

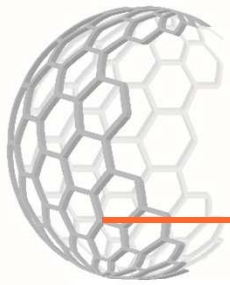


MEZIOBOROVÉ PŘÍSTUPY V HOJENÍ RAN

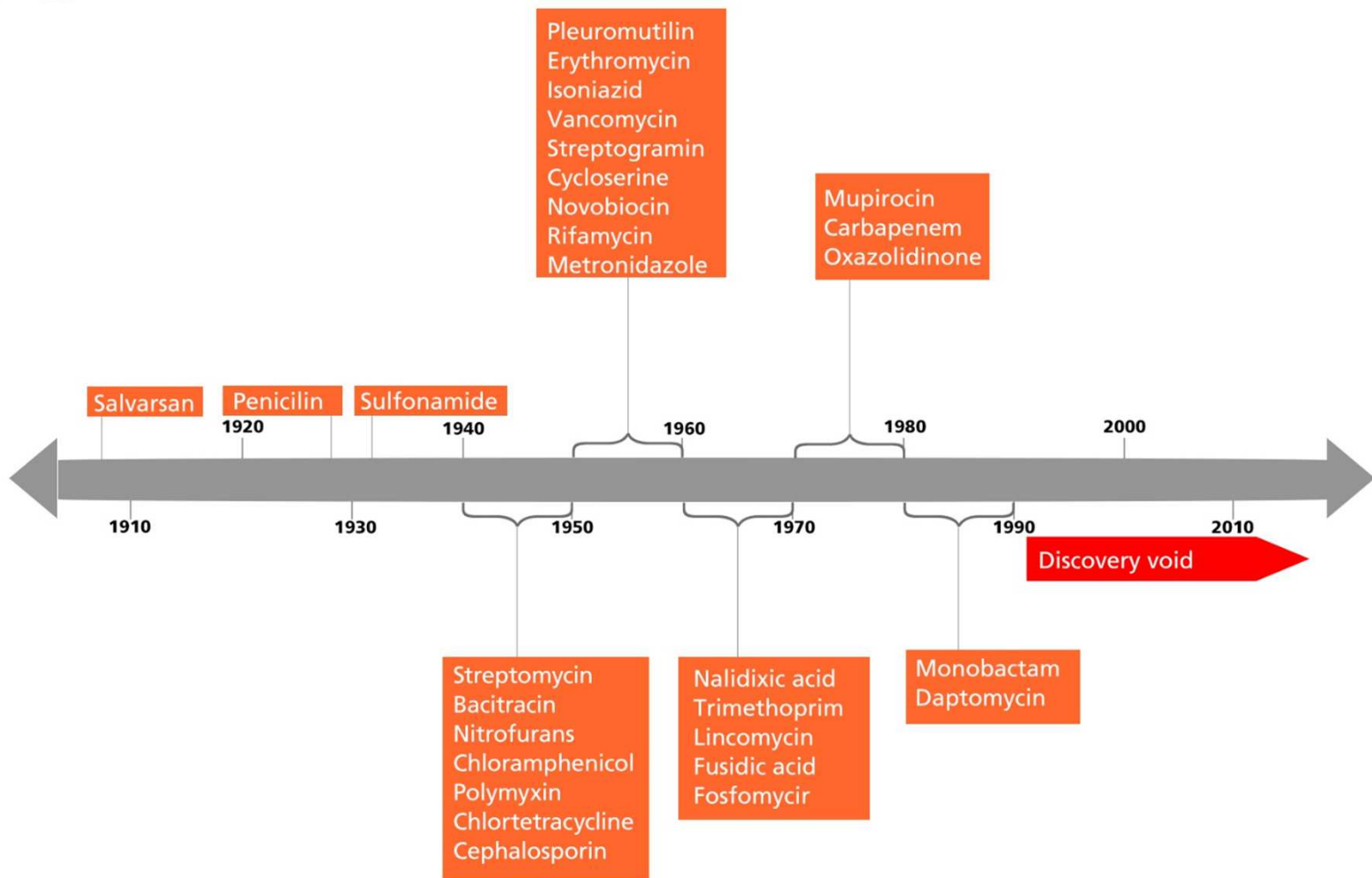
NANOMATERIALS, AN ALTERNATIVE TO ANTIBIOTICS OR DEAD-END STREET?

Kristyna Dolezelikova, Zuzana Bytesnikova, Frantisek
Ondreas, Kristyna Smerkova, Lukas Richtera, Zbynek
Heger, Lucy Vojtova, Vojtech Adam

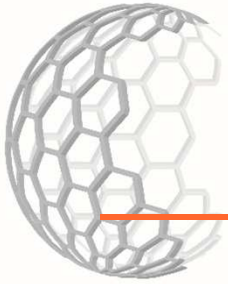
28. 11. 2019



Antibiotics

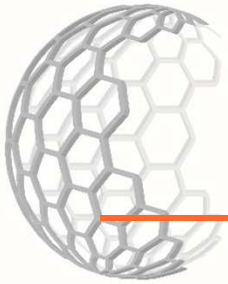


Adopted and Modified/Silver L.L. (2011), Crit. Microb. Rev., 71-100.



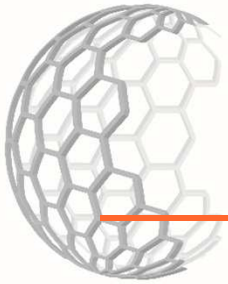
Resistance

- **Microbial resistance to antibiotics** has risen to dangerously high levels worldwide
- **New resistance mechanisms are emerging** and spreading globally, threatening our ability to treat common infectious diseases



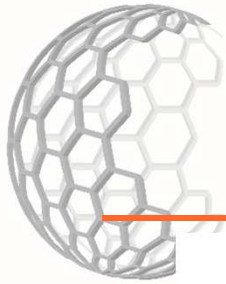
Resistance

- **Microbial resistance to antibiotics** has risen to dangerously high levels worldwide
- **New resistance mechanisms are emerging** and spreading globally, threatening our ability to treat common infectious diseases
- **Antibiotics are misused** as a prophylactic agricultural supplements to maintain health and productivity of livestock
- The conventional antibiotics development is lagging behind the need and the recently used **antibiotics are losing their efficacy**

