Connecting evidence to outcomes

The silver release profile of antimicrobial wound dressings: standardizing *in vitro* evaluations

Sharon Lindsay, Michelle DelBono, Ryan Stevenson, Sally Stephens, Breda Cullen
Systagenix Wound Management, Gargrave, UK

Systagenix WOUND MANAGEMENT

Abstract

Despite the abundance of silver-containing dressings to treat chronic wound infections, there is no standard method to evaluate their silver release, making it difficult for cross-study comparisons. This is compounded by the use of water or saline to elute silver from such dressings, which gives different results and does not adequately reflect the composition of wound exudate. To mimic the release of silver from elemental and compound (ionic) silver-containing dressings in exudating wounds, we have developed a method using an artificial wound fluid medium.

The silver release profile of two elemental and two compound silver dressings was determined using atomic absorption spectrometry (AA). Samples of uniform shape and size of each dressing were placed in either 20 mL of simulated wound fluid containing albumin, de-ionized water, or solutions containing sodium chloride, and incubated in a circulating water bath at 37ºC, 60 rpm for 7 days. These solutions were replaced periodically with an equal volume of fresh fluid: spent solution was retained for AA analysis.

Results demonstrate that from Day 1 to Day 7, the amount of silver released/detected for all dressings was substantially higher with simulated wound fluid or de-ionized water containing albumin than with solutions containing sodium chloride or de-ionized water only. We believe this is due to the presence of protein (albumin) in wound fluid, which can affect silver solubility.

Silver release evaluations should be standardized to draw meaningful comparisons between dressings: the amount of silver released from dressings tested differed according to the elution solution. We propose that an simulated wound fluid-containing albumin more closely mimics the composition of an exudating wound, and should be used when evaluating the silver release of dressings.

Objective

- To determine the silver-release profile of silver containing dressings in a range of different solutions.

Methods

- The silver-release profile of 4 dressings was investigated (SilverCel* Non-Adherent [Dressing A]; SilverCel* [Dressing B]; Aquacel* Ag [Dressing C]; Maxorb Extra* [Dressing D]). Samples (5 x 5 cm) of each dressing were placed in 20 mL of simulated wound fluid (2% bovine albumin, 0.02 M calcium chloride dihydrate, 0.4 M sodium chloride, 0.08 M tris methylamine in de-ionized water, pH 7.5) and incubated in a circulating water bath at 37ºC, 60 rpm for 7 days. Spent SWF was replaced every 24 hours with an equal volume of fresh SWF: the spent solution was retained for AA analysis (Perkin Elmer AAnalyst 200).
- To determine the affect of the elution medium on the silver-release profile of silver-containing dressings, the silver-release profile of Dressing A was investigated after 24 hours incubation in the following solutions:
  - De-ionized water
  - De-ionized water with 2% bovine albumin
  - De-ionized water with 5% bovine albumin
  - 0.9% sodium chloride (NaCl)
  - 0.9% sodium chloride (NaCl) with 2% bovine albumin
  - 1.8% sodium chloride (NaCl)
  - 1.8% sodium chloride (NaCl) with 2% bovine albumin
- All dressings were tested to at least quadruplicate and from 2 separate batches.

* This product is a trademark of its owner

How does the AA measure silver concentrations?

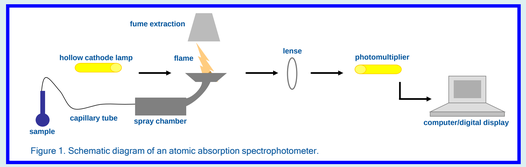
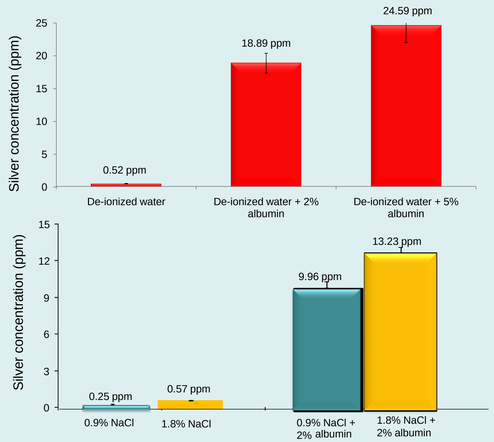


Figure 1. Schematic diagram of an atomic absorption spectrophotometer.

