HYBRID HYDROGEL CONTAINING MESOPOROUS SILICA NANOPARTICLES FOR TOXIN REMOVAL

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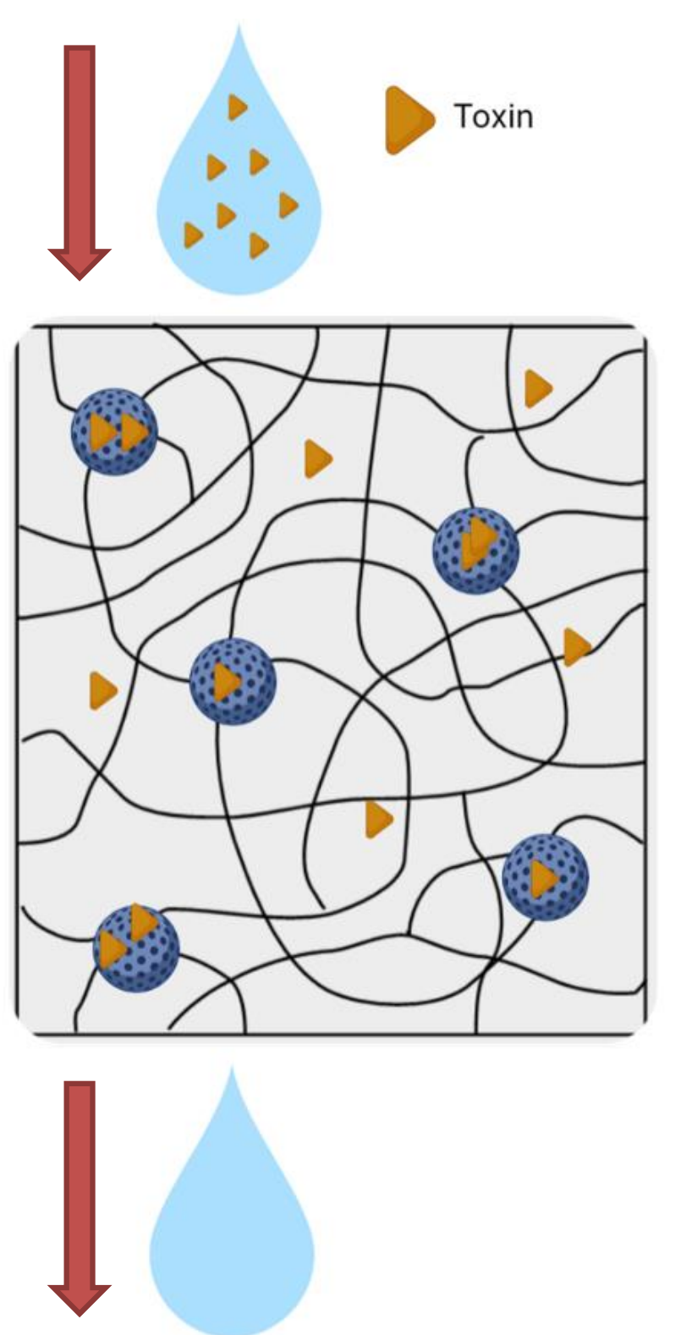
Background

Toxin elimination is a very serious problem that can surge in case of kidney disease and loss of kidney capacity to remove water and waste solutes content. The detention of toxins in the blood involves a variety of side effects especially on cardiovascular system such as hypertension and heart failure. The treatment, when the kidney transplant is not feasible involves dialysis which leads, however, to problems in terms of patient compliance. A wearable artificial kidney has been reported [1] that is capable of purifying the blood outside the hospital, however, none have yet to be successfully implemented clinically. This has led to the conception of a lot of different purification methods for this purpose.

The goal of this project is to have a material through which a fluid can pass and at the same time be purified from toxic substances; we want to obtain hydrogels with particular mechanical features, which can be covalently crosslinked with mesoporous nanoparticles. These nanoparticles must contain large and specifically functionalized pores in order to be able to bind and entrap toxins.

