



European Network for diagnosis  
and treatment of antibiotic-  
resistant bacterial infections  
(**EURESTOP- CA21145**)

<https://eurestop.eu/>

**Assoc. Prof. Didem ŞEN KARAMAN**  
**Young Researchers & Innovators**  
**Coordinator**

# YR&Is Coordinating TEAM



**Ivana Kovacevic (Serbia)**  
YR&Is committee member

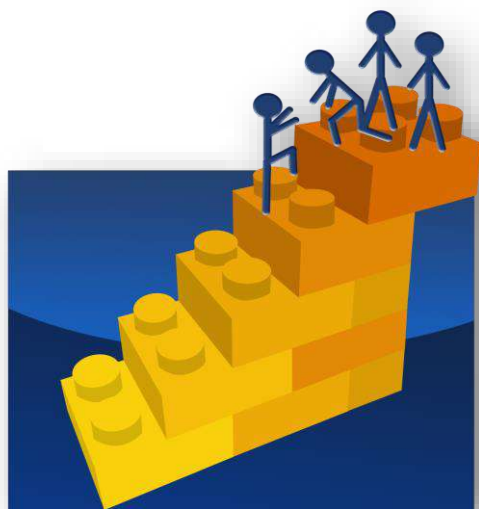


**Didem ŞEN KARAMAN (Turkey)**  
Coordinator



**Amar Osmanovic (Bosnia and Herzegovina)**  
YR&Is committee member

# EURESTOP ACTION



**Motivation** : Career development of Young Researchers and Innovators and research impulses in the Action - Inclusiveness Target Countries (ITC).

**Way** ;

- ✓ **Increase and disseminate the know-how on DR bacteria** from a multidisciplinary and translational perspective, and use this knowledge **in training young scientists** including Ph.D. students, ECIs, and established researchers via Short-Term Scientific Missions (STSMs).
- ✓ **Provide** young researchers&investigators **pre-access to the network** to create a link with the Action, **help them familiarise** themselves with the management **of a network** at European level, and **support their early career development.**



# Young Researchers & Investigators in EURESTOP Action :

- ✓ PhD candidates involved in the action ( Individual participaton or as a part of resarch group)
- ✓ Researchers with PhD degree ( less than 8 years between the date of the PhD/doctorate (or similar experience)
- ✓ Researchers with PhD/doctorate degree and involved in the COST Action under age 40



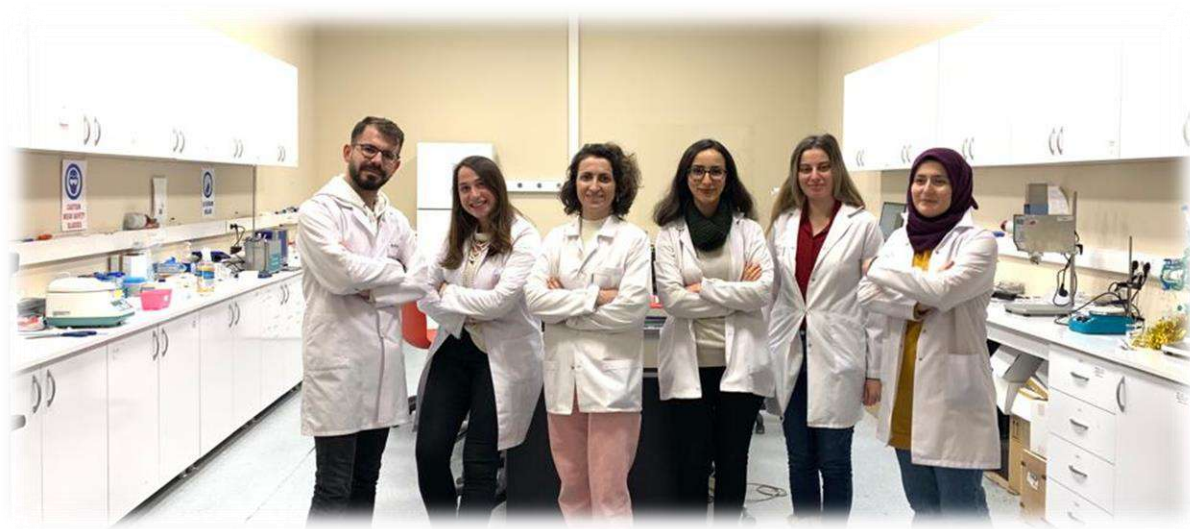




# YR&Is Coordinator & members

- ✓ Encouraging YR&I participation in EURESTOP Action events and research activities;
- ✓ Time slots for disseminations (as oral ppts ) at each Action conference and at WG meetings
- ✓ Training programs on topics;
  - 1) *bioinformatics and computational modelling;*
  - 2) *genomics, proteomics, and glycomics;*
  - 3) *bacterial culture and antimicrobial testing in vitro*
  - 4) *3D mimetic cell and tissue culture;*
  - 5) *drug synthesis and delivery,*
- ✓ Calls for STSMs.
- ✓ 3<sup>rd</sup> year (30<sup>th</sup> month) of the Action a meeting entirely by Young Researchers and Innovators