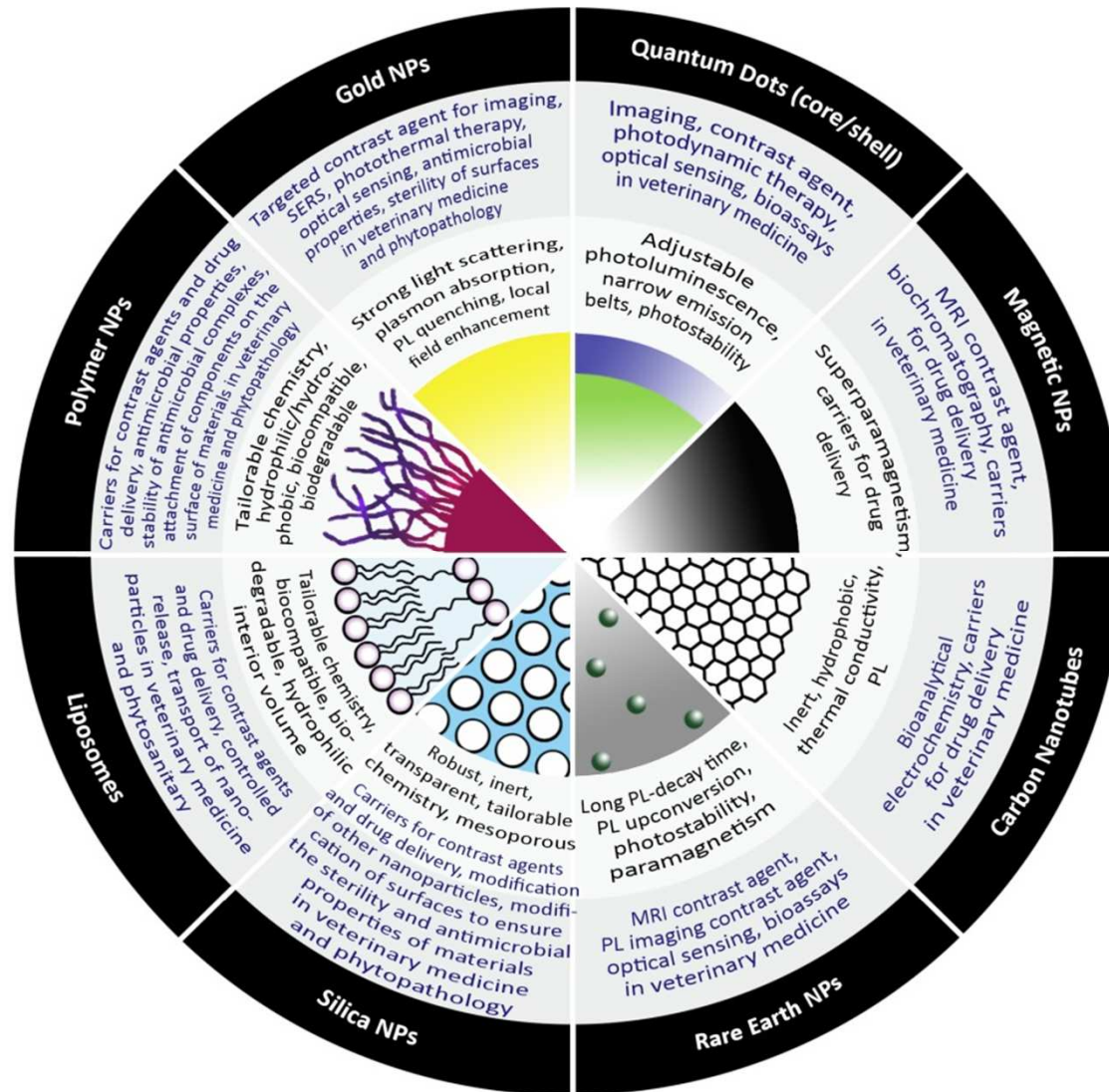


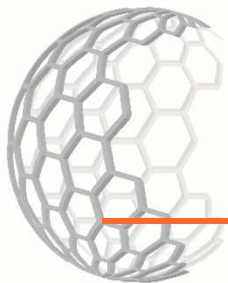
Resistance

- **Microbial resistance to antibiotics** has risen to dangerously high levels worldwide
- **New resistance mechanisms are emerging** and spreading globally, threatening our ability to treat common infectious diseases
- **Antibiotics are misused** as a prophylactic agricultural supplements to maintain health and productivity of livestock
- The conventional antibiotics development is lagging behind the need and the recently used **antibiotics are losing their efficacy**
- The **nanotechnology** can offer intelligent solution **for individual or combined therapy approaches**

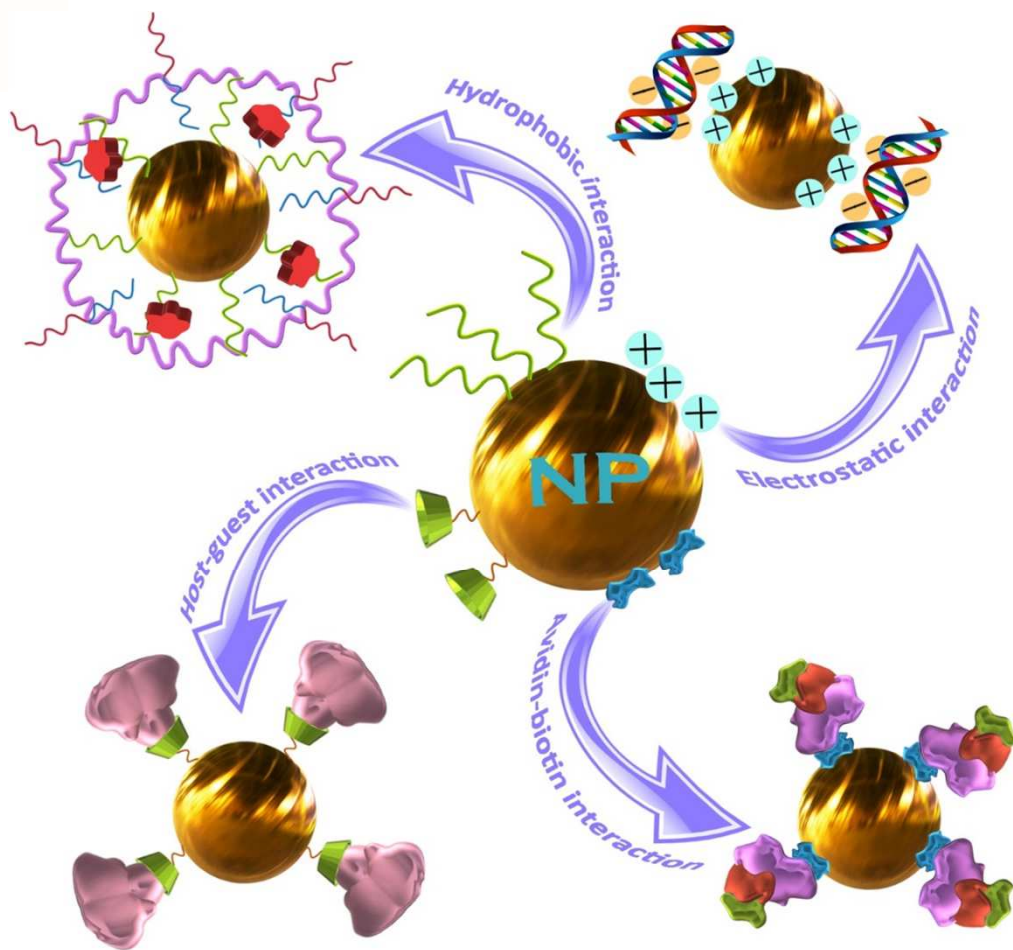


Nanomedicine, nanoparticles

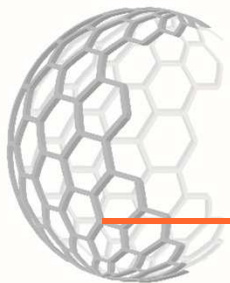




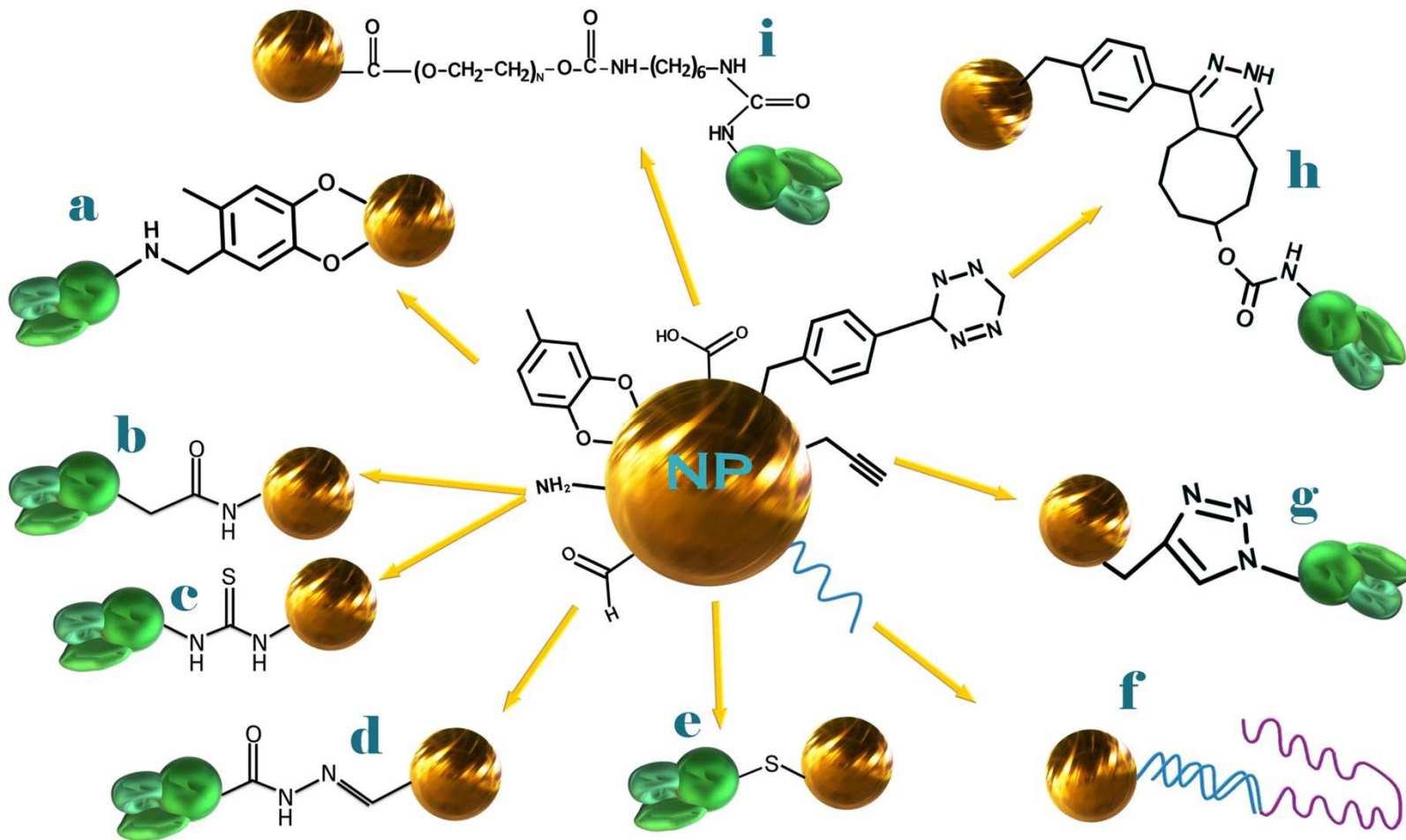
Nanomedicine, biomolecules

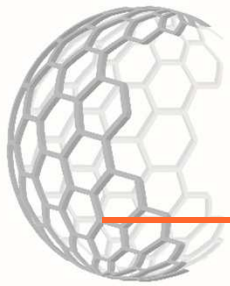


 therapeutic genes or siRNA,  therapeutic drug,  Amphiphilic polymer,
 Hydrophobic surface,  β -cyclodextrin,  Citric acid,  Streptavidin,
 Hydrophobic guest molecule,  Biotinylated biomolecule



