Systematic design of mesoporous silica nanoparticles to overcome the mucus barrier for targeted oral therapy of inflammatory bowel disease

Hanna Lavén[1,2,3], Era Mero[1], Ahmed Omar[1], Rebecca Fransson[3], Alexandra Teleki[1,2]

hanna.laven@uu.se

1. Department of Pharmacy, Science for Life Laboratory, Uppsala University, Sweden 2. The Swedish Drug Delivery Center, Department of Pharmacy, Uppsala University, Sweden
3. Advanced Drug Delivery, Pharmaceutical Sciences R&D, AstraZeneca, Sweden

1. Introduction

The incidence of **inflammatory bowel disease (IBD)** is increasing globally[1], necessitating effective treatments. IBD is a disease with complex pathogenesis and heterogenous treatment response, which complicates drug development.

This project aims to utilize **mesoporous silica nanoparticles** (MSNs) to enhance **targeted drug delivery** to diseased colonic tissue. One of the key challenges in **oral drug delivery** is hindered diffusion to disease targets due to nanoparticles becoming trapped in **mucus**. Our approach involves synthesising MSNs of varying **shapes and sizes** using a sol-gel method and employing an **artificial mucus model,** designed to simulate porcine mucus to investigate the **diffusion behaviour** of different MSNs through **particle tracking techniques**.

2. Synthesis of mesoporous silica nanoparticles

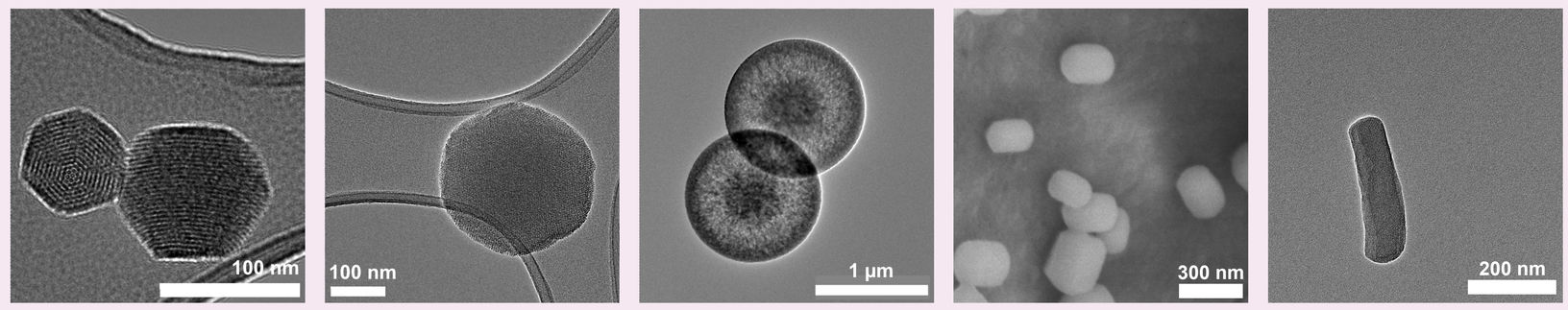


Figure 1. TEM characterization and DLS size distribution of mesoporous silica nanoparticles synthesized via the sol-gel method. TEM images demonstrate the successful preparation of MSNs with controlled particle size and shape, ranging from 100 to 1300 nm. The synthesized particles include spherical MSNs with mean diameters of 160, 260, and 1300 nm, as well as rod-shaped MSNs with dimensions of 165 × 240 nm and 140 × 400 nm.

3. Particle tracking in artificial mucus

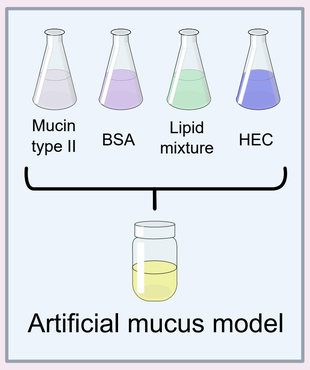
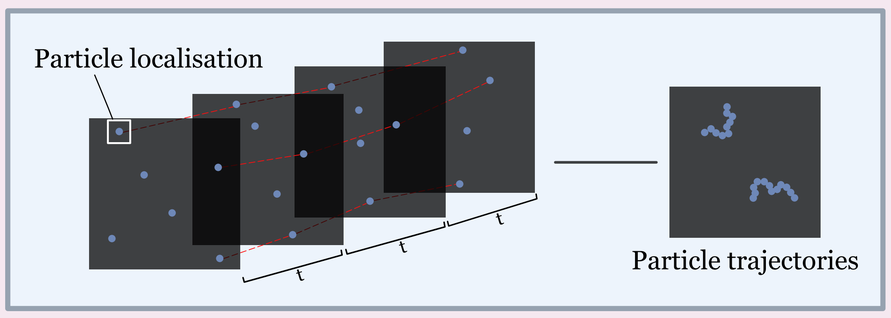


Figure 2. Artificial mucus model and particle tracking analysis of nanoparticle diffusion. Nanoparticle transport in artificial mucus[2] was analyzed using multiple particle tracking. Particle localization across time was used to reconstruct trajectories and quantify diffusion behavior, enabling evaluation of the effects of particle size and shape on mucus transport.