- Solutions of known concentrations of silver are prepared, analysed by the AA (Figure 1) and used to generate a standard curve relating absorbance to silver concentration.
- Unknown samples are analyzed by the AA - the silver concentration is determined by relating absorbance to silver concentration on the standard curve.

Release of Silver Ions from Dressing A



- Minimal silver ions released in water, saline & NaCl solutions
- The addition of protein (albumin) significantly increased silver release

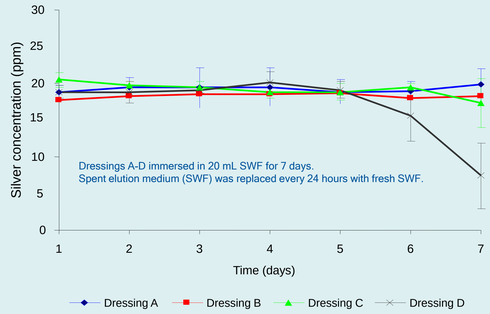
Silver Chemistry

- All silver-containing dressings, whether elemental (Ag/metallic) or ionic, achieve their antimicrobial action by releasing silver cations (Ag^+).
- Elemental silver exists as a neutral atom (Ag) and is relatively unreactive.
  - In the presence of oxygen, elemental silver (Ag) oxidises to form silver oxide and upon dissolution in fluid, silver oxide dissociates into its components releasing antimicrobial silver cations (Ag^+).
- Ionic silver (Ag^+/silver cation) is positively charged and has antimicrobial activity irrespective of the presence of oxygen.

Release of Silver from Dressings in Simulated Wound Fluid

Since protein significantly affects silver release its important to control this in release studies

Simulated wound fluid was used for release studies as it best represents the clinical situation

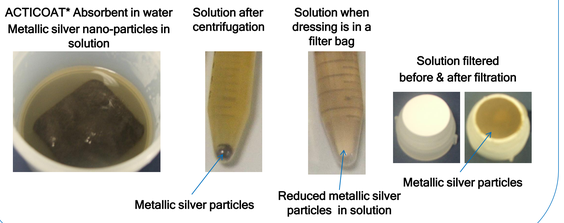


When elution solution is controlled a similar amount of silver is released from all dressings until their silver reservoir is depleted.

With exception to Dressing D, all dressings released a sustained amount of silver (approximately 17-20 ppm) over 7 days in SWF.

ACTICOAT Silver Release Studies

- When ACTICOAT* Absorbent was incubated in Deionised Water particulate silver was observed to fall from the dressing
- This leads to over estimation of silver concentration by AA analysis as it cannot differentiate between metallic silver & ionic silver
- Centrifugation, & filtration reduced total silver levels, however nano-particles of metallic silver too small and could not be fully removed
- Therefore ACTICOAT* was not assessed in further release studies with simulated wound fluid as results were misleading



Conclusions

- Addition of albumin affects the amount of silver released from dressings
  - Increasing the concentration of albumin in the solutions increased the amount of silver released.
  - Higher concentrations of silver were detected when dressings were incubated in solutions of de-ionized water and 2% albumin compared to sodium chloride with 2% albumin.
- Solutions used for silver release evaluations should be standardized to enable meaningful comparisons between dressings. Standardization should be focused on clinical relevance.
- It is proposed that an simulated wound fluid-containing 2% albumin (Falanga, 1992) more closely represents the composition of an exudating wound. In these studies all silver releasing dressings release ~20ppm until the silver is depleted.

Reference

- Falanga V, *J. Dermatol.* 1992; 19: 667-72.