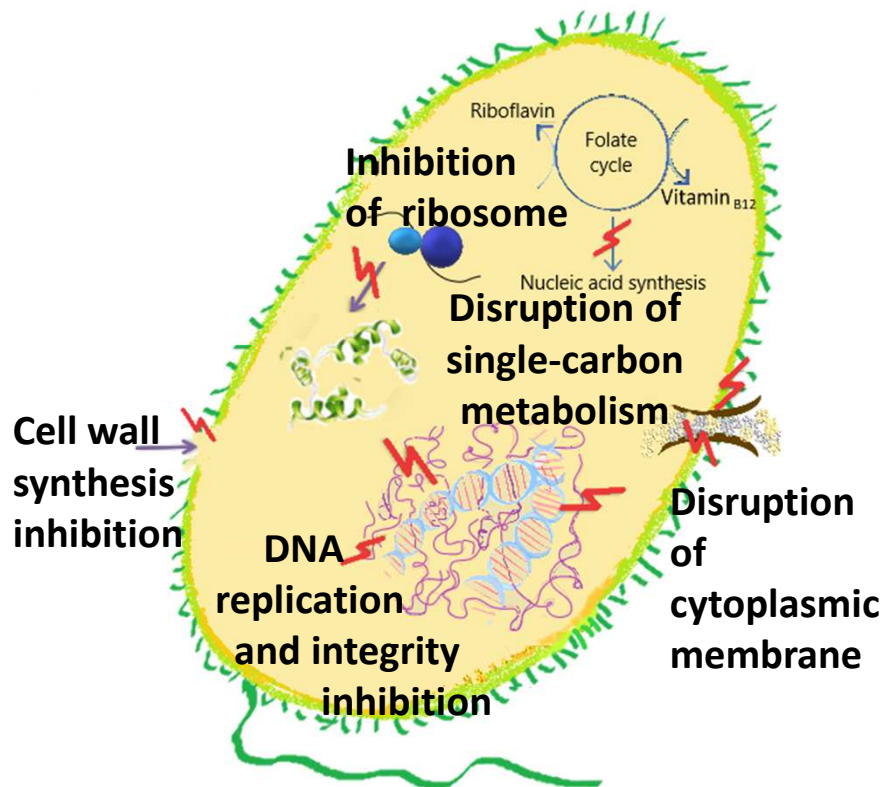
Nanomedicine, chemical substances

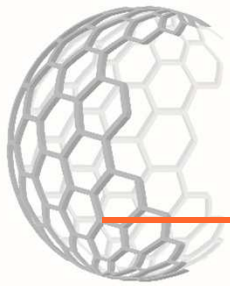




Nanoparticles vs. current antibiotics

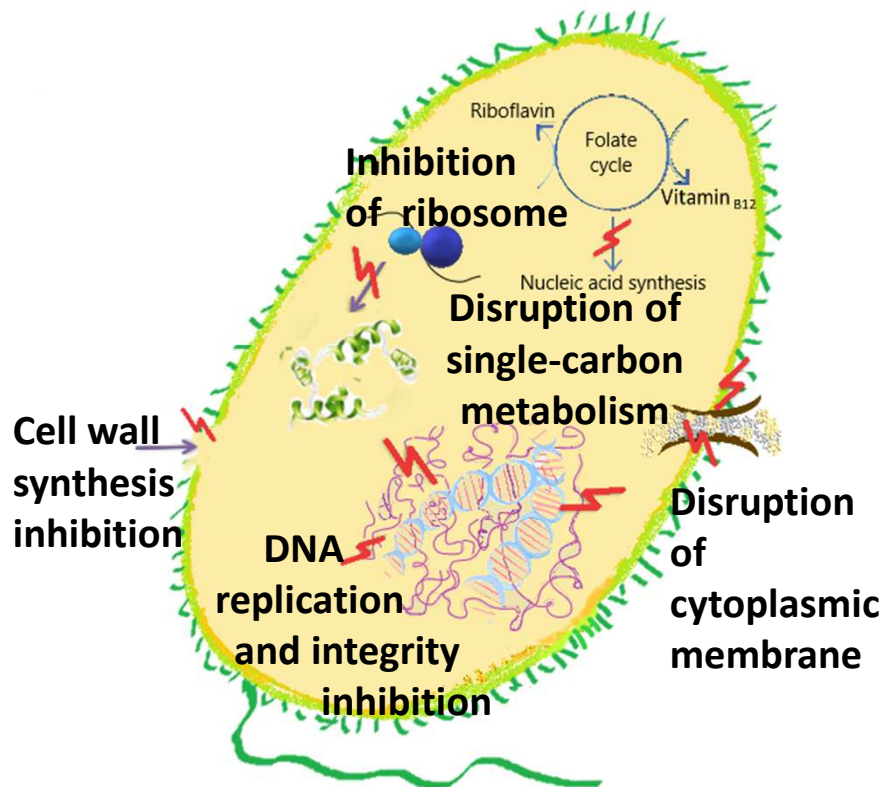
Current antibiotics



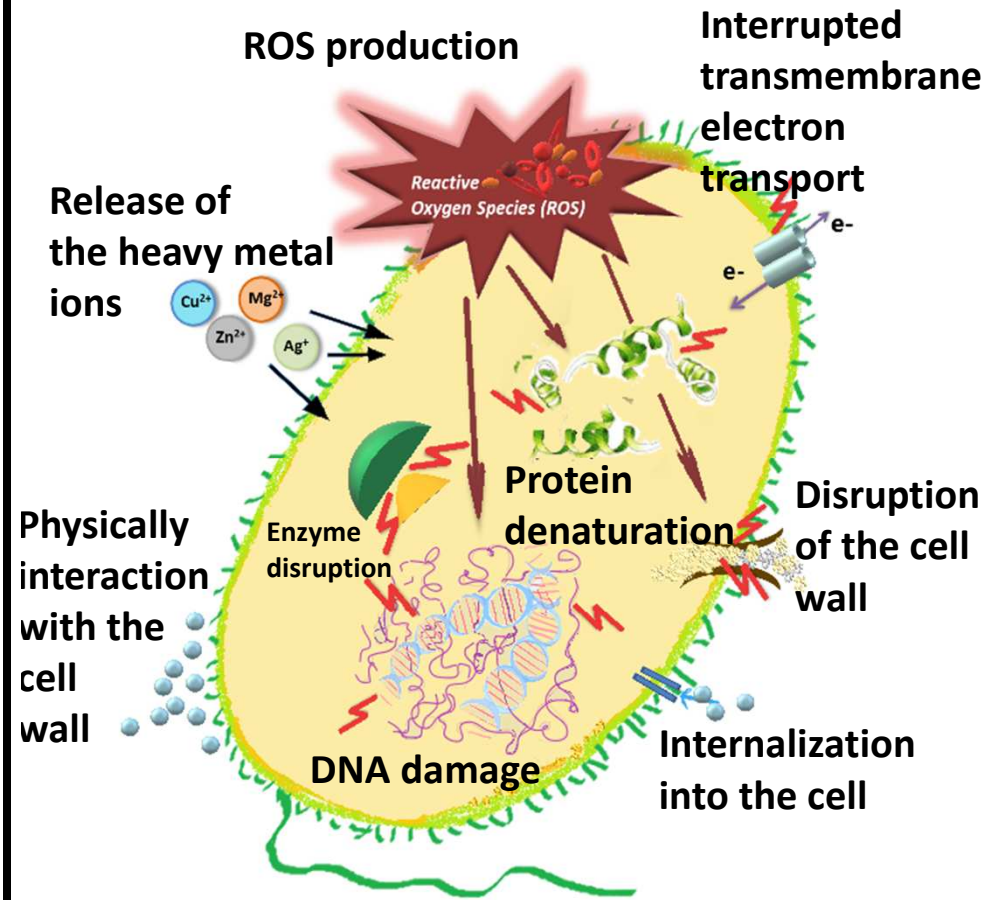


Nanoparticles vs. current antibiotics

Current antibiotics



Nanoparticles





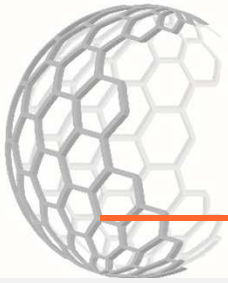
CONTENT

- Nanoparticles/Nanomaterials
- Use cases
 - Zinc nanoparticles
 - Metal composite nanoparticles
 - 3D materials



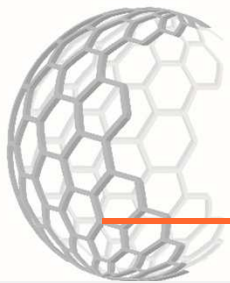
CONTENT

- **Nanoparticles/Nanomaterials**
- Use cases
 - Zinc nanoparticles
 - Metal composite nanoparticles
 - 3D materials