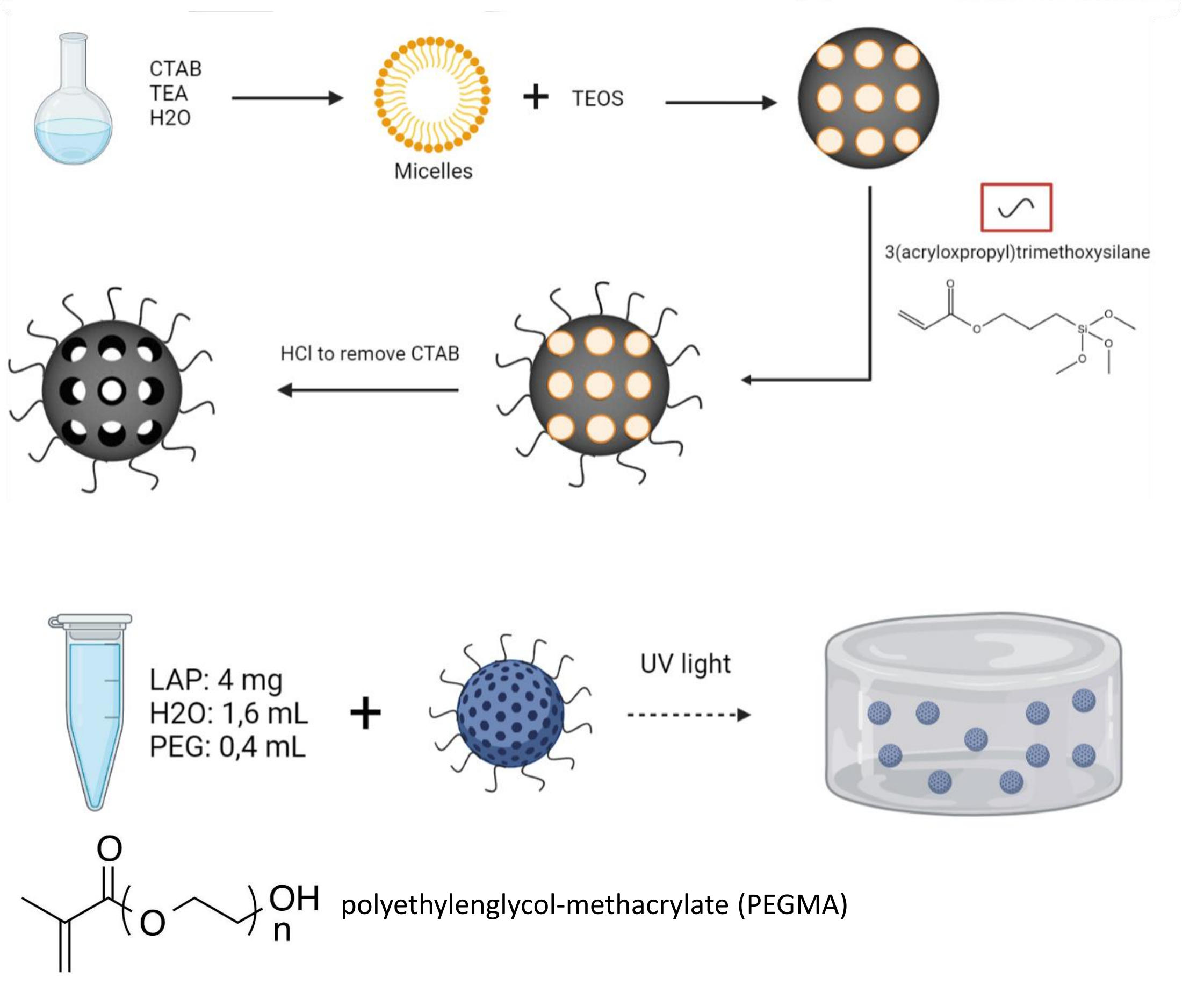


Methods

Mesoporous nanoparticles: Synthesized using CTAB as surfactant to form the micelles and TEOS as source of silica. Once the nanoparticles are formed, they were externally functionalized with (3 acryloxypropyl) trimethoxysilane in order to be able to crosslink them with the hydrogel. Then the CTAB was removed with HCl to obtain mesoporous nanoparticles.[2]

PEG hydrogel: Hybrid materials were synthesized using polyethylenglycol-methacrylate (PEGMA). Lithium phenyl-2,4,6-trimethylbenzoylphospinate (LAP) was adopted as photo-initiator to trigger the crosslinking using UV light.

