RAS AG
materials & technologies
INTRODUCTION RAS AG
RAS AG founded in 2016 as merger of

- rent a scientist GmbH scientific services since 1995
- ras materials GmbH production and sales of nanomaterials since 2010

RAS AG offers development services, technologies and materials for the creation of technology based product innovations.
## RAS AG

### Company Data

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turnover</td>
<td>2,0 mio. € p.a.</td>
</tr>
<tr>
<td>Personnel</td>
<td>17</td>
</tr>
<tr>
<td>Areas</td>
<td>1,000 m²</td>
</tr>
<tr>
<td>- Chemical lab</td>
<td></td>
</tr>
<tr>
<td>- Process lab</td>
<td></td>
</tr>
<tr>
<td>- Microbiological lab</td>
<td></td>
</tr>
<tr>
<td>- Customer specific development areas</td>
<td></td>
</tr>
<tr>
<td>- Nanomaterials production</td>
<td></td>
</tr>
</tbody>
</table>

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business units

rent a scientist®
- Our R+D services bring innovation to companies. We shape markets with creativity and knowhow.

agpure®
- Antimicrobial additive with outstanding properties and maximum safety for man and nature.

ECOS®
- Silver nanowire technology. Transparent, conductive surfaces for a variety of applications.

new materials
- Together with our partners we are always working on absolutely new materials and technologies.
markets

Healthcare
- agpure®, specialities, paints, laquers and resins for disinfection, implants, bone cement, wound treatment, panels, ceramics, colouring

Agriculture
- agpure®, NanoFe and Qpur for plant strengthening

Polymers + Fibers
- ECOS®, agpure®, smart release in thermoplastic polymers for antimicrobial, conductive and repelling function-alization

Electronics
- ECOS® coatings and formulations for high performance flexible transparent electrodes, IR-reflection applications and ESD shielding

Textile Coatings
- agpure®, ECOS® and smart release in coatings for antimicrobial, repelling and shielding textiles

Specialities
- Qpur as additive for high temperature lubricants and lubricating liquids
INTRODUCTION NANOSILVER
REVIEW ARTICLE

Silver nanoparticles: the powerful nanoweapon against multidrug-resistant bacteria

M.K. Rai, S.D. Deshmukh, A.P. Ingle and A.K. Gade

Department of Biotechnology, Sant Gadge Baba Amravati University, Amravati, Maharashtra, India

Keywords
antimicrobial, methicillin-resistant

Summary
Introduction Nanosilver

- The use of nanosilver as medicinal product is ancient

<table>
<thead>
<tr>
<th>Product</th>
<th>Use</th>
<th>Particle Size (nm)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argyrol</td>
<td>Anti-Infective (early 1900s)</td>
<td>35 nm</td>
<td>DLS Study, NanoHorizons, 2009.</td>
</tr>
<tr>
<td>Collargol</td>
<td>Anti-Infective (early 1900s)</td>
<td>10-20 nm</td>
<td>Muller, 1926 (1). Bogdanchikova, 1992 (2).</td>
</tr>
<tr>
<td>Protargol</td>
<td>Anti-Infective (early 1900s)</td>
<td>2 nm</td>
<td>Bogdanchikova, 1992 (2).</td>
</tr>
</tbody>
</table>

Nanosilver – mode of action

Release of Ag⁺
Nanosilver – mode of action

Antimicrobial activity

Activity of nanosilver against MDR germs

State of scientific knowledge

- Antimicrobial effect of nanosilver is well described
  - Nanosilver – Coating for medical devices
  - Nanosilver containing wound dress is active against bacteria with NDM-1 carbapenemase (Acinetobacter baumannii, Citrobacter freundii, Enterobacter spp., Escherichia coli and Klebsiella pneumoniae)

- Synergistic effect of nanosilver + antibiotics
  - Imipenem, Gentamicin, Ciprofloxacin and Vancomycin + 100 µg/g nanosilver
  - 20 – 35 % Increase of antibiotic sensitivity
Activity of nanosilver against MDR germs

State of scientific knowledge

- Table shows further bacterial strains sensible against nanosilver

- Conclusion:
  Scientific studies show a very strong activity of silver nanoparticles against multidrugresistant germs.