# ***Hybrid nanoantibiotic designs for combating bacterial infections***



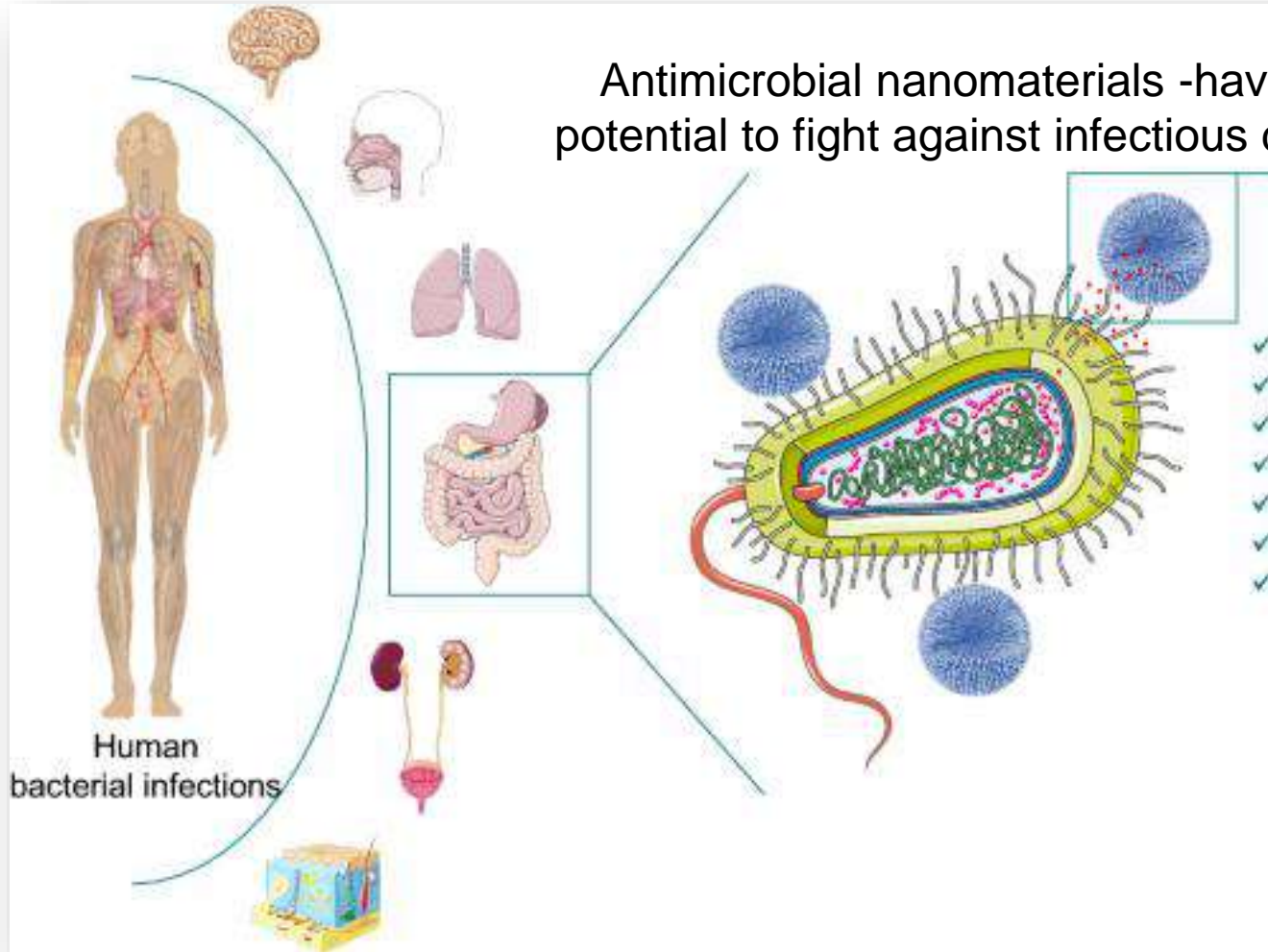
***Nanomedicine and Biomaterials Laboratory Group  
at Department of Biomedical Engineering,  
İzmir Katip Çelebi University***

# Nanomaterials as non-traditional antibiotic agents: “*nanoantibiotics* as promising therapeutic tools against bacterial infections “

Antimicrobial nanomaterials -have great potential to fight against infectious diseases.