PEG hydrogel with nanoparticles: An aqueous solution 1% w/w of nanoparticles externally functionalized was added to the polymer solution before the crosslinking. The presence of the acrylate group allows the formation of a covalent bond between the polymer and the nanoparticles.



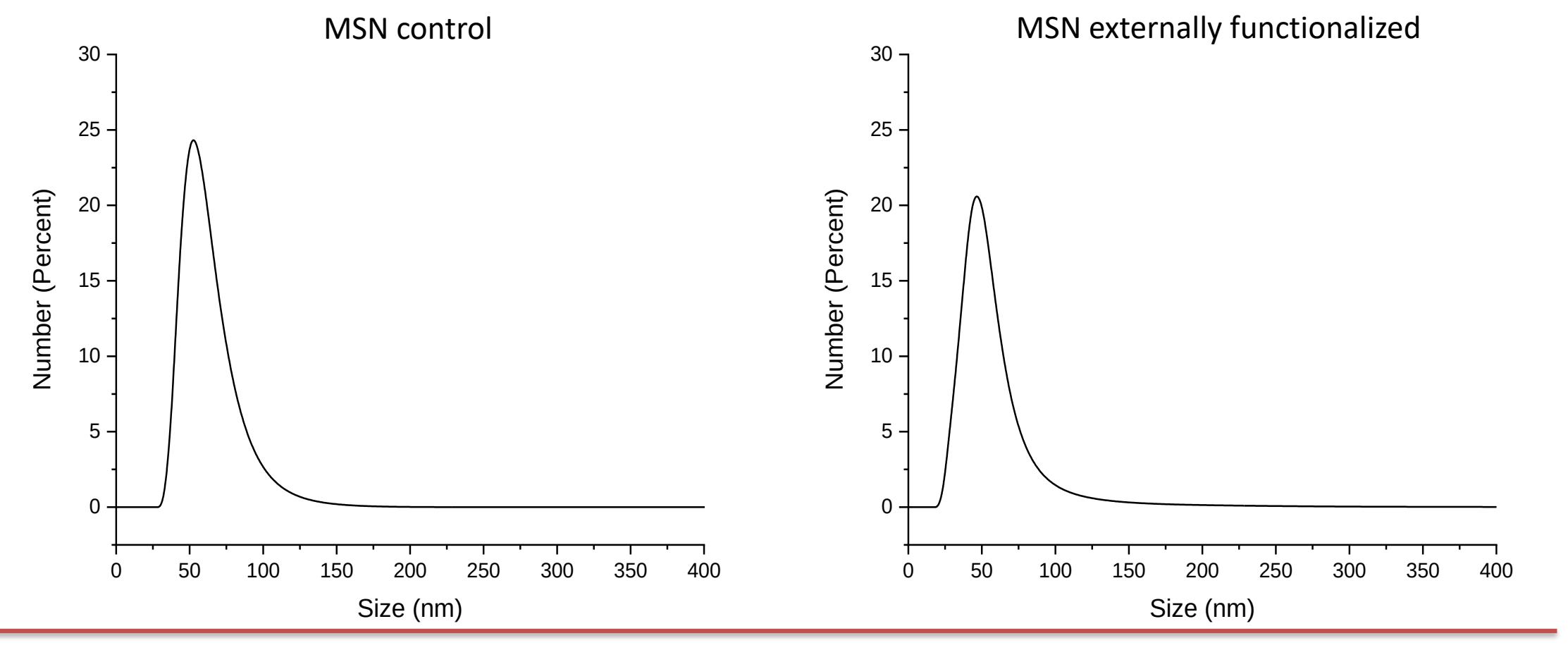
polyethylenglycol-methacrylate (PEGMA)