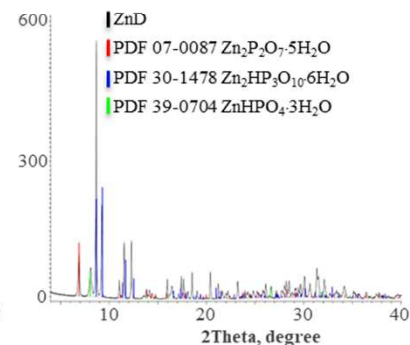
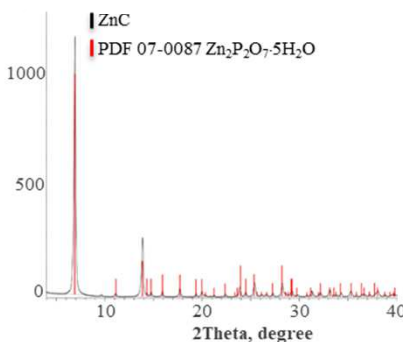
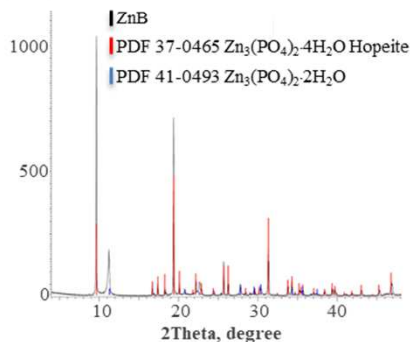
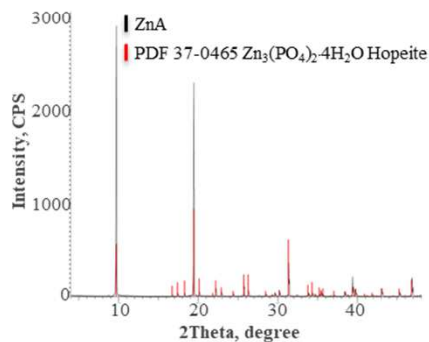
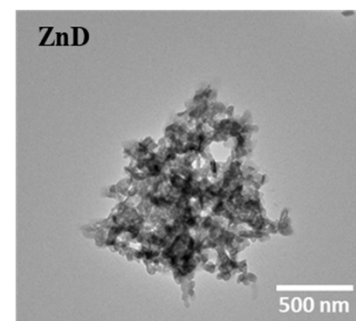
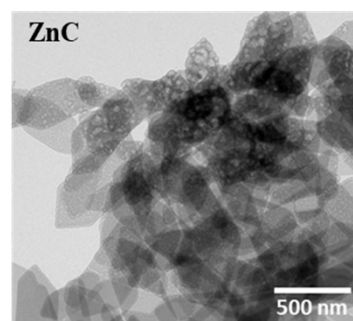
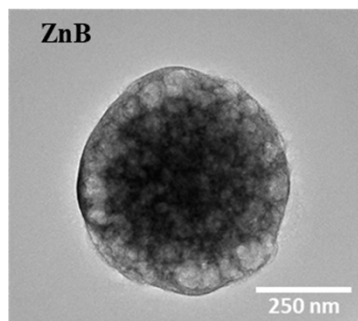
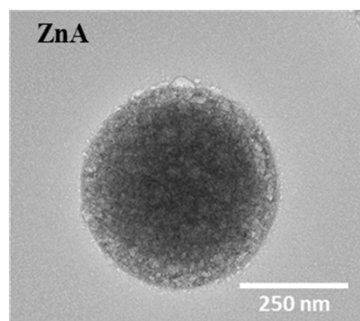
Zinc phosphate-based nanoparticles

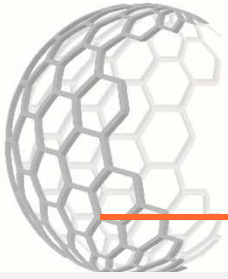
- **Precursors** – hydrogen phosphate (ZnA and ZnB), diphosphate (ZnC), and triphosphate (ZnD)
- ZnA and ZnB **spherical shape** (477 and 521 nm)
- ZnC and ZnD **irregular shape** (452 and 1035 nm) - tendency to form small aggregates



Zinc phosphate-based nanoparticles

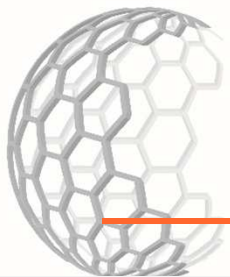
- **Precursors** – hydrogen phosphate (ZnA and ZnB), diphosphate (ZnC), and triphosphate (ZnD)
- ZnA and ZnB **spherical shape** (477 and 521 nm)
- ZnC and ZnD **irregular shape** (452 and 1035 nm) - tendency to form small aggregates





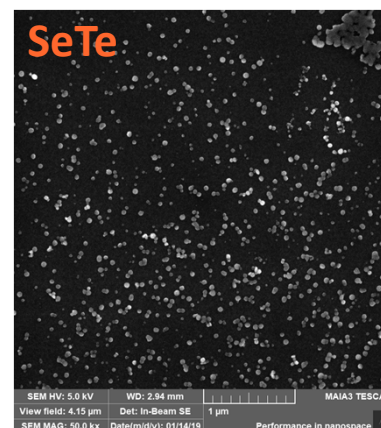
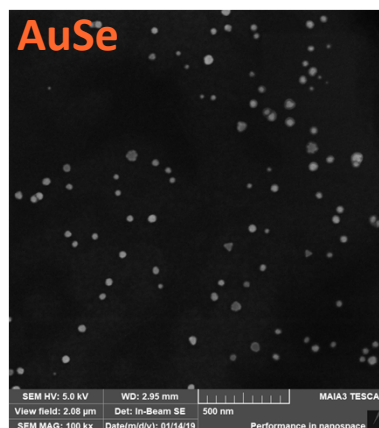
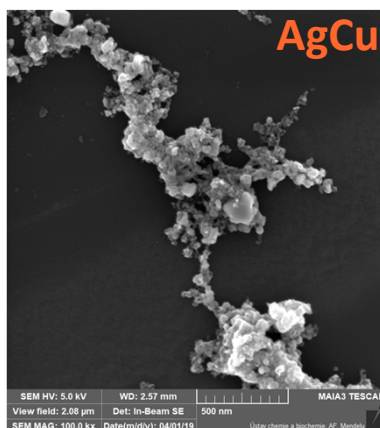
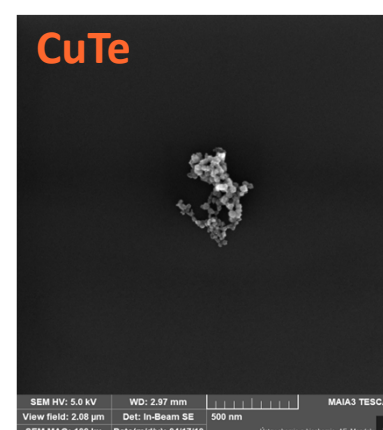
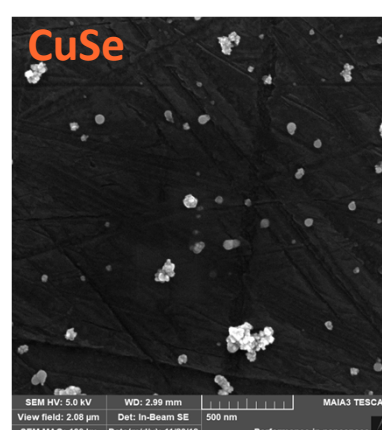
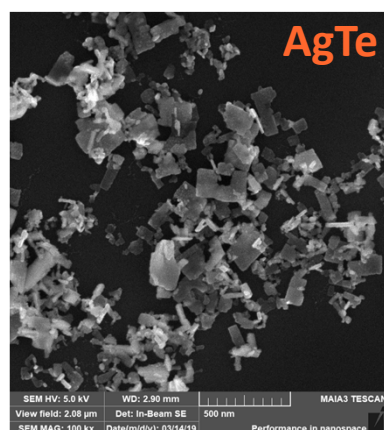
Metal composite nanoparticles

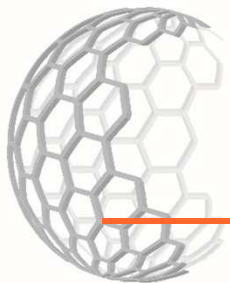
- Combination of various **elements**: Cu, Ag, Au, Se, Te at various **ratios**
- Various **shapes** (spheres, plates, cubes) and **size** (5 - 1000 nm)