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Mechanism of Action</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinobacter baumannii</td>
<td>Alteration of cell wall and cytoplasm.</td>
<td>[26,27]</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>Alteration of membrane permeability and respiration</td>
<td>[26,28–44]</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>Alteration of cell wall and cytoplasm.</td>
<td>[42,45,46]</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>Alteration of membrane</td>
<td>[28,41,47]</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>Morphological changes, separation of the cytoplasmic membrane from the cell wall, plasmolysis</td>
<td>[47]</td>
</tr>
<tr>
<td>Micrococcus luteus</td>
<td>Alteration of membrane</td>
<td>[28]</td>
</tr>
<tr>
<td>Nitrifying bacteria</td>
<td>inhibits respiratory activity</td>
<td>[31]</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Irreversible damage on bacterial cells, Alteration of membrane permeability and respiration</td>
<td>[17,28,32,33,36,41–44,48–50]</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Alteration of cell wall and cytoplasm.</td>
<td>[43,44]</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Irreversible damage on bacterial cells</td>
<td>[17,26,31,34,37,39–41,48,51,52]</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>Inhibition of bacterial DNA replication, bacterial cytoplasm membranes damage, modification of intracellular ATP levels</td>
<td>[36,52]</td>
</tr>
<tr>
<td>Salmonella typhi</td>
<td>cytoplasm membranes damage, modification of intracellular ATP levels</td>
<td>[33,36,48,51]</td>
</tr>
<tr>
<td>Vibrio cholerae</td>
<td>Alteration of membrane permeability and respiration</td>
<td>[33]</td>
</tr>
</tbody>
</table>
Dimensions
- Mean diameter 15 nm
- 99% of particles < 20 nm

Formulations
- Stable in aqueous and organic dispersions
- Incorporation in polymers and resins

Permanence
- No release of nanoparticles (Ag⁰) from solid matrices
- Continuous release of smallest amounts of silver ions (Ag⁺)

RAS AG
Some of our products

**agpure® W10**
- 10 wt.-% nanosilver, stabilized, solvent: water

**agpure® W50**
- 45 wt.-% nanosilver, stabilized, pasteous

**agpure® MB6500**
- 0,65 wt.-% nanosilver masterbatch,

→ No agpure® nanopowders
Coatings
- Dispersion colours
- Laquers and resins
- Sol-gel coatings
- Polymer based dispersions

Polymers
- Textiles – fibers and fleece
- Commodities
- Films and Tubing

Medical devices
Research in Healthcare

- Project with starting date (Funding organisation)
  - 2008 Development nanosilvercoating for Osteosynthesis (HessenAgentur)
  - 2009 Development bone cement with nanosilver (BayMedTech)
  - 2010 Research on the biocompatibility of nanosilver containing medical devices (BMBF)
  - 2012 Development glasfiber-reinforced wall panels with nanosilver (BayMedTech)
  - 2015 Optimisation of nanosilver-containing bone cement (BMWi – AIF ZIM)
  - 2017 Investigation of antimicrobial surfaces inside emergency rooms (BMBF)
Products and Applications in Healthcare containing nanosilver

- Products in research
  - Bone-cement
  - Wound-treatment
- In approval
  - Osteosynthesis
- On the market
  - Glasfiber-reinforced wall panels
  - Silicone pressure protection articles for podiatry
  - Antimicrobial coating for cryostats
  - Antibacterial lacquer for hard otoplastics and hearing aids
  - Antimicrobial polymer products
  - Paints and lacquers for walls and furniture in hospitals
Publications related to agpure® nanosilver

- Attached you find a list with publications where agpure® nanosilver or NM 300 K was used
- Structure
  - Phys-chem- Data and Reference material
  - Medical / Antimicrobial efficacy
  - Humantoxicity
  - Ecotoxicity
  - Exposure / Migration / Textile
Regulation and Safety Assessment
Biocidal products regulation (EU-BPR)

- Antimicrobial → Biocidal product →
- REGULATION (EU) No. 528/2012:
  - Silver (CAS 7440-22-4) is notified (Product Type 2, 4, 5, 9, 11)
  - Substance dossier for nanosilver has been submitted acc. to Art. 95
  - “The approval of an active substance shall not cover nanomaterials except where explicitly mentioned.” (§ 4 (4))
  - “… where nanomaterials are used in that product, the risk […] has been assessed separately. “ (§ 19 (1 f))
  → Risk assessment for silver nanoparticles needed
  → agpure® is continuously marketable
Regulation and Safety Assessment
International standard reference material

- Data for nanospecific risk assessment required

- agpure® W10
  - The official nanosilver reference- and testing material (NM 300 K) for the “OECD WPMN - sponsorship program”
  - Certified Reference Material BAM-N001 at the Federal Institute for Materials Research and Testing (German BAM)
Regulation and Safety Assessment

OECD WPMN sponsorship program
Regulation and Safety Assessment

agpure® exposure assessment

- **Nanoparticle inside ≠ nanoparticle release**
- Safe use of silver nanoparticles:
  - Exposure of silver nano particles during production unlikely
    - *REACH-NanoHazEx: Rip-oN 3*
  - No abrasion of nano particles is detectable from polymer materials
  - Similar results on abrasion in all the other projects related to nanorisks

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Thank you

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