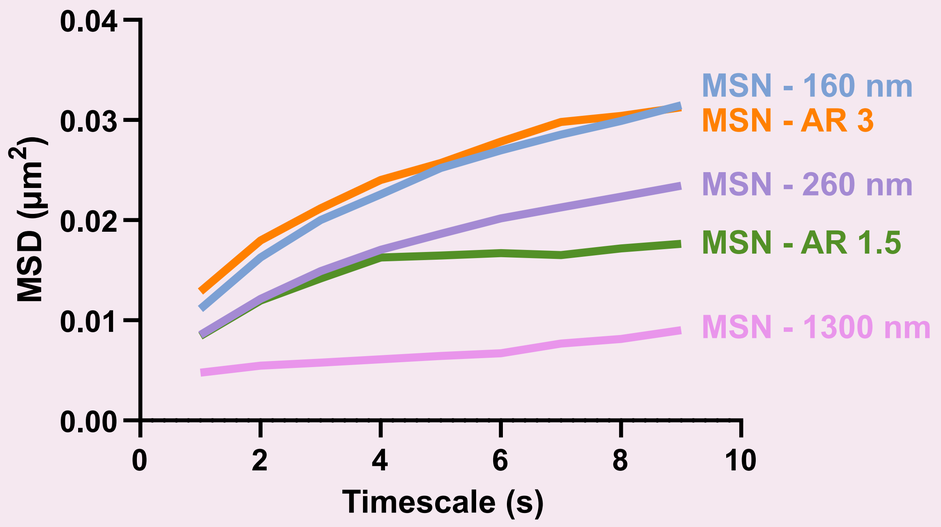


Figure 3. Diffusion behavior of MSNs as a function of particle size and shape. Spherical MSNs showed a clear size-dependent decrease in mobility, with larger particles diffusing more slowly. Notably, 160 nm spherical MSNs exhibited diffusion behavior similar to elongated MSNs with an aspect ratio (AR) of 3. This suggests that AR 3 MSNs may provide higher drug-loading capacity while maintaining transport properties comparable to smaller spherical particles, highlighting shape as an important design parameter.

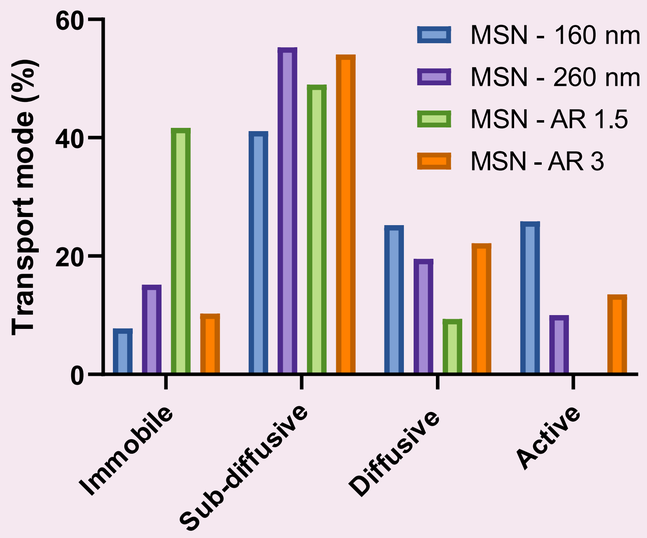


Figure 4. Transport mode distribution of MSNs in the mucus model. Across all particle types, the sub-diffusive transport mode was predominant, which is consistent with the hindered motion expected in a mucus environment. In contrast, MSN with AR 1.5 showed a higher proportion of immobile particles than the other particles, suggesting increased trapping within the mucus network.

4. Safety in zebrafish

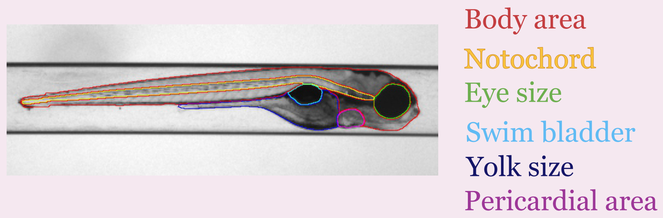


Figure 5. Developmental effects of mesoporous silica nanoparticles in zebrafish embryos. Preliminary results suggest that zebrafish embryos injected with mesoporous silica nanoparticles showed no significant developmental delay compared with the control group. Further studies will assess higher dose levels and compare toxicological effects across different particle shapes.

5. Key Findings

- MSNs were synthesized in a size range of 100-1300 nm with spherical and elongated shapes.
- Spherical MSNs showed size-dependent mobility, with larger particles diffusing more slowly in artificial mucus.
- Elongated MSNs with AR 3 showed diffusion comparable to 160 nm spherical MSNs.
- Elongated MSNs may therefore offer improved drug-loading capacity while retaining favorable mucus transport.
- Sub-diffusive transport was the dominant transport mode across all particle types.
- Preliminary zebrafish studies showed no significant developmental delays after injection with MSNs.

References

1. Kuenzig, E., et al. *Gastroenterology, 162* (2022)
2. Tjakra, M., et al. *Molecular Pharmaceutics, 22* (2025)

Acknowledgements

UPPSALA UNIVERSITET
Swedish Foundation for Strategic Research
SweDeliver Shaping the future of drug delivery
AstraZeneca