Composition and antibacterial mode of action of Atrauman Ag

Dressings containing silver have been proven to reduce the infection risk in wounds. In addition it is also crucial to prevent cytotoxic effects on the wound itself.

Conclusion

The bactericidal action of Atrauman Ag has been tested in extensive microbiological in-vitro tests following standardised test procedures. The laboratory tests confirm a rapid and long lasting efficacy of the impregnated tulle dressing containing silver on a wide spectrum of bacteria. Atrauman Ag is only antibacterial effective when in direct contact with bacteria.

Composition of Atrauman Ag

The support fabric for Atrauman Ag consists of a water-repellent polyamide textile. It is coated with metallic silver which is chemically bound, i.e. firmly fixed, to the support fabric. The silver-coated support fabric is in turn impregnated with a hydrophilic ointment which consists mainly of triglycerides. The complete system has a high exudation as well as air and water vapour permeability (Diag. 1)

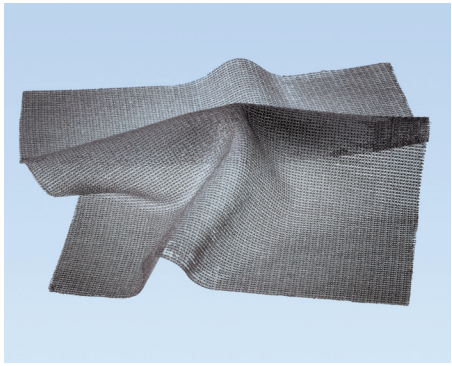
Mode of action and cytotoxicity

Silver is an almost inert metal. If it comes into contact with liquids, silver ions (Ag+) are released instantly which then combine with the surface proteins of cells, e.g. bacteria, and develop their effect there (Br J Nurs 2004; 13:S6). In Atrauman Ag the antibacterial mode of action is comparable. When in contact with wound exudate Atrauman Ag forms silver ions on its metallic surface. The silver ions are kept within the dressing where they bind to and therefore destroy bacteria. The wound exudate together with the dead bacteria and endotoxins produced by this process are absorbed into the secondary dressing (Diag. 2).

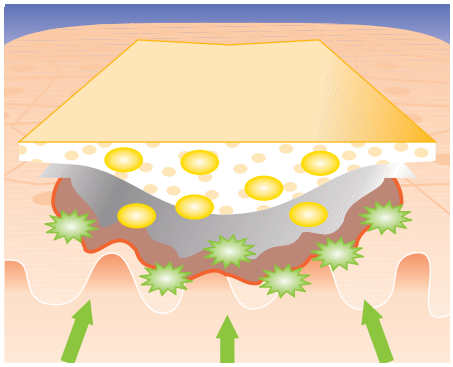
The fewer the silver ions that are released into the wound and into the cell tissue, the lower the toxicity of a dressing containing silver. At the same time it has to be guaranteed though that the concentration of the silver ions is sufficient to enable the development of an effective bactericide effect. The quantity of silver ions released into the wound differs greatly from silver dressing to silver dressing (Ostomy Wound Manag 49; 2003 49:19). This is mainly dependent on the method by which the silver is integrated into the wound dressing.

We were able to prove an excellent 'use to risk'- relationship for Atrauman Ag. Due to its mode of action, in which the formed silver ions are kept within the dressing, the cytotoxicity is kept to a minimum. The effective bactericide action is limited to the surface of the wound dressing.

The low cytotoxicity of Atrauman Ag was proven by tests with the human keratinocyte cell line HaCaT. The effect of Atrauman Ag and two other dressings containing silver on cell-growth was tested referring to the toxicity test to ISO 10993. In this test, the human keratinocytes were incubated for 24 hours in 96 well plates allowing sufficient time for adhesion and proliferation. An eluate was produced from Atrauman Ag and two further dressings; 1 ml cell culture medium was added per 6 cm^2 area, at 37° C for 24 hours and shaken at 300 rev/min; the eluate was sterile-filtered and thinned 1:4. The cell culture medium from the 96 well plates was replaced by the eluate, using a cytostatic as positive control and a fresh cell culture medium as negative control. The human keratinocytes were then incubated together with the eluates from the three products at 37° C for 72 hours. Afterwards, the vitality of the keratinocytes was determined by using an "In Vitro Toxicology Assay Kit MTT based". This kit measures the toxic effect by making the metabolic activity of the human keratinocytes visible through a colour reaction. This reaction can then be quantified spectrometrically and is a direct measure of the cell vitality.



