NANOCRYSTALLINE SILVER:
WHAT IS IT AND WHAT DOES IT DO?

Robert E. Burrell
Professor and Chair Department of Biomedical Engineering,
Canada Research Chair and Professor,
Department of Chemical and Materials Engineering
University of Alberta
Nanomedicine

Nanomedicine is defined as the design, synthesis, or application of materials, devices, or technologies in the nanometer-scale for the basic understanding, diagnosis, and/or treatment of disease.

Key to this definition is that phenomena and materials at the nanometer scale are known to have properties that are uniquely attributable to that scale length.
A nanomaterial is one that has at least one dimension on the nanoscale.

A nanocrystalline material is one that has crystals with at least one dimension < 20 nm.
Nanocrystalline materials are single- or multi-phase polycrystals, the crystal size of which is of the order of a few (typically 1-10) nanometres, so that about 50 vol.% of the material consists of grain or interphase boundaries. The basic feature of these materials is the utilization of the atomic arrangement in the cores of lattice defects (grain or interphase boundaries) to generate solids with a new type of atomic structure. Because of the constraints exerted by the two adjacent lattices on the atoms in the core of an incoherent interface, the atomic arrangements in the cores of grain or interphase boundaries differ from the unconstrained atomic arrangements of glass and crystals.

How are they formed?

Using an advanced materials process….Physical Vapor Deposition.
Physical Vapor Deposition

Unique conditions: lower temperature, higher pressure
Physical/Chemical Characterization
Species Released During Dissolution

• By changing the physical properties at the crystal lattice level, a metastable, high-energy, metal matrix composite surface coating of silver is produced.

• Releases multiple species of silver ($\text{Ag}^+$ and $\text{Ag}^0$) (Fan and Bard, J Phys Chem B 2002, 106, 279-287).
Silver Species

\[Ag^0\] - only released from nanocrystalline silver.
- occurs as a cluster of atoms/ions.
- anti-inflammatory compound?

\[Ag^+\] - most common form of silver released by silver dressings.

\[Ag^{+++}\] - released from nanocrystalline silver?
Silver released (mg/L)
80 40 0
hours 24 hours 48 hours

Note: Flow rate - 0.33 ml/hr of water through 10 in² of Acticoat® dressing

TOTAL NANOCRYSTALLINE SILVER DISSOLUTION
SEM Analysis
Comparison of atomic concentration of total oxygen and oxygen bonded to silver, as determined via XPS, to crystallite size and biological activity\(^5\) \((S. \text{aureus})\) after exposure of the dressing to various temperatures for 24 hours.
Antimicrobial Activity.
MRSA Death Curve

Exposure Time (Hours)

Viable Bacteria (Log CFU/mL)

- Acticoat
- SSD
- AgNO3
- Arglaes
- Silverlon
## RESULTS: LOG REDUCTION

<table>
<thead>
<tr>
<th>Dressings</th>
<th>Parent Strain (P. aeruginosa)</th>
<th>Resistant Strain (P. aeruginosa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ag nylon</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Na CMC with Ag</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nanocrystalline Ag</td>
<td>&gt;5</td>
<td>&gt;5</td>
</tr>
</tbody>
</table>
Anti-inflammatory Activity
Histology

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative Control</td>
<td>![Image]</td>
<td>![Image]</td>
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<tr>
<td>Positive Control</td>
<td>![Image]</td>
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<tr>
<td>Silver Nitrate</td>
<td>![Image]</td>
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<tr>
<td>Nanocrystalline Silver</td>
<td>![Image]</td>
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</tbody>
</table>

Histological images showing the effects of different treatments over a period of three days.
Wound Healing: Acticoat vs Kerlix AMD

![Graph showing wound healing comparison between Acticoat and Kerlix AMD. The graph plots the percentage of wounds re-epithelialized over time (in days). The x-axis represents time post-wounding (in days), ranging from 0 to 20. The y-axis represents the percentage of wounds re-epithelialized, ranging from 0% to 100%. The graph includes two lines: one for Acticoat and one for Kerlix AMD. Acticoat shows a quicker re-epithelialization rate compared to Kerlix AMD.](image-url)
Admission Image
Burn (Day 3)
No pseudo eschar or exudate
Re-epithelialization ongoing
Burn (Day 21)
Complete re-epithelialization
10 y Tx w/ 2 y SSD

70 d Acticoat

60 d Acticoat
MMP-9 and MMP-2 Levels During Healing

![Graph showing MMP-9 and MMP-2 levels during healing. The x-axis represents the duration of treatment in days, ranging from 0 to 40. The y-axis represents protein level in ng, ranging from 0 to 2000. The graph shows two lines: one for MMP-9 (diamonds) and one for MMP-2 (squares). MMP-9 levels decrease sharply initially and then remain relatively stable. MMP-2 levels remain relatively constant throughout the treatment period.]
• Chemical burn from alcohol wipe

• Premature neonate with burn injury.
Why did the dressing work?

Multiple species of Ag released from nanocrystalline silver

Potent antimicrobial

Potent anti-inflammatory activity
The Future

Identification of Ag species and mechanism of action

Work on other noble metals

Work on other site-specific applications

• eg. pulmonary
Microscopic Examination Of Infected Lungs Treated With Nanocrystalline Silver & TOBI
Key Points

Nanotechnology is about functionality not size.

Understanding how materials behave at the nanoscale is essential.

We need to develop a market pull for technology through vehicles such as AiiMIT.

We need to use groups such as BERRI to develop products that meet Regulatory requirements.
Thank you