Metal composite nanoparticles

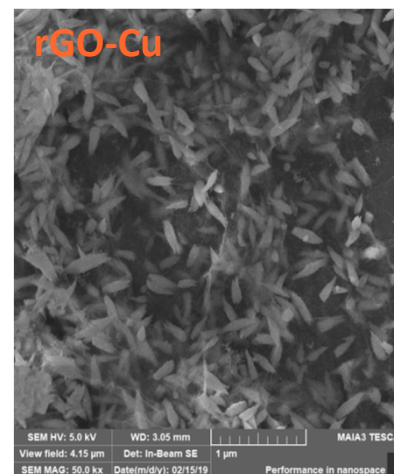
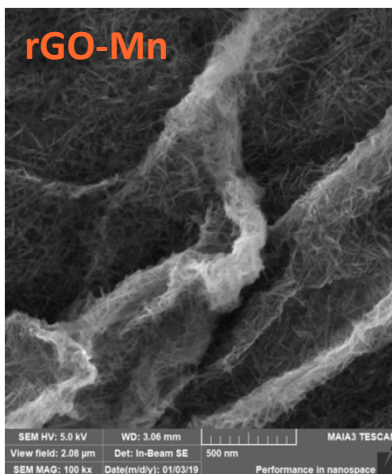
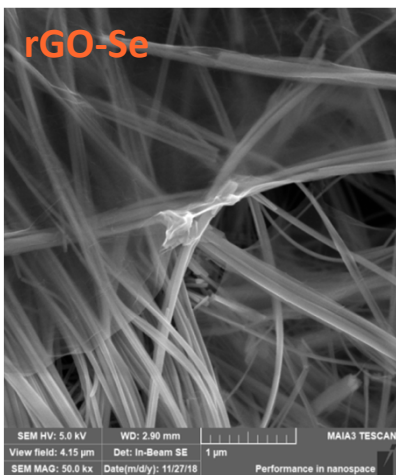
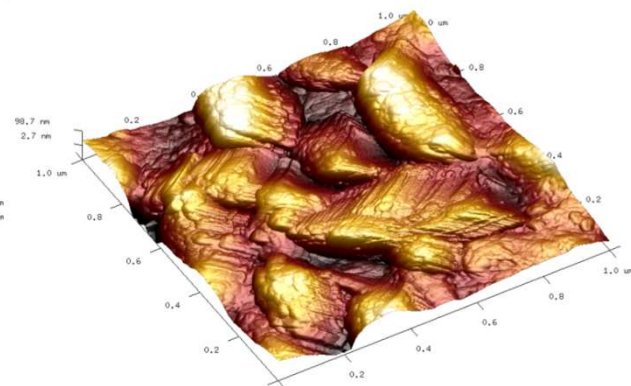
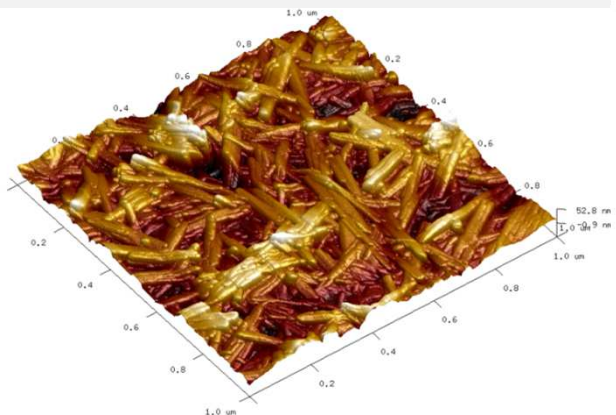
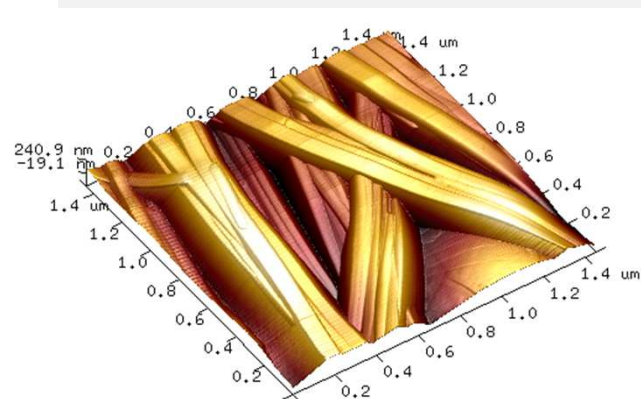
- Combination of various **elements**: Cu, Ag, Au, Se, Te at various **ratios**
- Various **shapes** (spheres, plates, cubes) and **size** (5 - 1000 nm)





Graphene based nanocomposites

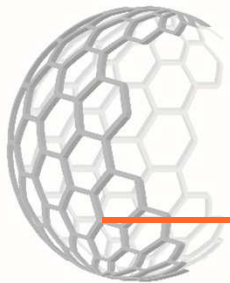
- Combination of various elements: Se, Mn, Au, Ti, Ce, Bi, Ni, Zn, Cu at various ratios and combinations with graphene oxide





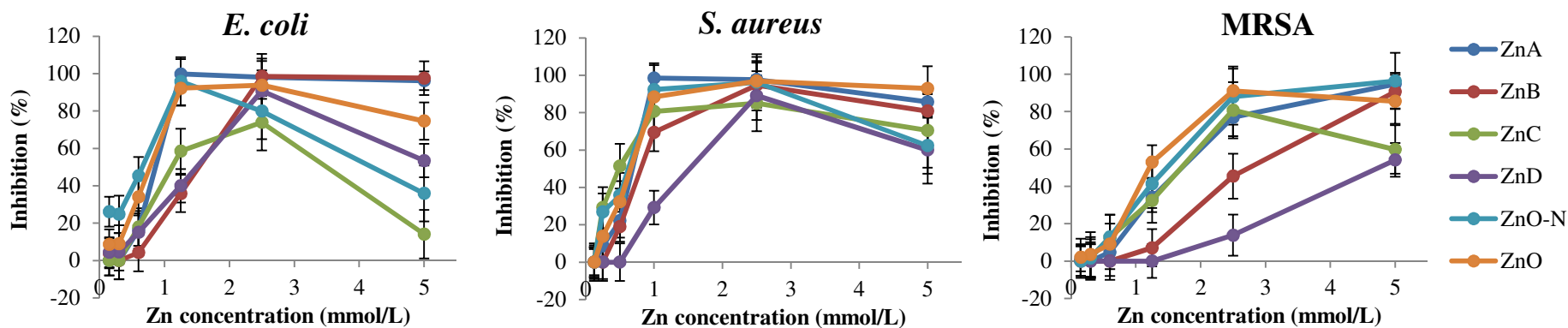
CONTENT

-
- Nanoparticles/Nanomaterials
 - Use cases
 - **Zinc nanoparticles**
 - Metal composite nanoparticles
 - 3D materials

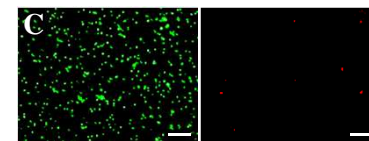
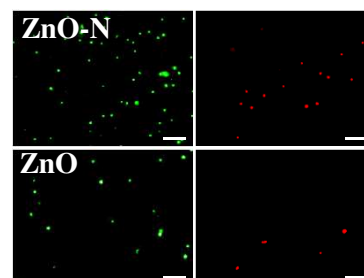
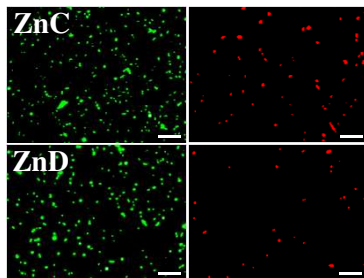
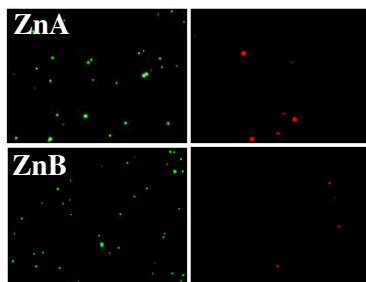


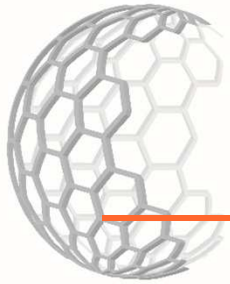
Zinc phosphate-based NPs I

- Antibacterial activity *in vitro* (compared with ZnO and ZnO NPs)



MRSA
live/dead
assay





Zinc phosphate-based NPs II



- Rats were fed with 2000 mg Zn/kg diet for 30 days x compared with control
- Oxidative stress and changes in liver and duodenum tissues was not observed
- Influence on gut microbiota

Horky et al. *Journal of Animal Science and Biotechnology* (2019) 10:17
<https://doi.org/10.1186/s40104-019-0319-6>

Journal of Animal Science and
Biotechnology

RESEARCH

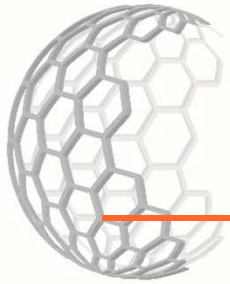
Open Access



Zinc phosphate-based nanoparticles as a novel antibacterial agent: *in vivo* study on rats after dietary exposure

Pavel Horky¹, Sylvie Škalickova¹, Lenka Urbankova¹, Daria Baholet¹, Silvia Kociova², Zuzana Bytesnikova², Eliska Kabourkova², Zuzana Lackova^{2,3}, Natalia Cernei^{2,3}, Milica Gagic², Vedran Milosavljevic^{2,3}, Vendula Smolikova^{2,3}, Eva Vaclavkova⁴, Pavel Nevrlida⁵, Pavel Knot¹, Olga Krystofova^{2,3}, David Hynek^{2,3}, Pavel Kopecl^{2,3}, Jiri Skladanka¹, Vojtech Adam^{2,3} and Kristyna Smerkova^{2,3*}