## *State-of-the-art nanoparticles*

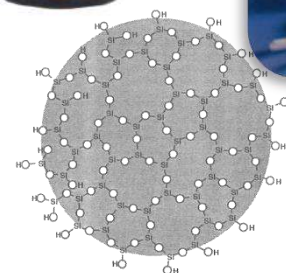
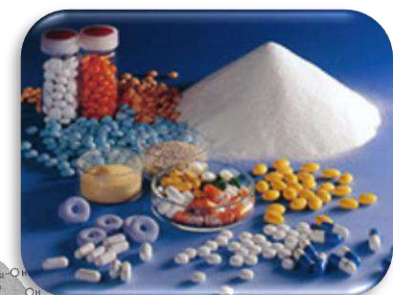
- ✓ Antibacterial effect
- ✓ High antibiotics loading
- ✓ Antibiotics targeting
- ✓ Antibiotics penetration increase
- ✓ Antibiotics retention increase
- ✓ Antibiotics efflux reduction
- ✓ Promotion of host immunity



**Silica: SiO<sub>2</sub>** Amorphous silica (SiO<sub>2</sub>), "silica", is a body-like substance, which is a lot of especially in hair, skin and nails is also taken as a dietary supplement. Not to be confused with crystalline silicates (eg asbestos, quartz) !!! An essential component of whole body cells (SiO<sub>2</sub> in human tissues varies from 10 to 200 mg / 100 grams dry weight)

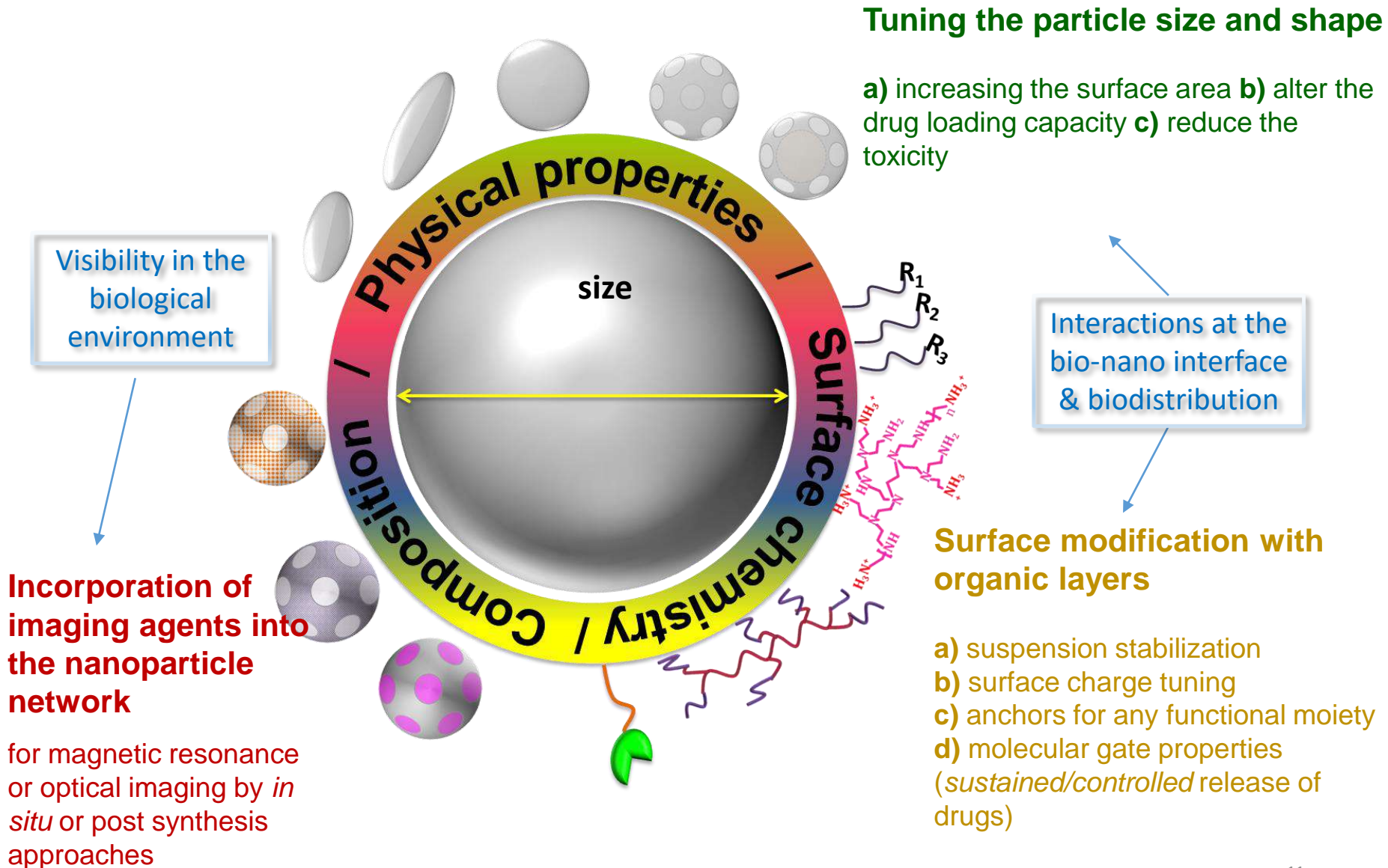
Silicon dioxide (E 551) is authorised as a food additive in the European Union (EU) in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008 on food additives and specific purity criteria are defined in the Commission Regulation (EU) No 231/2012.

- ✓ Versatile applicability
- ✓ Used as a filler in tablets over 50 years (GRAS)
- ✓ In traditional solid preparations improves ; compactibility and flowability, promote disintegration, adjust hygroscopicity, and prevent excessive adhesion
- ✓ In 1983, research began in the use of SiO<sub>2</sub> gels as a drug carrier due to their high porosity
- ✓ The forms of synthetic amorphous silica (SAS) used as E 551 include fumed silica and hydrated silica (precipitated silica, silica gel and hydrous silica) comprised of aggregated nanosized primary particles.

