exposed skin sites. Dermal flux of silver in healthy subjects and AD patients was respectively 0.23 and 0.20 ng/cm^2/h. The urine silver concentrations showed no increase after exposure. Furthermore, exposure to silver did not lead to the changes in the profiles of IL-1α and IL-1RA. Dermal absorption of silver under "real life scenario" was lower than the current reference dose. Furthermore, dermal exposure did not lead to altered expression of inflammatory IL-1 cytokines in the skin.

1. Introduction

Antimicrobial properties of silver have been recognized since ancient times. Silver has mainly been used for medical purposes *e.g.* in wound care, medicating clothing for health care personnel and in garments designed to combat superinfections in patients with atopic dermatitis (AD). The treatment of wounds and burns with silver evolved from topical application of the silver nitrate solution

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followed by silver sulfadiazine cream and more recently by medical garments and dressings containing silver salts or metallic silver (including nanosilver) (Moiemen et al., 2011). Nowadays, silver is also increasingly used in functionalized products for consumers like in outdoor- and sport clothing, and personal hygiene products aiming at prevention of malodour. The most used form of silver in textiles are silver salts (79%) followed by metallic silver and silver ion exchangers (respectively 13% and 8%) (Windler et al., 2013). As silver containing textiles are in direct contact over large body surface areas for prolonged periods this has raised concerns over possible adverse health effects, also realizing that these products are worn by individuals who might be increasingly susceptible, *e.g.* children and individuals with skin diseases. For substances in textiles no registration is required in many EU countries, since textiles in the EU are treated as articles (von Götz et al., 2013). Substances in articles also do not need to be listed on a product label or be evaluated according to their potential for consumer exposure (von Götz et al., 2013). Dermal exposure to silver might potentially lead either to local skin effects or systemic adverse effects after its absorption in the body (Samberg et al., 2010). The likelihood of such effects is dependent on the amount of silver which penetrates into and across the skin. The *in vivo* data on percutaneous penetration of silver from clothing and garments under "in use scenario" are scarce. Furthermore, little is known on dermal absorption of silver in the individuals with impaired skin barrier. Reduced skin barrier can be intrinsic, like in patients with AD, or acquired, *e.g.* due to skin irritation caused by sweating or exposure to skin irritating chemicals, UV light or mechanical friction. In addition to the skin barrier condition, actual exposure can be influenced by various factors that can influence migration of silver from fabrics like skin pH and temperature, physical stress acting on the fabrics (wear -and- tear), type of silver and the way it is incorporated in the textile (von Götz et al., 2013).

In fabrics, silver can be present as metallic silver in a natural crystalline or nano state which ionizes in the presence of water or body fluids. The antimicrobial action of silver or silver compounds is believed to be proportional to the bioactive silver ion (Ag^+) released.

In the present study we investigated the percutaneous absorption of silver in healthy individuals and patients with AD under "real life" scenario. AD patients have been selected from two reasons. Firstly, AD patients, in particular children, are frequent users of silver containing garments due to often occurring bacterial superinfections. Secondly, one of the main features of AD is reduced skin barrier, thus they represent a model for damaged skin barrier (Kezic et al., 2014). In addition to percutaneous penetration we investigated for possible proinflammatory effects associated with dermal exposure to silver and measured the levels of the inflammatory mediators, interleukin (IL) cytokines, IL-1 and IL-1RA in the skin after exposure to silver.

2. Materials and methods

2.1. Investigational material

For this study the Argentum company (Geneva, IL 60134, USA) provided two sleeves marked with "L" (left arm) and "R" (right arm) in 5 different sizes to avoid that the sleeves are not too tight or too loose. One sleeve contained silver, the other one was a placebo, *i.e.* silver free. The participants got 2 pairs of sleeves. The silver containing garment, registered as medical device class I powered by Silverlon® technology, consisted of 79% Micromodal fibre, 13% Polyamide Ag and 7% Lycra. The surface of the fibers are covered by a layer of 0.2–0.4 μm of pure metallic silver using an electroless chemical plating method. The content of silver in the textile was 3.6% (w/w). A fiber coated with pure silver is knitted in such a way that silver yarn lies exclusively on the inside of the textiles. The SEM/EDX (Scanning Electron Microscopy/Energy-dispersive X-ray spectroscopy) images of the fibers containing silver (Spectrum 2) and silver free fibers (Spectrum 1) are shown in Fig 1. The area of

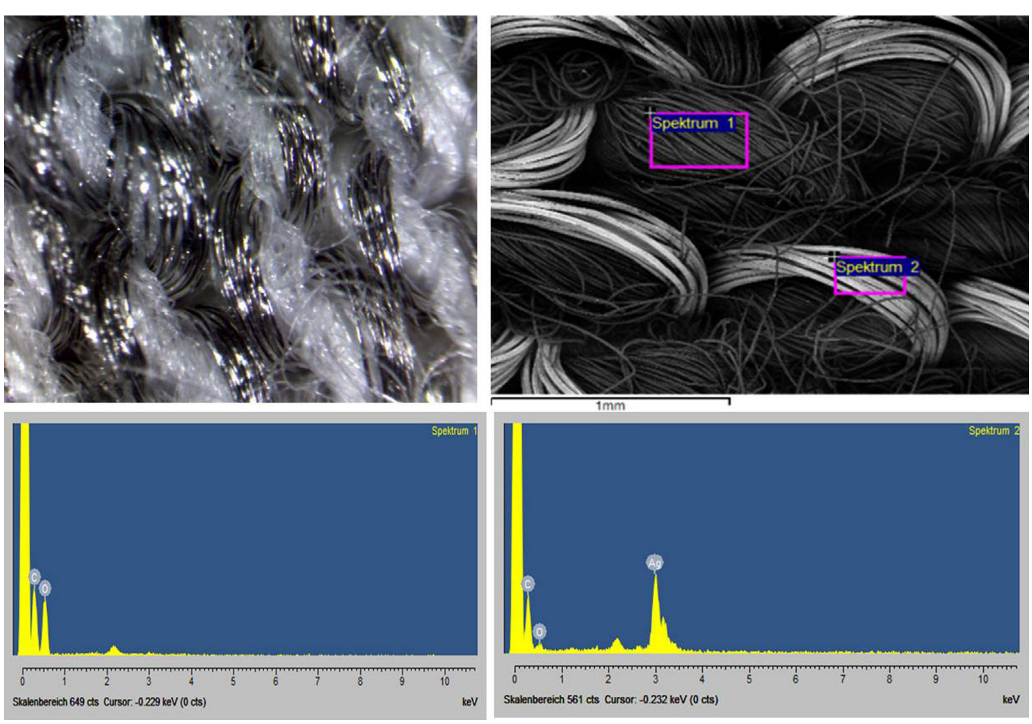

Fig. 1. Scanning Electron Microscopy images of the Silverlon® sleeve (Upper level) and Energy-dispersive X-ray spectra of the silver free fiber (Spektrum 1) and silver coated fiber (Spektrum 2) (Lower panel).