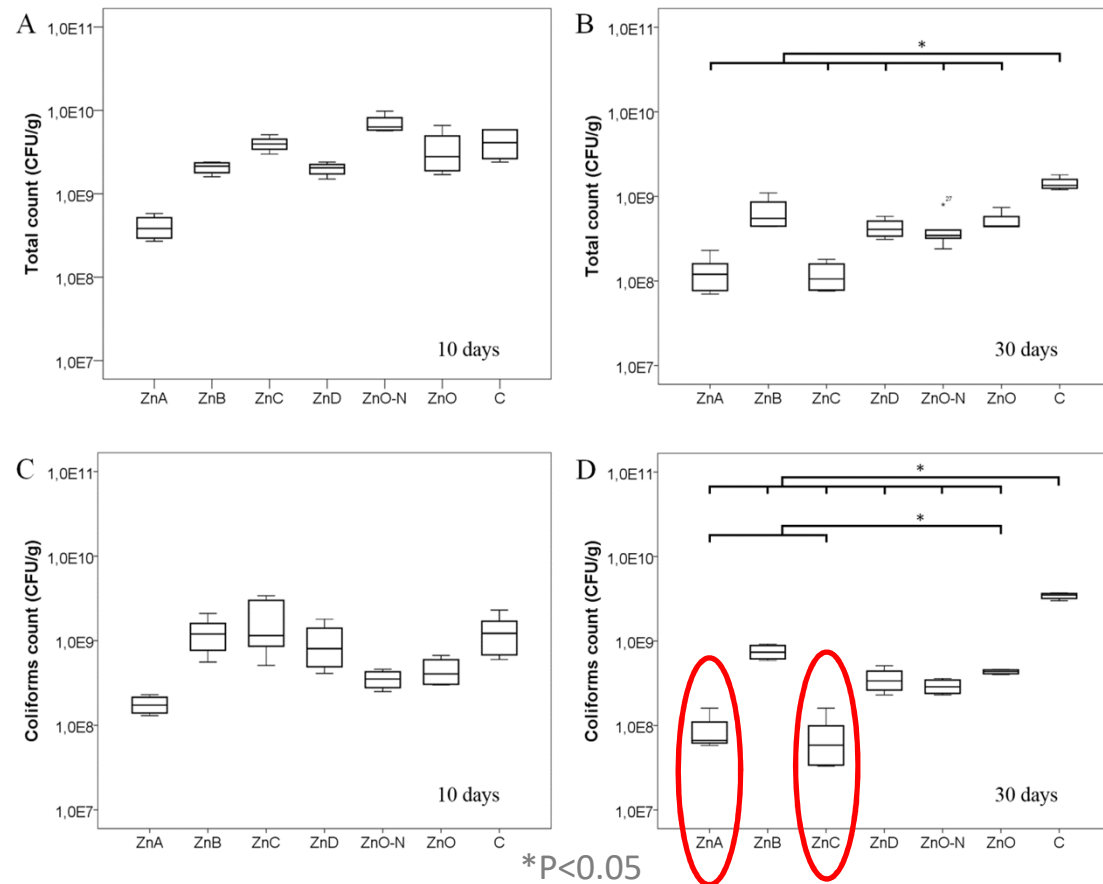
Horky et al., *Journal of Animal Science and Biotechnology* (2019)



Zinc phosphate-based NPs II



The counts of total aerobic and coliform bacteria in rat feces at day 10 and day 30



- Rats were fed with 2000 mg Zn/kg diet for 30 days x compared with control
- Oxidative stress and changes in liver and duodenum tissues was not observed
- Influence on gut microbiota

Horky et al. *Journal of Animal Science and Biotechnology* (2019) 10:17
<https://doi.org/10.1186/s40104-019-0319-8>

Journal of Animal Science and Biotechnology

RESEARCH

Open Access



Zinc phosphate-based nanoparticles as a novel antibacterial agent: *in vivo* study on rats after dietary exposure

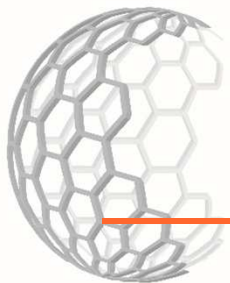
Pavel Horky¹, Sylvie Škalicková¹, Lenka Urbanková¹, Daria Baholet¹, Silvia Kociová², Zuzana Bytesniková², Eliska Kabourkova^{2,3}, Zuzana Lackova^{2,3}, Natalia Cernei^{2,3}, Milica Gagic², Vedran Milosavljevic^{2,3}, Vendula Smollikova^{2,3}, Eva Vaclavkova⁴, Pavel Nevrlka⁵, Pavel Knot¹, Olga Krystofova^{2,3}, David Hynek^{2,3}, Pavel Kopeck^{2,3}, Jiri Skladanka¹, Vojtech Adam^{2,3} and Kristyna Smerkova^{2,3*}

Horky et al., *Journal of Animal Science and Biotechnology* (2019)



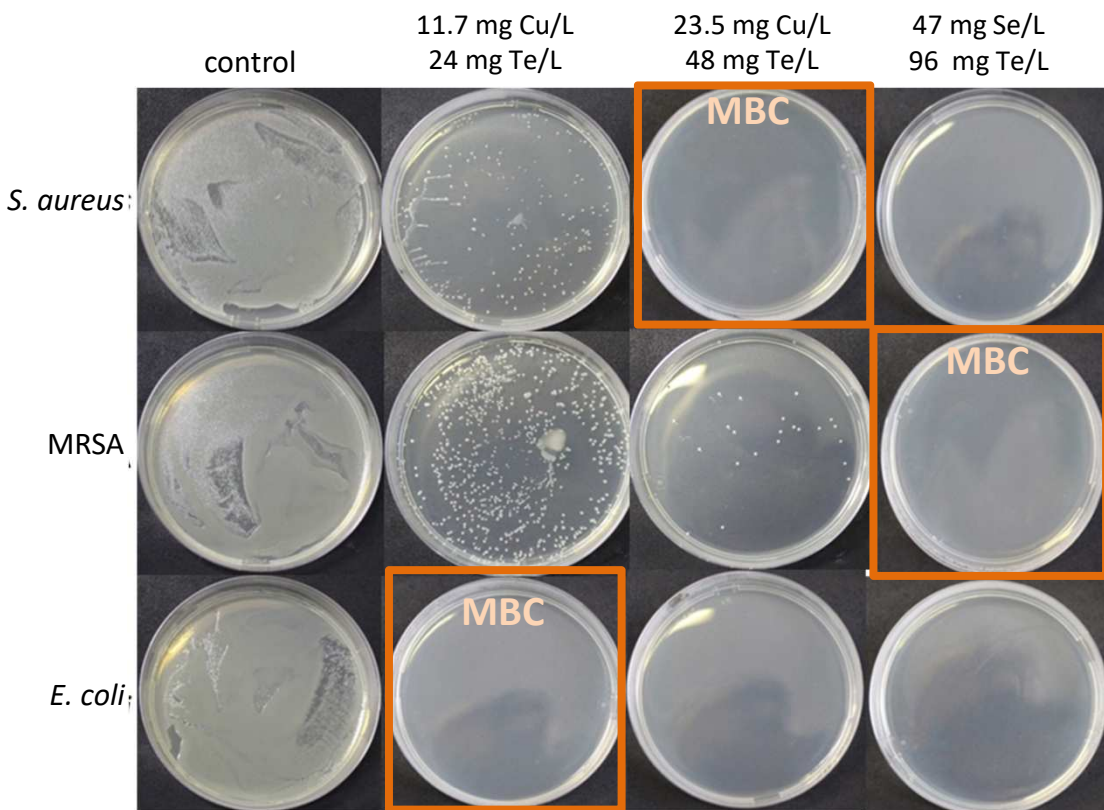
CONTENT

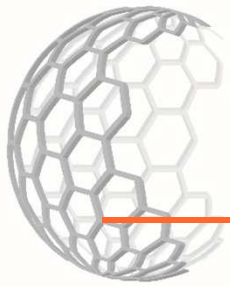
- Nanoparticles/Nanomaterials
- Use cases
 - Zinc nanoparticles
 - **Metal composite nanoparticles**
 - 3D materials