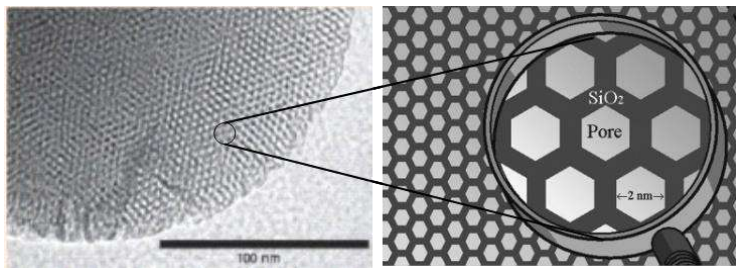


EFSA J. 2018 Jan 17;16(1):e05088. doi: 10.2903/j.efsa.2018.5088.

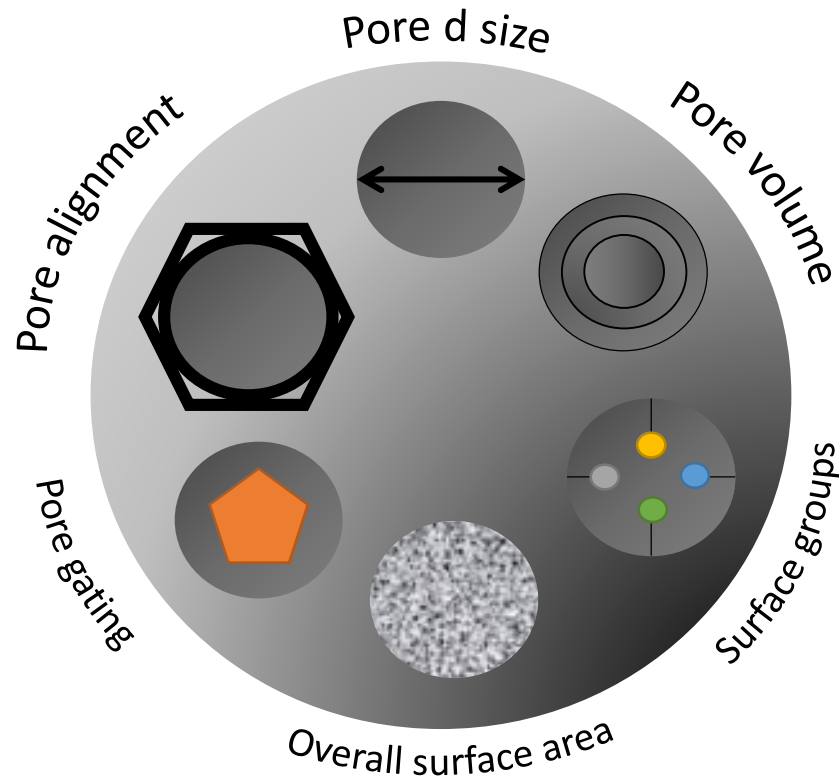
# Flexible designs options with Nanoparticles



# Mesoporous silica framework serve for antibiotics and AMP delivery



- **Pore sizes** can be *tuned* in the molecular size range → ideal for *hosting molecular agents, e.g. drugs*
- Extremely **high surface areas** and **pore volumes** → *hosting of a large amount of cargo* (drugs, imaging agents, proteins...)
- The **ordered pore structure** provides a *homogeneous distribution* of guest molecules → *sustained or controlled release*
- The inner **pore walls** can be surface functionalized to **provide anchoring points** for the cargo molecules and **enhance drug immobilization**
- The outer **particle surface** can be functionalized independently to **regulate the drug release, tune the surface charge**, provide **suspension stability** and/or attach functional moieties by **bioconjugation reactions etc.**