Diag. 1
Atrauman Ag, the silver containing tulle dressing.



Diag. 2
Antibacterial action of Atrauman Ag; bacteria (green) are destroyed after contact with Atrauman Ag. The wound secretion with the dead bacteria and the resulting endotoxins are absorbed into the secondary dressing.

As shown in diag. 3, Atrauman Ag is clearly less cytotoxic on human keratinocytes than the other two dressings containing silver. The reason for this lower toxicity: compared to other dressings containing silver is that Atrauman Ag releases noticeably fewer silver ions to the surrounding area.

This lower release of ions was confirmed by the Agar plate diffusion Test. The Agar plate diffusion Test to DIN EN ISO 20645 is a method by which the anti-bacterial effect of anti-microbial textiles and other materials can be tested. For Atrauman Ag, only those bacteria were destroyed (in this test set-up: Staphylococcus aureus) which were in immediate contact with the dressing. Because the silver ions formed by Atrauman Ag remain within the dressing, no zone of inhibition was observed on the edge of the specimen. The result for two other tested dressings containing silver looked completely different. Here, a clear zone of inhibition was recognisable around the dressing because considerably higher concentrations of silver ions were released into the surrounding area.

Broad-spectrum mechanism of action, rapid and long-lasting effect.

Open wounds – acute or chronic – are vulnerable to a permanent risk of infection from pathogenic bacteria. Particularly Staphylococci, streptococci and gram-negative bacilli pose a substantial danger. MRSA strains (methicillin resistant Staphylococcus aureus), too, are the reason for more and more serious infections in hospital (J Wound Care 2002; 11:125). In order to reduce the risk of infection, it follows that dressings containing silver not only have to be effective against as many strains of bacteria as possible, but also act quickly and over a long period of time.

All these essential properties were confirmed for Atrauman Ag in laboratory tests. The test series were carried out according to standard method of the American Society for Testing Materials (ASTM 2180). This method examines the antibacterial efficacy of substances which are combined with polymers or hydrophobic materials. The chosen culture medium was fluid agar which had been inoculated with the bacterial strains to be tested. The cell culture was then put on the dressing as a thin layer by pipette and incubated. This test method guarantees a consistent contact of the inoculate with the dressing. Afterwards, the surviving bacteria are eluated, the colonies resulting from the eluate counted and from there the percentage of bacteria destroyed is calculated.

In these microbiological tests, Atrauman Ag effectively destroys not only problem germs like methicillin-resistant Staphylococcus aureus strains (MRSA), but also a great number of other gram-positive and gram-negative strains of bacteria (Diag. 4). Also, the bactericide action starts very quickly. Using the example of a gram-negative and gram-positive strain of bacteria, it is clear that even with an initial germ count of 10^6 germs per ml, complete destruction is achieved for Staphylococcus aureus after four hours (Diag. 5); and for Klebsiella pneumoniae after only 2 hours (Diag. 6). Even with a contamination of 10^7 germs per ml of culture solution, Atrauman Ag destroys all bacteria in the specimen within 24 hours (Diag. 7).

In a further laboratory test (method ASTM 2180) it could also be proven that the bactericide effect is not only short term but sustained for a long period of time. In this case Atrauman Ag effectively destroyed both Staphylococcus aureus as well as Klebsiella pneumoniae - despite repeated new injections of the medium for 9 days maintaining a continuous high contamination (Diag. 8).

A wound is recognised as infected if it has 10^5 or more germs per ml of fluid in the wound. In order to treat such an infected wound effectively, the dressing containing silver should be able to act as a bactericide for even higher germ counts as well as for bacteria of different virulence. Atrauman Ag fulfils these prerequisites, as proven by microbiological tests.