CuTe NPs

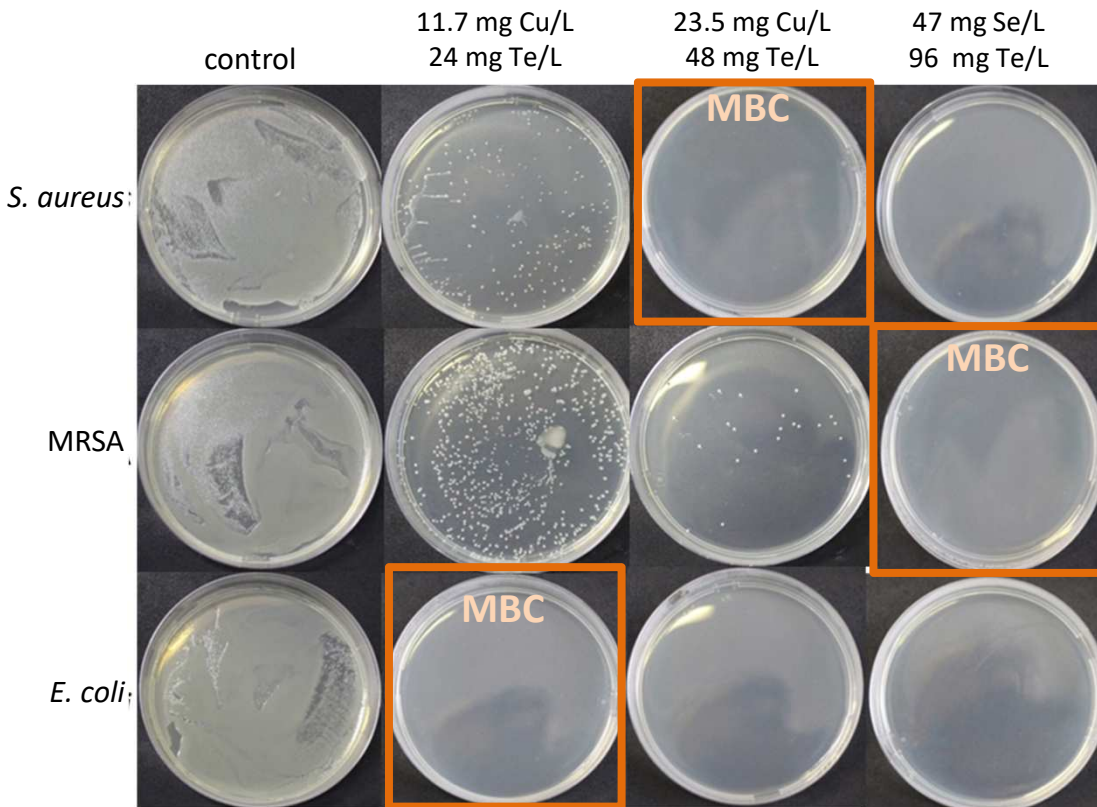
- Antibacterial activity



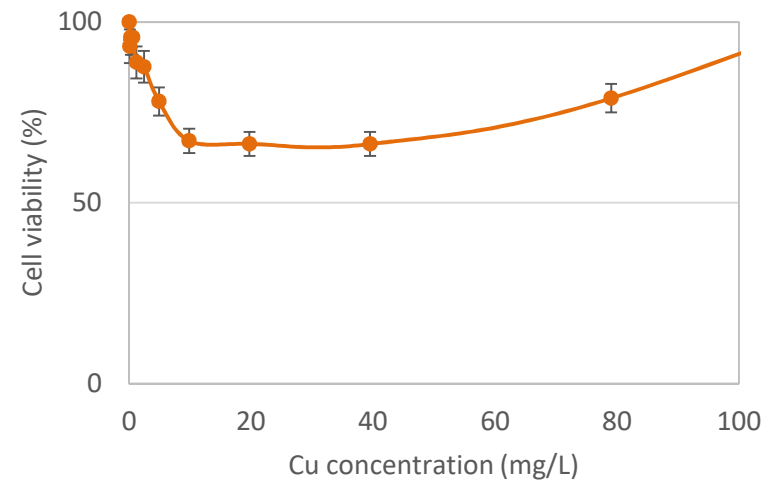


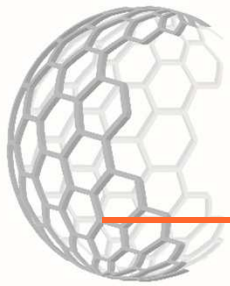
CuTe NPs

- Antibacterial activity



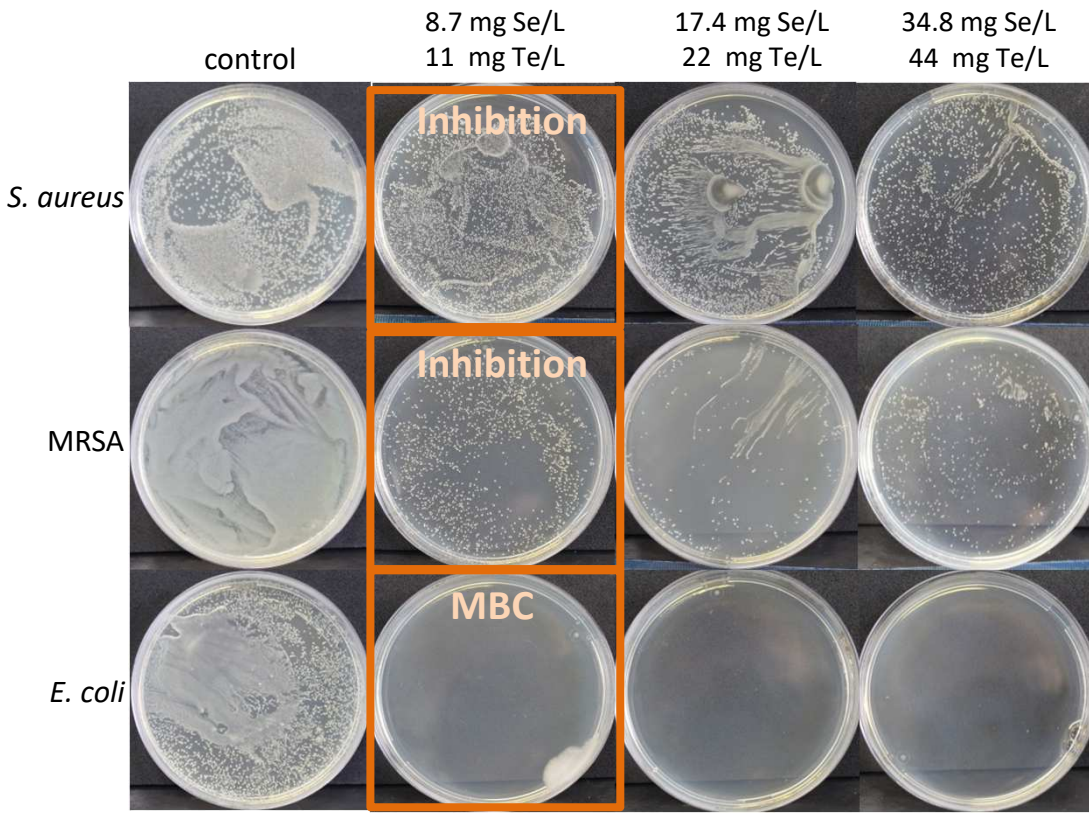
- Viability assay of HUVEC

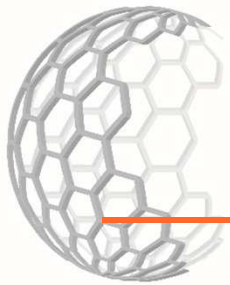




SeTe NPs

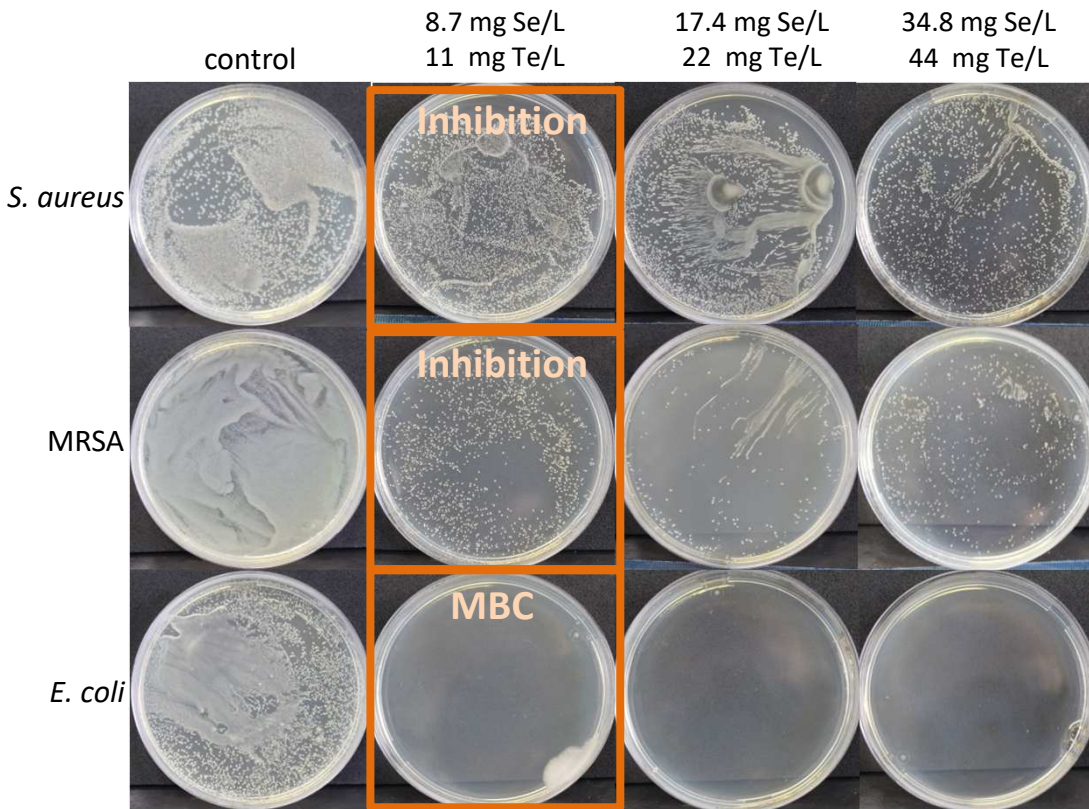
- Antibacterial activity



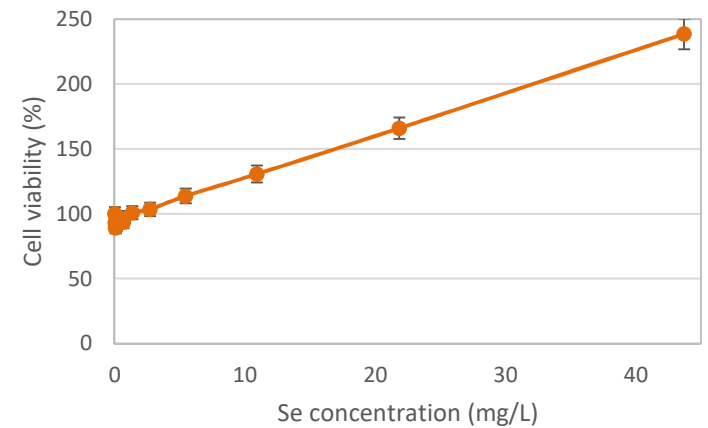


SeTe NPs

- Antibacterial activity



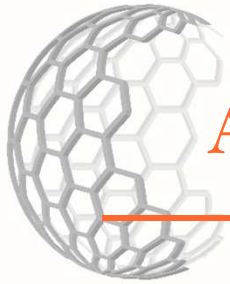
- Viability assay of HUVEC





CONTENT

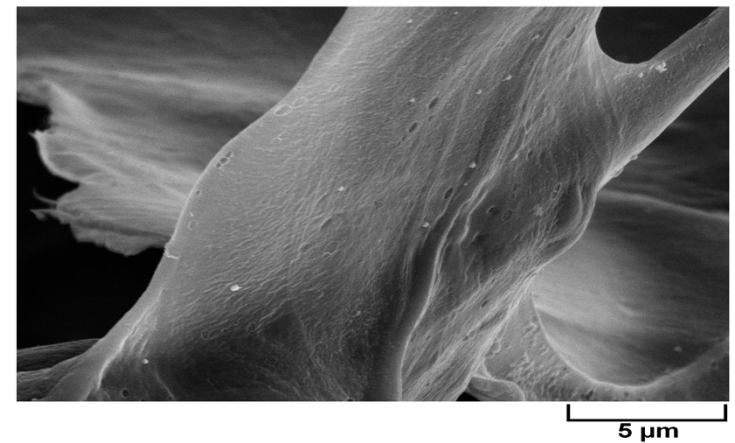
- Nanoparticles/Nanomaterials
- Use cases
 - Zinc nanoparticles
 - Metal composite nanoparticles
- **3D materials**



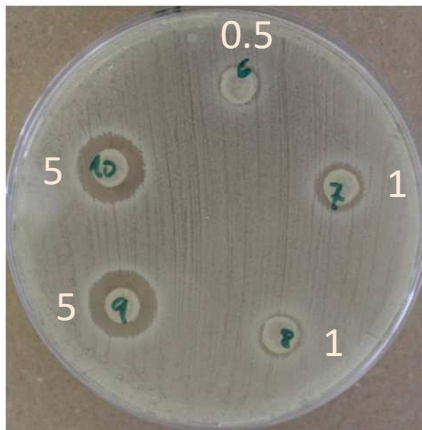
Antibacterial 3D porous collagen scaffolds

- Collagen/chitosan scaffolds doped with SeNPs
- For soft tissue regeneration

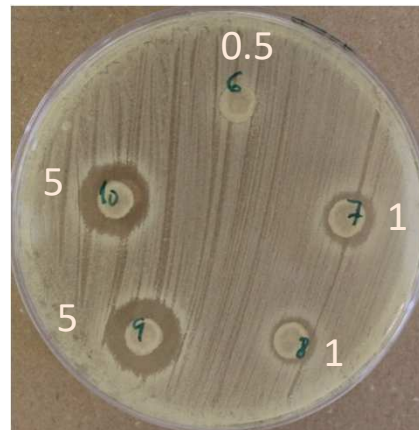
Morfology of scaffold with SeNPs



S. aureus

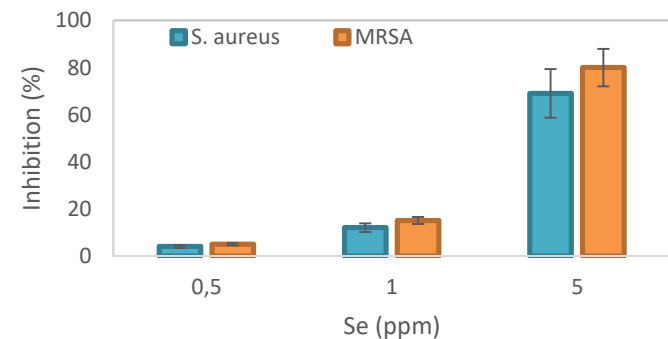


