UNCOVERING THE POTENTIAL OF GALLIUM-DENDRITIC ZEOLITES FOR ADVANCED ANTIMICROBIAL THERAPY

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CRS2026 ANNUAL MEETING & EXPOSITION LISBON PORTUGAL — MULTISECTOR INNOVATION for ADVANCING DELIVERY SCIENCE — JULY 6-9, 2026

BACKGROUND

Antimicrobial resistance

4.7 Million Deaths Annually

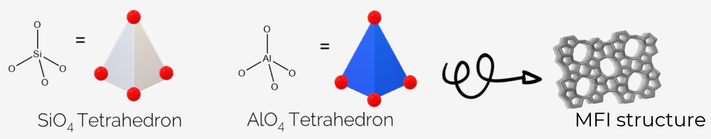
10 Million Deaths by 2050

$1 Trillion Economic Impact

The rise of antimicrobial resistance represents a major global health challenge that requires innovative therapeutic solutions. Nanomedicine offers new opportunities to tackle this problem.

...What are zeolites?

❖ Silica microporous materials



Silicate and aluminate tetrahedron form the primary building units which interconnect forming the zeolitic structures.

Properties:

✓ high stability
✓ microporosity (pore size < 2nm)
✓ high surface area (up to 700 m²/g)
✓ adjustable hydrophilicity
✓ ion-exchange capacities

x alluminum toxicity
x pore size limits drug loading

OBJECTIVES

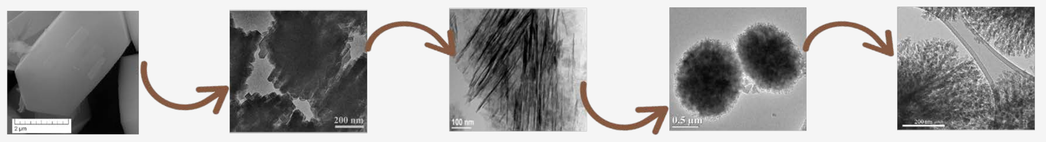
The development of gallium-dendritic zeolitic nanoparticles to be used as drug delivery system to combat antimicrobial resistance, specifically, cutaneous infections.

For this, the material have to posses different properties:

➢ Biocompatible
Substitution of Al with Ga

➢ Antimicrobial activity
Using a metal with antimicrobial activity as Ga and loading different drugs

➢ Nanometric size and accessible porosity



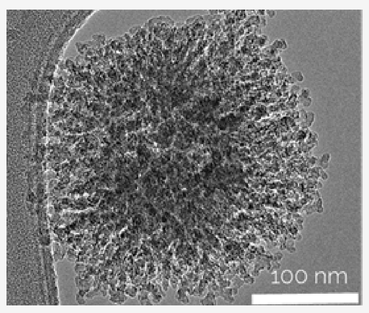
RESULTS

PHYSICOCHEMICAL CHARACTERIZATION

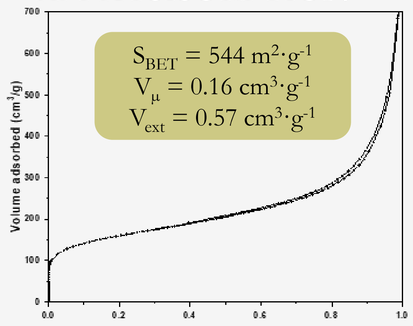
✓ Hierarchical trimodal porosity with high accessibility

✓ Particle size <200 nm

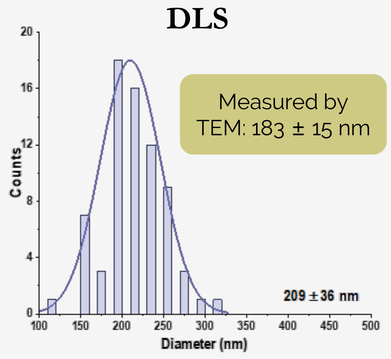
HR-TEM



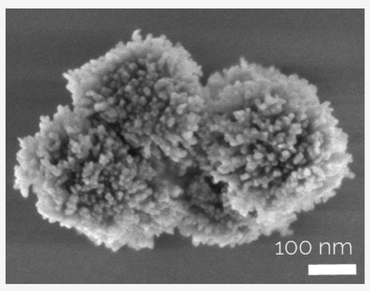
Ar PHYSISORPTION



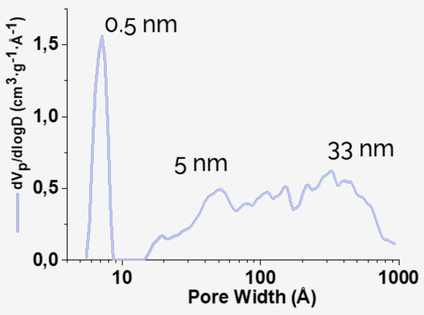
DLS



HR-SEM

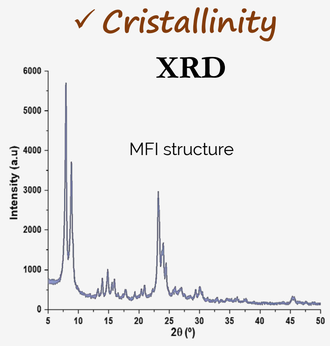


Pore Size Distribution



✓ Cristallinity

XRD



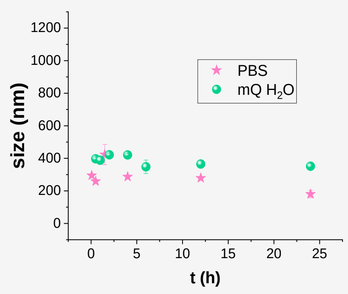
The dendritic architecture features a highly accessible trimodal porosity (with micro-, meso- and macropores). Particle size is < 200nm, as infered from TEM images and DLS measurements. XRD diffractogram corresponds to a zeolite with MFI structure.