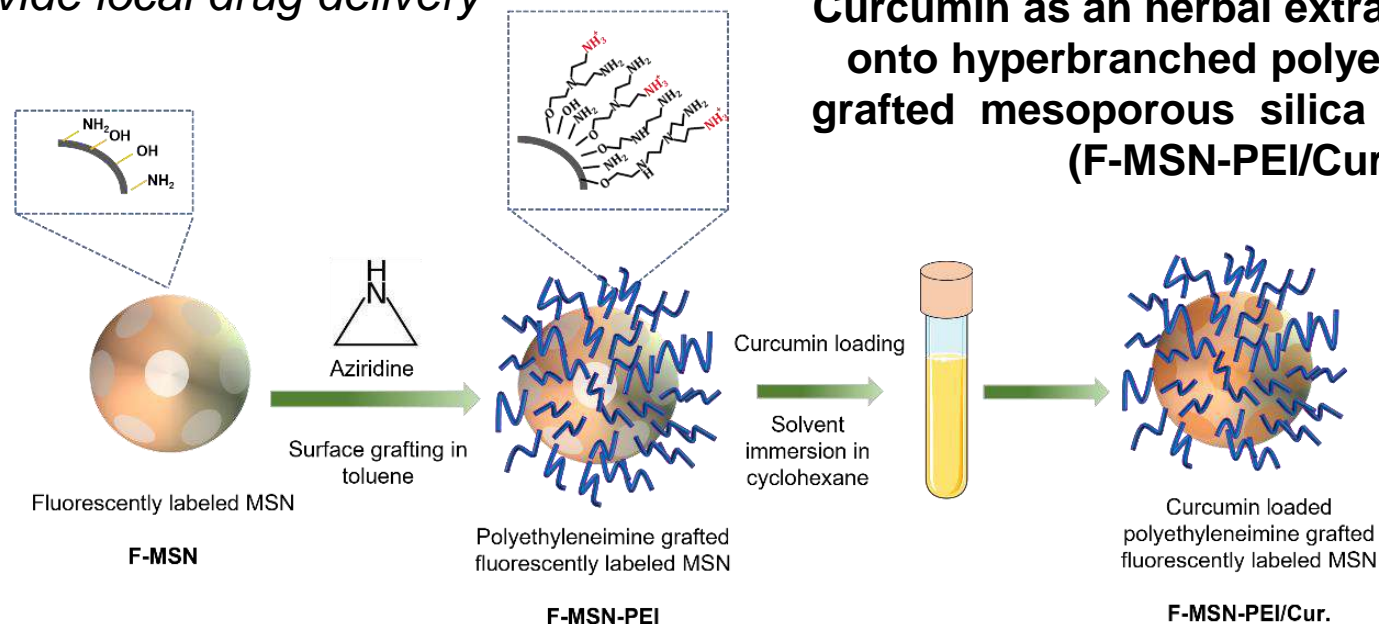


**RESEARCH ARTICLE**

# Polyethylenimine-grafted mesoporous silica nanocarriers markedly enhance the bactericidal effect of curcumin against *Staphylococcus aureus* biofilm

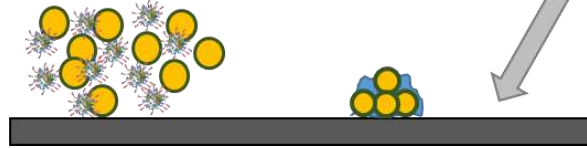
*Biofilm-associated infections difficult to treat & limited repertoire of antibiotics*  
A potential solution to biofilm-associated infections ;

- ✓ Attack biofilms from many fronts
- ✓ Target biofilm matrix
- ✓ Provide local drug delivery



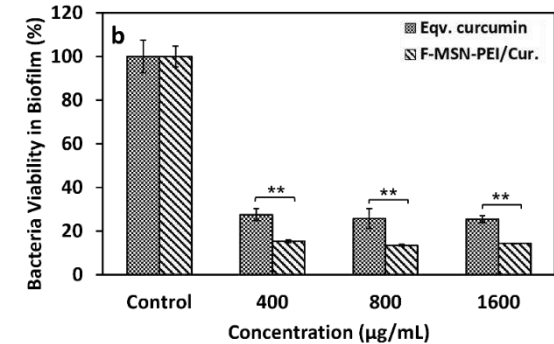
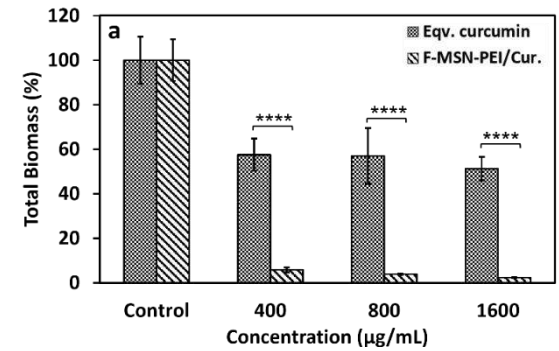
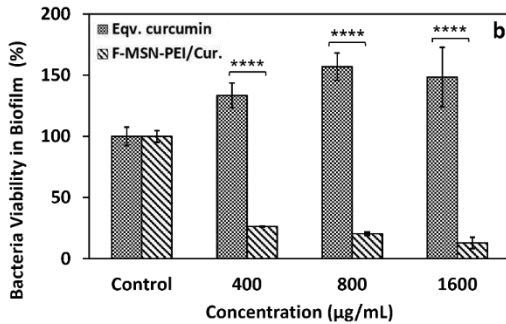
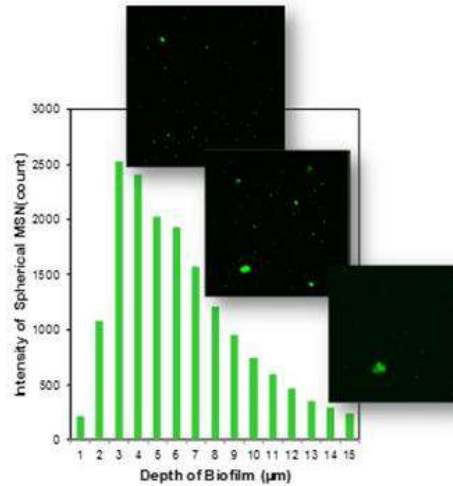
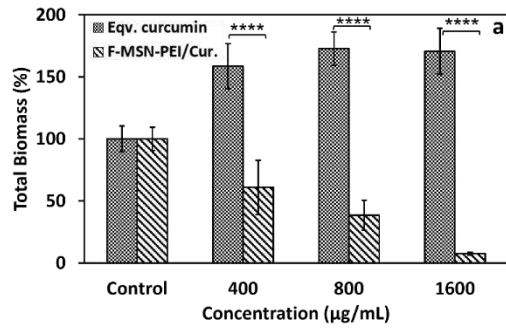
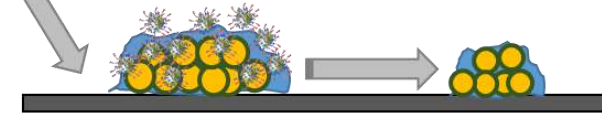
**Curcumin as an herbal extract was loaded onto hyperbranched polyethylenimine-grafted mesoporous silica nanoparticles (F-MSN-PEI/Cur).**