Results

Mesoporous nanoparticles characterization

Dynamic Light Scattering

Figure 1. DLS of mesoporous silica
DLS was performed with an aqueous solution of both the nanoparticles externally functionalized and not.
The hydrodynamic diameter is:
MSN control: 59 ± 0.41 nm
MSN functionalized: 51 ± 7.81 nm



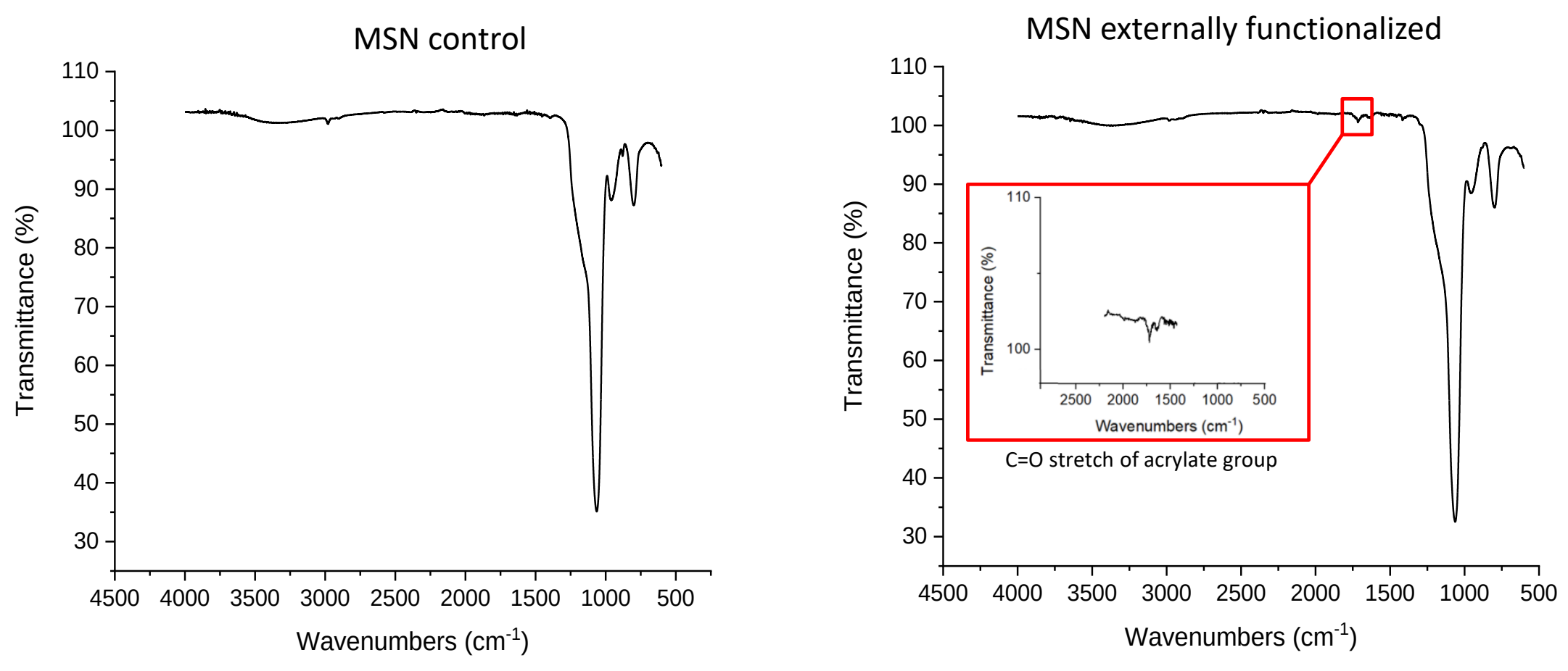
Z-potential

Figure 2. Z-potential determination
The Z-potential is negative for both the nanoparticles since the molecule we have used to functionalize them ((3 acryloxypropyl) trimethoxysilane) is not charged.