MRSA



Collagen scaffolds with different SeNPs concentrations (ppm)

Bacterial growth inhibition

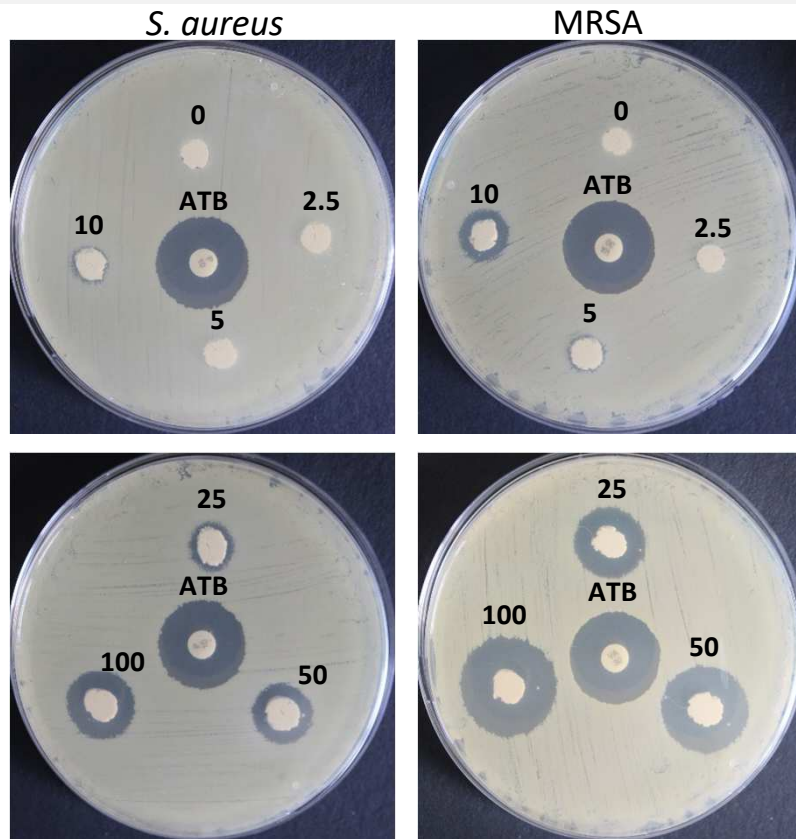
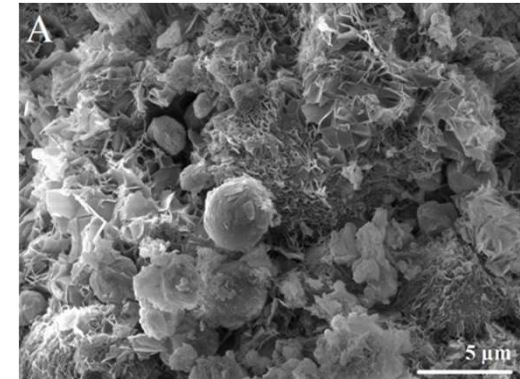




Antibacterial Polymer-Phosphate Bone Cement

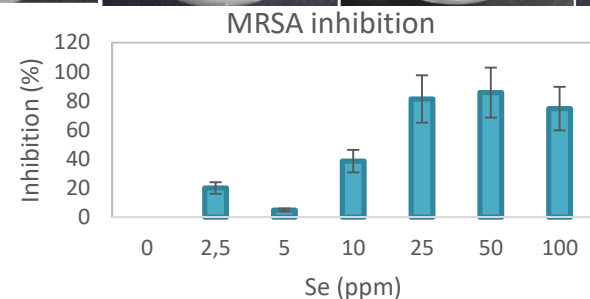
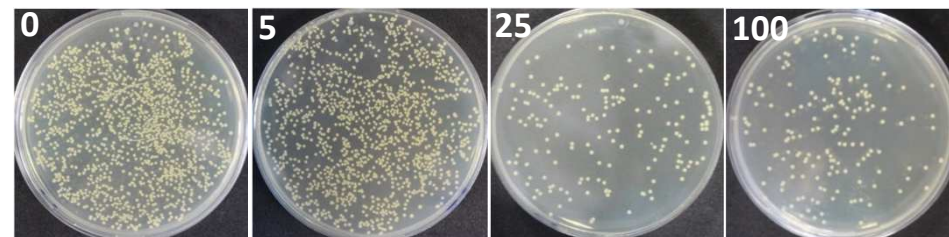
- Based on calcium phosphate with copolymer
- Doped with SeNPs
- Injectable, resorbable, porous bone substitute

Microstructure of bone cement with SeNPs



Bone cement with different SeNPs concentrations (ppm)

Recultivated MRSA colonies after incubation with bone cement (Se concentration in ppm)





DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY



Thank you for your attention



EVROPSKÁ UNIE
Evropské strukturální a investiční fondy
OP Výzkum, vývoj a vzdělávání



MINISTERSTVO ŠKOLSTVÍ,
MLÁDEŽE A TĚLOVÝCHOVY

Mendel
University
in Brno



středoevropský technologický institut
BRNO | ČESKÁ REPUBLIKA

Vojtech Adam, vojtech.adam@mendelu.cz