**Inhibiting *S.aureus* biofilm formation**



24h

**Eradication of *S.aureus* biofilm**

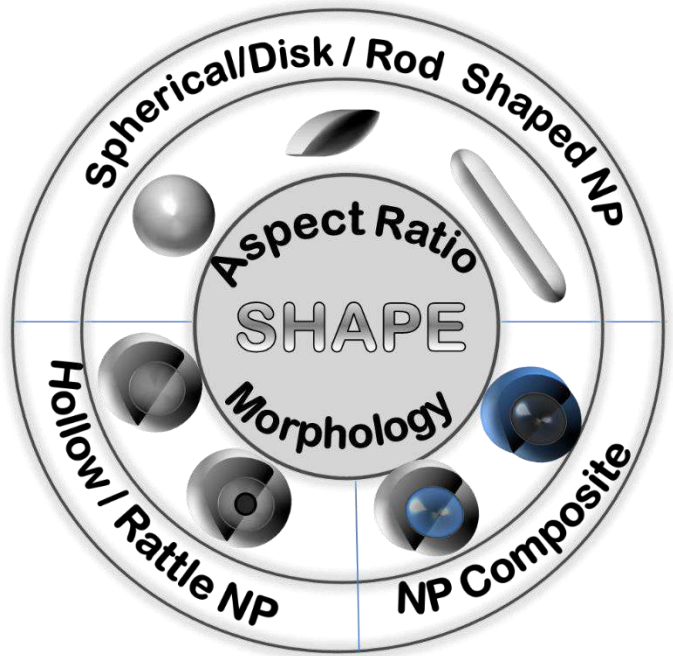
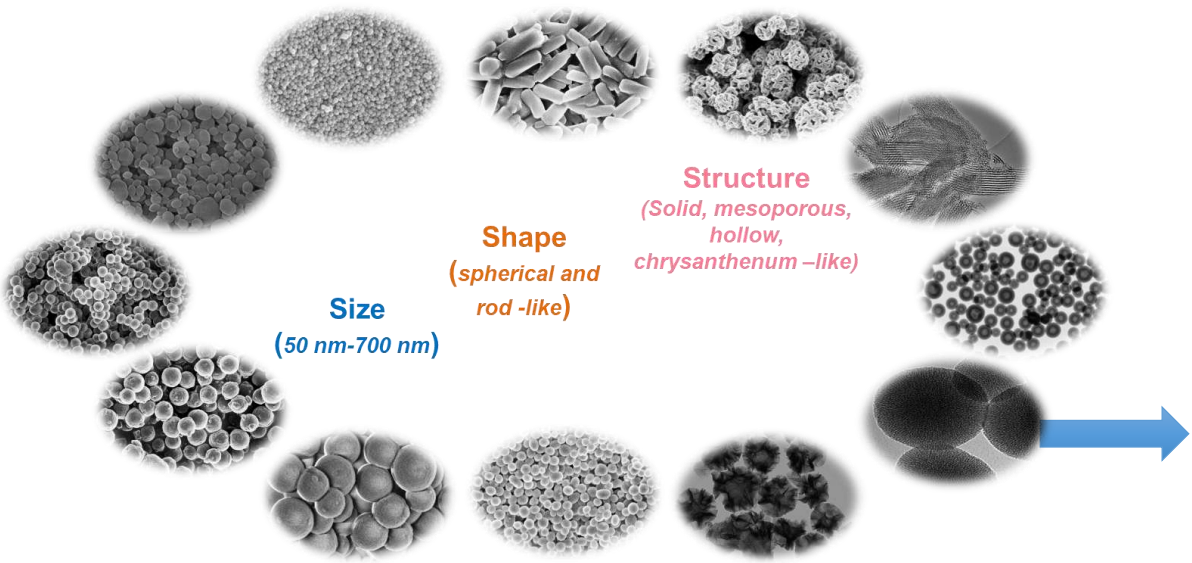


a) safranin assay for reduction in biomass, b) resazurin assay for reduction in bacterial viability

