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Evaluation of the penetration of nanocrystalline silver through various wound dressing mediums: An in vitro study

Magnus D. Potgieter [a,*], *Parastu Meidany* [b]

[a] *Department Plastic and Reconstructive surgery, Faculty of Health Sciences: School of Medicine, PO Box 667, Pretoria, 0001, South Africa*
[b] *Cnr Steve Biko and Dr Savage Road, Prinshoff Campus, Pretoria, Gauteng, South Africa*

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ABSTRACT

Background: The nanocrystalline silver (NCS) dressing Acticoat is commonly used in clinical practice for the treatment of burns and other open wounds as a topical antimicrobial. The dressing may dry resulting in traumatic dressing changes; hence the variety of contact layer dressings used in conjunction with it. Dressing combinations that do not permit NCS penetration are not cost effective and deprives the wound of the needed anti-microbial.
Methods: Common wound pathogens were subjected to a variety of contact layer dressings underlying the NCS dressings. The zone of inhibition (ZOI) obtained was measured and compared to a control.
Results: Intrasite gel demonstrated a synergistic effect with Acticoat. Iruxol exhibits antagonism by preventing penetration and is known to be partially deactivated by NCS. Intrasite conformable and Adaptic allowed partial penetration while the discs of Biobrane, unstretched/non-fenestrated Pelnac and Telfa transparent film did not allow for sufficient penetration to inhibit the underlying bacteria in this study. The cadaver skin from the South African skin bank (Tshwane university of Technology) displayed a greater antimicrobial effect than even the Acticoat control.
Conclusion: Our results illustrate that we should perhaps reconsider dressing combination choices with Acticoat in view of their redundancy or synergistic effect.

1. Introduction

Acticoat (Smith and Nephew) is a nanocrystalline silver (NCS) dressing which releases the silver into the wound bed, acting as a topical antimicrobial. Being the uncharged form of the molecule (Ag^0) NCS is much less rapidly deactivated by chloride anions than the charged (Ag^+) ions in some other silver dressings. The Acticoat dressing releases silver over days rather than hours as for silver

Abbreviations: ANOVA, analysis of variation; CFU, colony forming units; MIC, minimum inhibitory concentration; MRSA, Methicillin Resistant Staphylococcus aureus; MSSA, Methicillin Sensitive Staphylococcus aureus; NCS, nanocrystalline silver; ZOI, Zone(s) of Inhibition.

* *Corresponding author.*
E-mail addresses: Mdpotgieter.article@gmail.com (M.D. Potgieter), parastu.meidany@lancet.co.za (P. Meidany).
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nitrate [1]. Also, what further distinguishes NCS from other forms of silver is a dramatically increased surface area and better solubility to enter the wound environment [2]. NCS is a broad spectrum antimicrobial and antifungal agent [1]. Acticoat has also been shown to inhibit biofilm formation for *Pseudomonas aeruginosa* and *Acinetobacter baumannii* by more than 90% in vitro [3].

In our experience, the dressing sometimes desiccates and adheres to the wound bed, leading to painful dressing changes that often also bleed and damage underlying healing tissue. Therefore, many doctors and nurses use another contact layer dressing under the Acticoat that will not adhere to the wound bed.

There are a few reports in the literature of Acticoat being used in combination with such dressings. Hydrogels are sometimes used since the regular moistening of Acticoat can be labour-intensive and impractical [4]. Synergy has been demonstrated between NCS and the haemostatic dressing chitosan [5] and also between aztreonam and NCS in vitro against *P. aeruginosa* [6]. However, not all the findings were as encouraging. Acticoat has been shown to decrease the effect of collagenase by more than 50% in an in vitro study using a 1:1 ratio of dressings [7].