	Z-pot
MSN externally functionalized	- 19.56 ± 3.26
MSN control	- 20.21 ± 0.55

Fourier-Transform Infrared Spectroscopy

Figure 3. FTIR Spectroscopy
IR analysis, performed with the nanoparticles previously dryed, show the characteristic peak of silica. At 1714 cm^{-1} there is the weak C=O stretch peak of the acrylate group.



Thermogravimetric Analysis

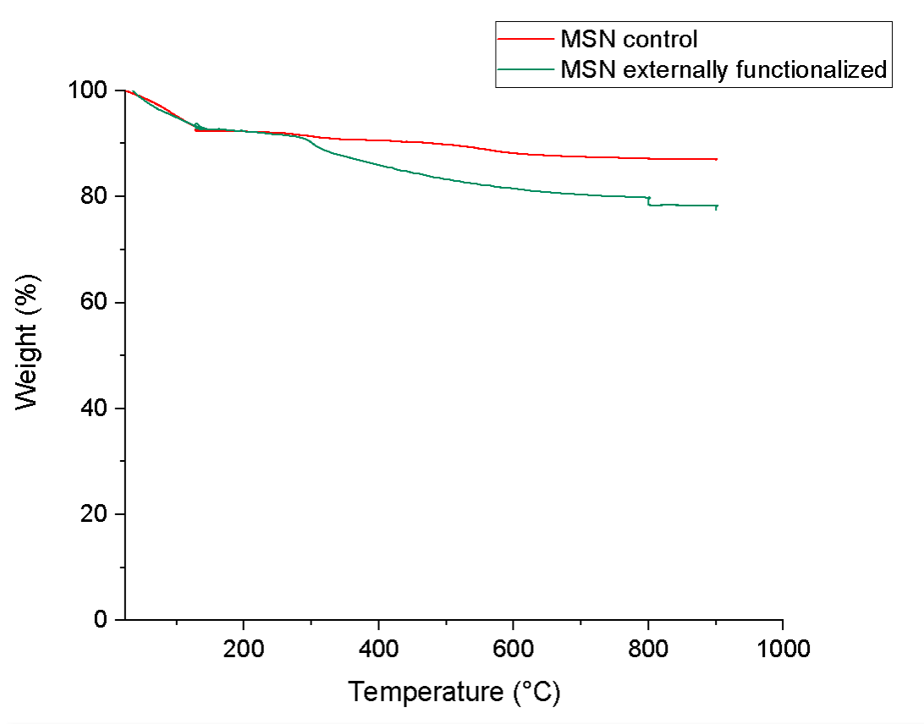
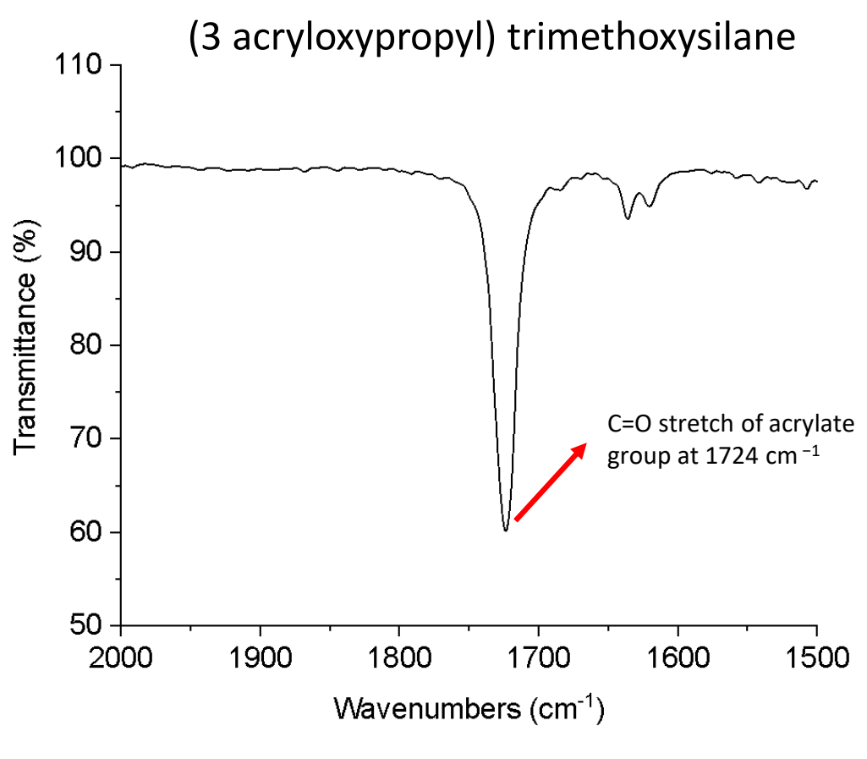
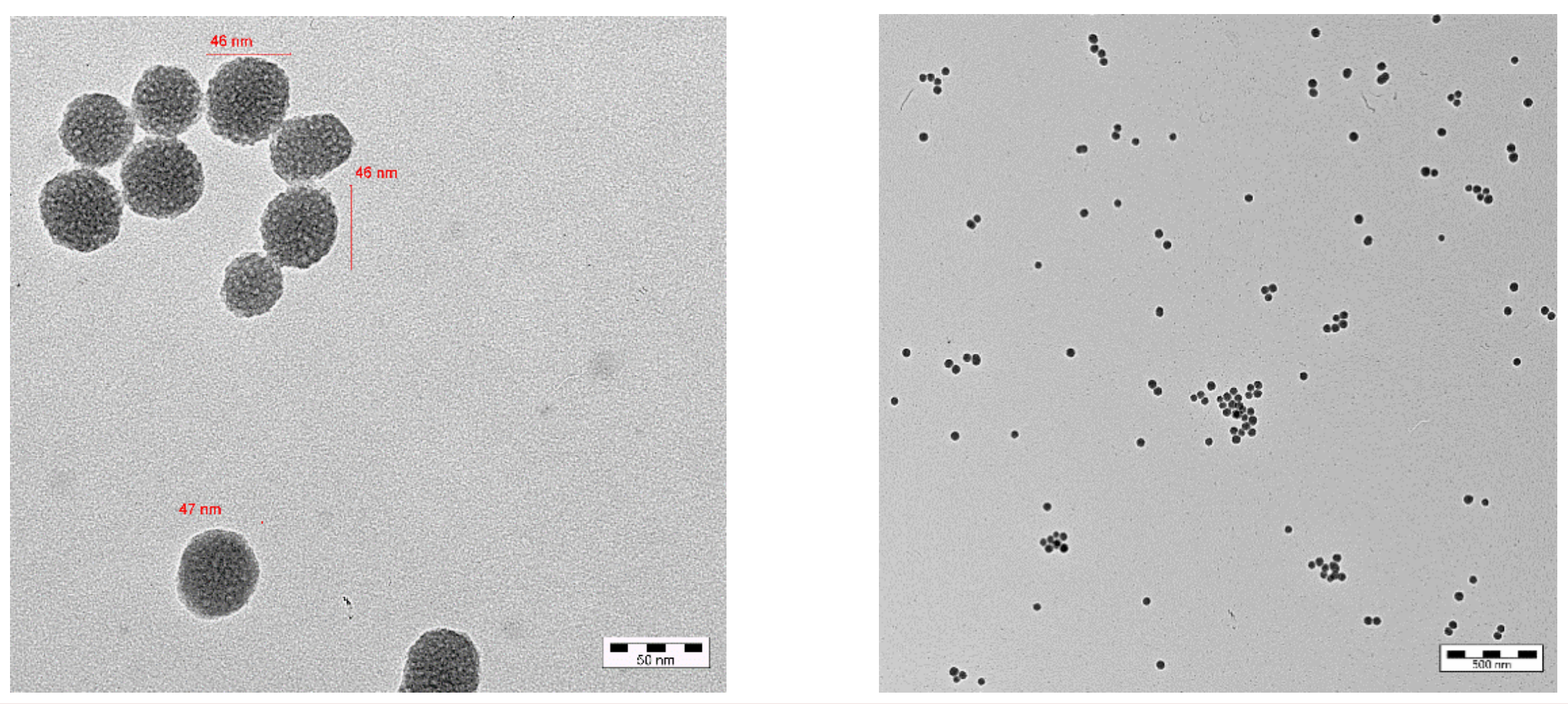


Figure 4. Thermogravimetric Analysis
TGA confirms the successful functionalization of nanoparticles surface. The nanoparticles externally functionalized show a bigger weight loss in comparison with the control ones.