# Tuning the physicochemical properties of MSN for antibacterial activity

## Biological fate: Size, surface charge, shape

- The carrier *physicochemical properties*, i.e. **size**, **surface charge**, and **shape** are the main determining factors that affect a nanoparticle's fate within a biological system (e.g. pharmacokinetics and biodistribution)

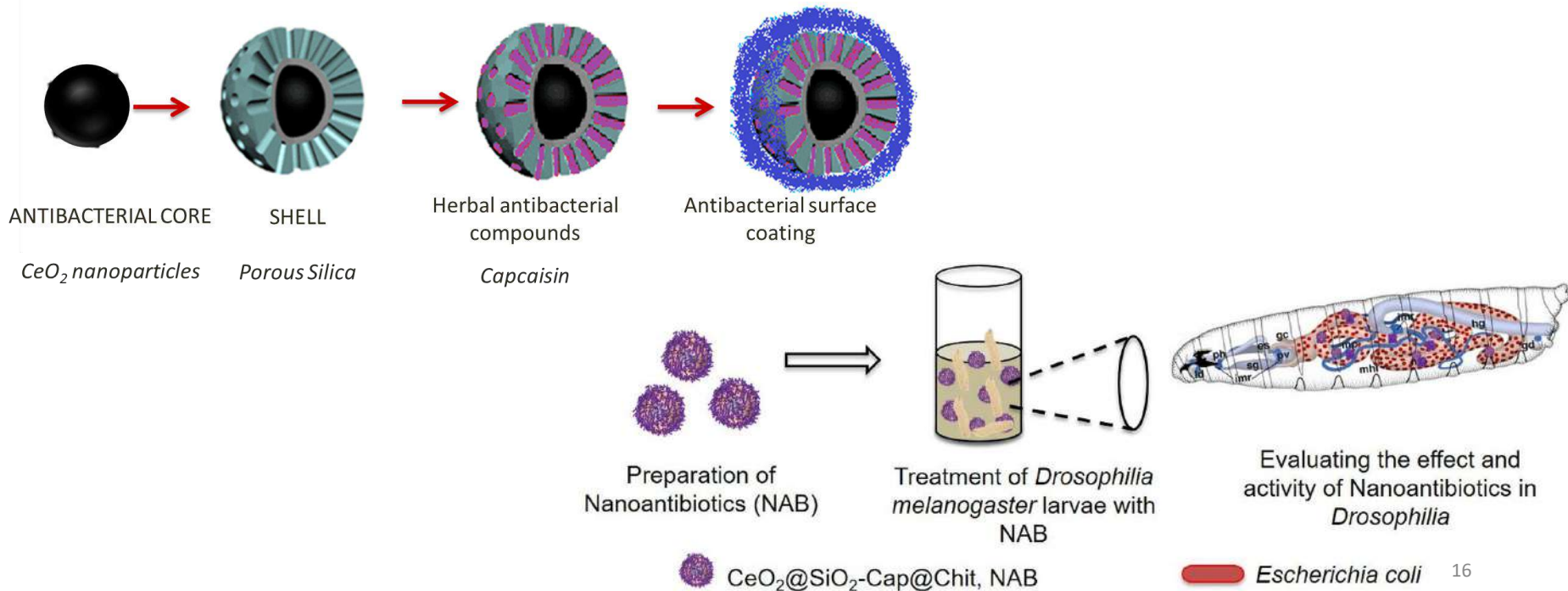


Also to maximize Bacteria interactions

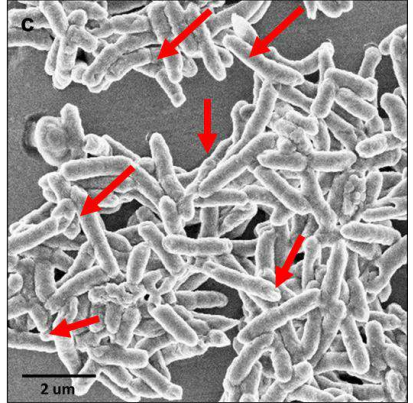
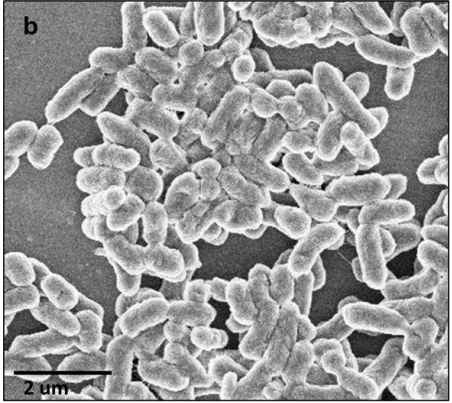
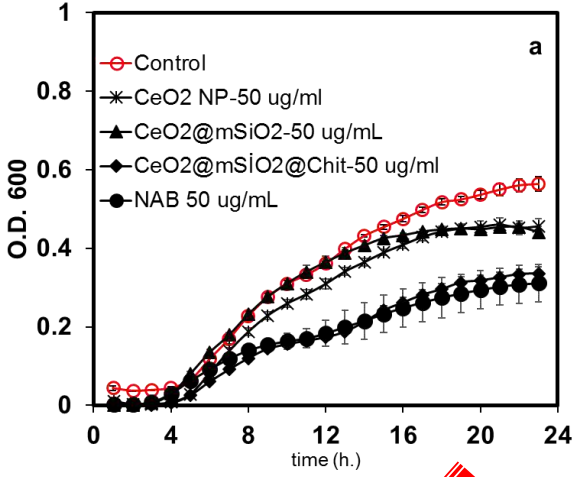
Core@shell structured ceria@mesoporous silica nanoantibiotics restrain bacterial growth *in vitro* and *in vivo*