POTENTIAL AS DRUG DELIVERY SYSTEMS

BIOLOGICAL PROPERTIES

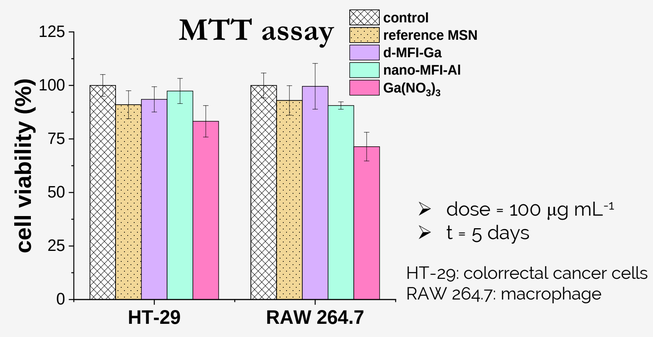
✓ Colloidal stability

DLS



✓ Biocompatibility

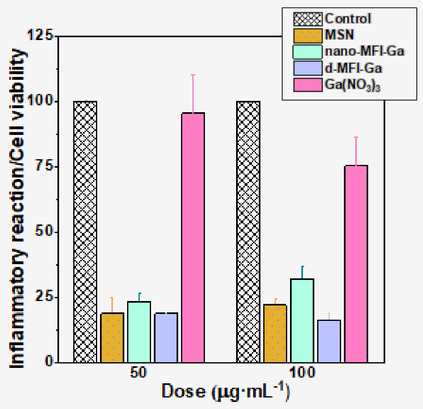
MTT assay



➢ dose = 100 μg mL⁻¹
➢ t = 5 days

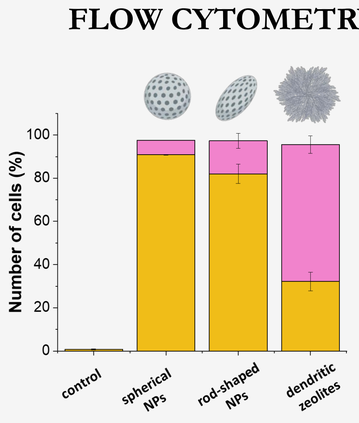
HT-29: colorrectal cancer cells
RAW 264.7: macrophage

✓ Antiinflammatory properties



✓ High uptake rate

FLOW CYTOMETRY

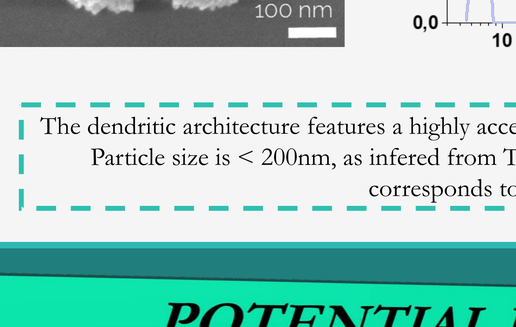


➢ dose = 100 μg mL⁻¹
➢ HT-29 cells

The dendritic morphology imparts the material with a higher internalization rate than spherical and rod-shaped nanoparticles.

POTENTIAL FOR CUTANEOUS INFECTION TREATMENT

DRUG LOADING

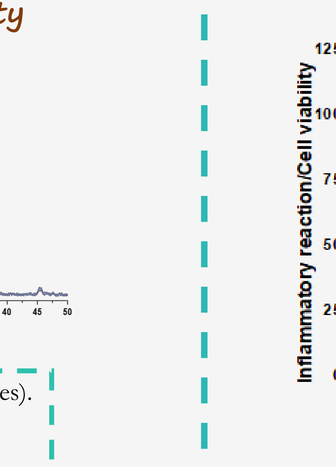


SBET = 95 m²·g⁻¹
Vμ = 0 cm³·g⁻¹
Vext = 0.35 cm³·g⁻¹

Successful differential loading of the drugs according to their size into the micro- or meso- and macropores.

TRANSDERMAL DRUG DELIVERY

Dendritic zeolite enhances drug permeation, probably due to their higher internalization rate.



ANTIBACTERIAL PERFORMANCE

➢ dose = 100 μg mL⁻¹
➢ *S. aureus* cells

CONCLUSIONS

The dendritic architecture imparts the material with a highly **accessible trimodal porosity, high internalization rate** by colorectal cancer cells and **enhanced transdermal penetration**.
The particle size was <200 nm and presented colloidal stability.

The substitution of aluminium by gallium lead to a **biocompatible** material with **intrinsic anti-inflammatory properties**.

Dual-drug loading was successfully achieved taking advantage of the different porosity of the material.

The introduction of gallium along with two antimicrobials endowed the material with **antibiotic activity**.

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FUNDING:
MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES — AGENCIA ESTATAL DE INVESTIGACIÓN — Funded by the European Union — European Research Council — Todenze Towards Dendritic Zeolites