Combination with selected dressings

As with all other tulle dressings, Atrauman Ag is used in combination with a secondary absorbent dressing. If the doctor decides to temporarily treat the wound with a silver dressing, he can continue to use the previously applied wound dressing. In laboratory tests carried out to the Standard Test Method of the American Association of Textile Chemists and Colorists (AATCC 100), as well as in a practice test, Atrauman Ag was able to be combined with hydroactive as well as with traditional wound dressings. The active bactericide and healing-promoting effect was confirmed in combination with the following dressings:

- Polyacrylate wound pads (e.g. TenderWet24 active, TenderWet active cavity)
- Calcium alginate (e.g. Sorbalgon)
- Traditional dressings (e.g. Zetuvit, ES gauze swabs)
- Foam dressings (e.g. PermaFoam, PermaFoam cavity)

In particular, the combination with TenderWet active was examined more thoroughly. The wound pad is activated with Ringer's solution which contains chloride ions. In aqueous solutions, silver ions with chloride ions form a salt which is difficult to dissolve, which could diminish the bactericide effect of the silver ions. However, as laboratory tests have shown, Atrauman Ag develops its effective bactericide action also in Ringer's solution (Diag. 9). The action of the tulle containing silver is therefore not impaired when used in combination with TenderWet active for wound treatment.

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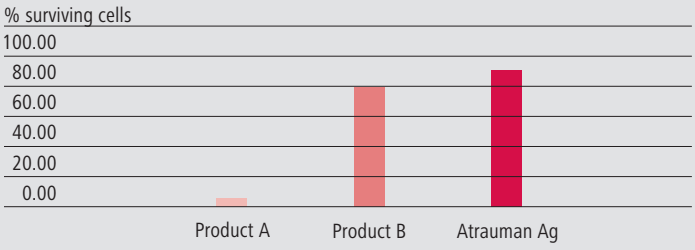
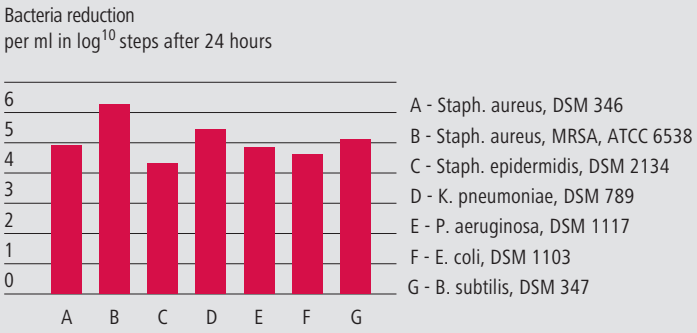
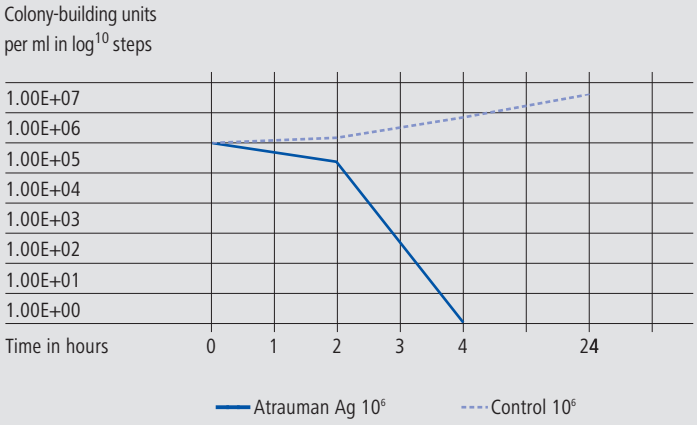
Diag. 3: Survival rate of human keratinocytes



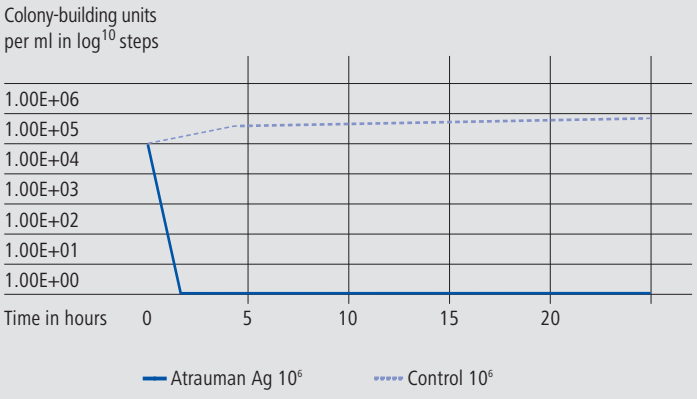
Diag. 4: Atrauman Ag, bacteria reduction, different bacteria