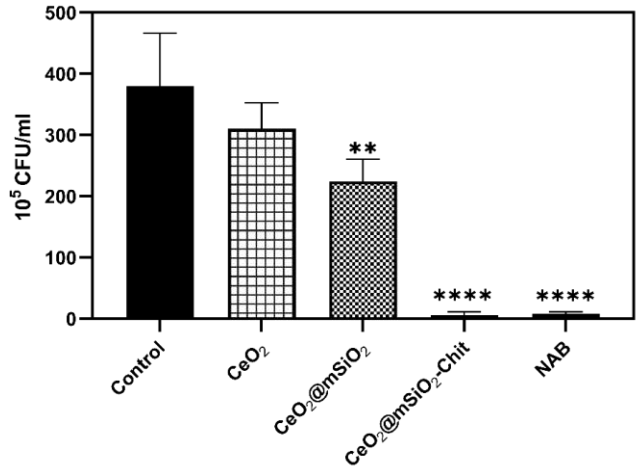
**“Nanoantibiotics”**: herbal extract loaded core@shell  $\text{CeO}_2$ @MSN@Chitosan hybrid materials and evaluating their antibacterial properties on *Drosophila melanogaster* (fruit fly) as an *in vivo* model for human intestinal diseases.



# In vitro E.coli growth inhibition

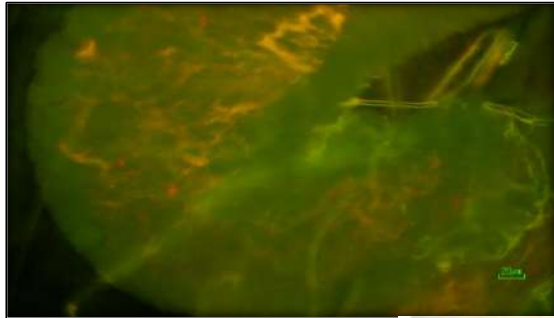


Exponential phase re-culturing

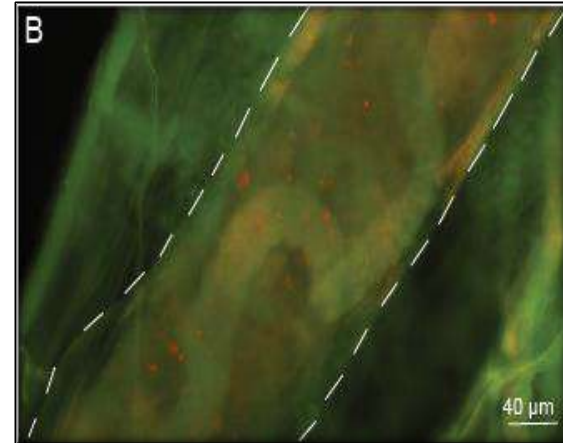
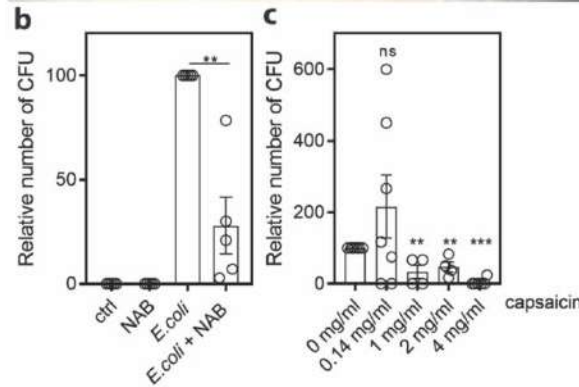


## In vivo evaluation in the GIT of flies

Nanocomposites with fluorescent dye (DiI) loading was imaged



1mg/ml of nanocomposites fed through food for 2 hours



Nanocomposites in the posterior midgut of the larvae of *Drosophila melanogaster*.

# Nanomed & Biomat Group in EURESTOP

## WG 2-Microbiology, Microbiota;

-Investigating the safety and bioactivity of available antibacterial compounds available for WG3 to prioritize novel putative antibacterial agents of biological, natural or synthetic origin as pre-clinical candidates by in vitro investigations.

## WG 3-Drug Design and Delivery ;

-Providing delivery systems to encapsulate various hydrophobic therapeutic agents, and offering different surface modification strategies in order to make it possible to adapt the pharmacological behavior of the nanocarrier to suit the intended application.

-Providing adjuvan NP systems for novel immunotherapies using existing antibodies