If the NCS does not penetrate the contact layer dressing, or acts antagonistically, we are depriving the patient of topical antimicrobial therapy and squandering valuable resources. Conversely if some of these dressings can be used in combination, we can combine their different attributes to achieve a synergistic effect. Our research question therefore was whether sufficient NCS penetration occurs through these dressings to inhibit underlying bacteria. Observing silver staining of the wound bed has been anecdotally reported as evidence of penetration but the concentration of the silver has not been proven to exert a significant anti-microbial effect.

2. Methods

This was an experimental in vitro study using a standard Kirby Bauer disc diffusion test. Antimicrobial resistance or sensitivity can only be objectively tested with in vitro methods. This, however, usually correlates well with clinical practice if clinical factors are taken into consideration [8]. The method involves placing an antimicrobial soaked disc onto agar which has been inoculated with a particular organism after which the antimicrobial will diffuse into the agar and inhibit bacterial growth. The area of inhibited growth around the disk is the Zone of inhibition (ZOI) and was measured in millimetres when present. In this instance the "antimicrobial" was a 4mm diameter circular disc of Acticoat Flex resting on a 6mm diameter disc of numerous contact layer dressings. When the contact layer was an ointment or gel a 0.05ml drop was used correlating with a 1.76mm height at a diameter of 6mm. We used this as a reasonable estimate of a layer of cream applied to the dressing in clinical practice. The Acticoat was moistened as per manufacturer instructions with sterile water (0.01ml). The purpose of making the Acticoat disc smaller than the underlying contact layer dressing was to prevent water from spilling down the edge of the combination rather than through the contact layer dressing.

The bacteria included in the study were:

1. *Methicillin Resistant Staphylococcus aureus* (MRSA)
2. *Methicillin Sensitive Staphylococcus aureus (MSSA)*
3. *Pseudomonas aeruginosa*
4. *Streptococcus pyogenes*

These were chosen because they are common, virulent wound pathogens, are fast growing, non-fastidious and were proven to be sensitive to NCS in a pilot study before we embarked on the main experiment. The bacteria were plated out onto Mueller-Hinton agar and incubated aerobically at 37°C to simulate body temperature for 24h with our chosen dressing combinations at an inoculums concentration corresponding to a McFarland Standard of 0.5 (1.5×10^8CFU/ml) as measured by a standard turbidometer.

The dressing combinations used were:

1. Acticoat (Smith and Nephew) alone as control
2. Iruxol (Smith and Nephew): 0.05ml
3. Intrasite (Smith and Nephew): 0.05ml
4. Intrasite conformable (Smith and Nephew): 6mm a side squares
5. Adaptic (Systagenix) 6mm diameter discs
6. Biobrane (Smith and Nephew): 6mm diameter discs
7. Pelnac (Smith and Nephew, 2-stage type, with silicone film): 6mm diameter discs
8. Telfa transparent film (Covidien): 6mm diameter discs
9. Cadaver skin from the Centre for Tissue Engineering Tshwane University of Technology, preserved in 98% glycerol, 6mm diameter discs, washed in normal saline prior to application.

Note that in the case of Intrasite conformable squares were used instead of circles for practical purposes since it cannot be cut with a punch. We proved the difference in ZOI for these organisms between a circle and a square to be statistically non-significant as part of our pilot study ($p=0.192$).

The complete experiment, with 4 microbes and 9 dressing combinations (including the control) was repeated 5 times on different days with a new broth each day. The residual degrees of freedom for each bacterium were in excess of 30, which is the norm and suggests an adequate sample size. A one-way ANOVA (analysis of variation) for ranks was employed for data analysis and Barlett's test for equal variances was used for the variance testing after which testing was done at the 0.05 level of significance.

The ZOI was measured to the nearest 0.1mm and will be presented on the Y-axis of the results graph as a diameter. The 6mm disc in the centre of the ZOI is not included in this measurement. This was done so that non-penetrating values could be represented as "0" for more clarity in the graphic representations. In addition, the bacteria are colour-coded for easier comparison. It is important to note that since no minimum inhibitory concentration values exist for topical NCS like for most systemic antimicrobials, the comparison

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