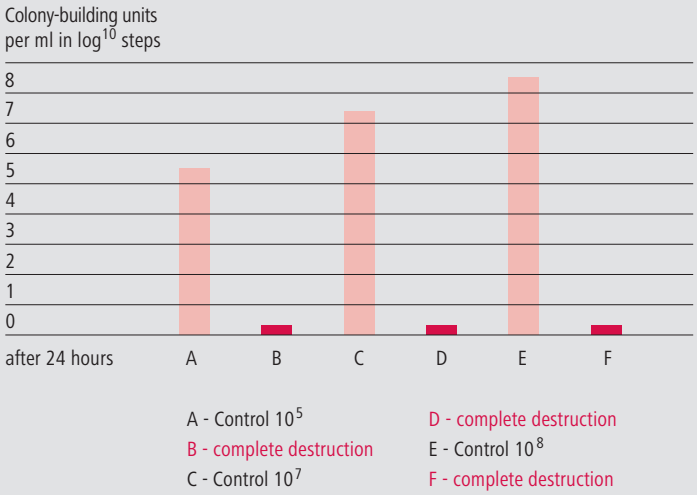
Diag. 5: Bacteria count reduction in Staphylococcus aureus



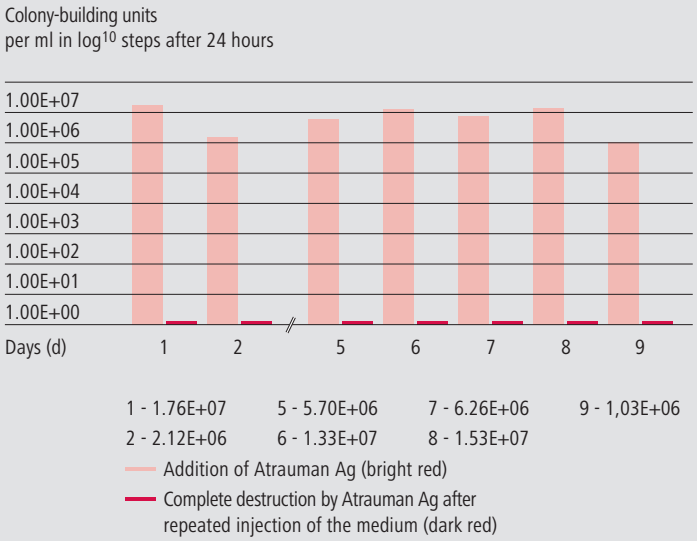
Diag. 6: Bacteria count reduction in Klebsiella pneumoniae



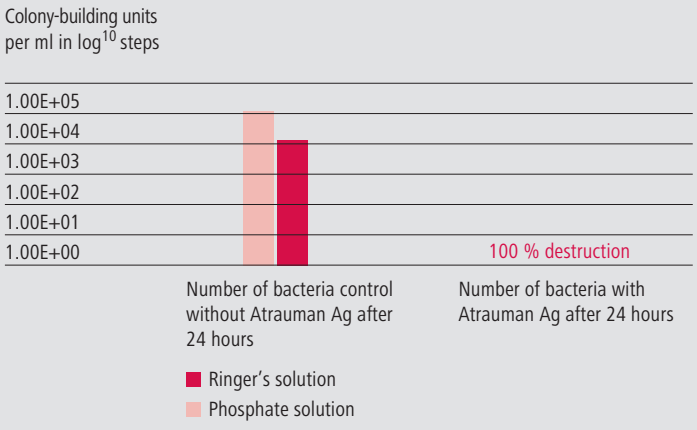
Diag. 7: Atrauman Ag: bacteria reduction, increasing number of germs (Staphylococcus aureus)



Diag. 8: Long term efficacy of Atrauman Ag in Staphylococcus aureus



Diag. 9: Bacteria count reduction in Staphylococcus aureus in Ringer's solution vs. phosphate solution



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