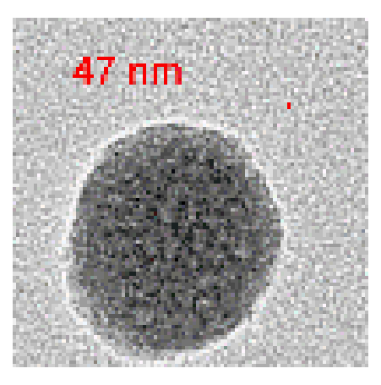
Transmission Electron Microscopy

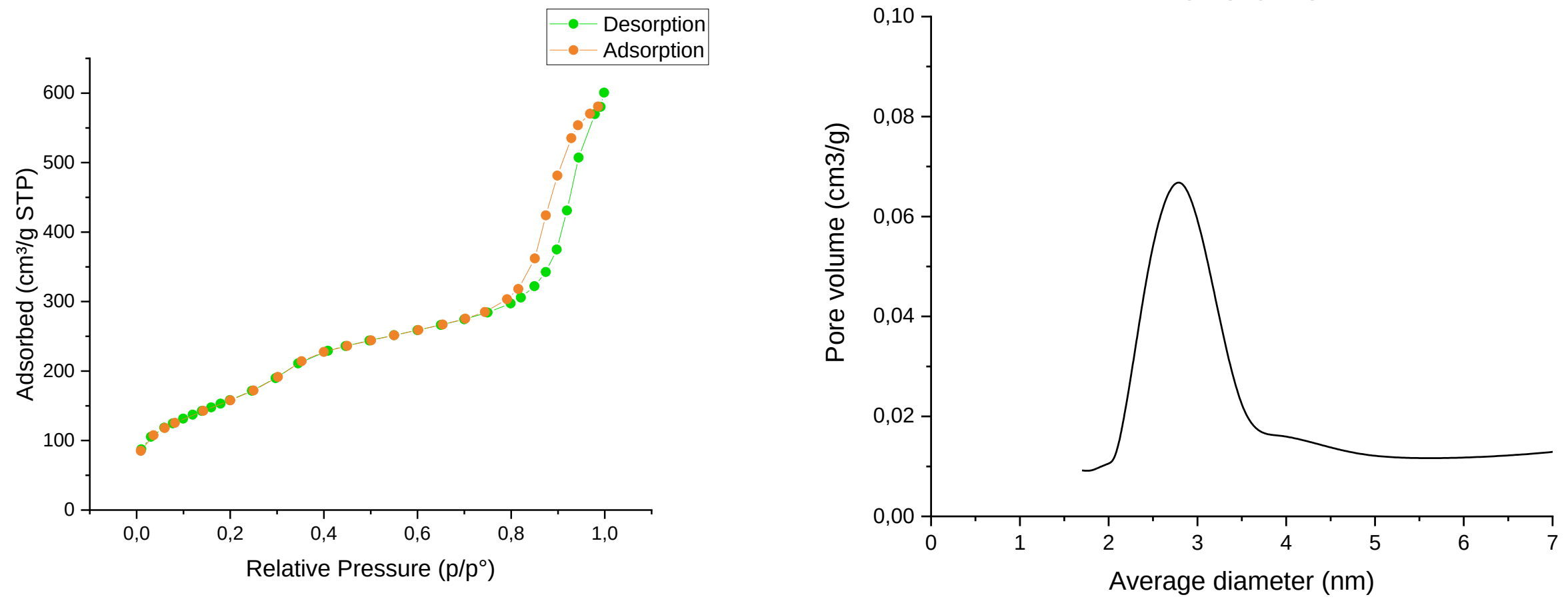
Figure 5. TEM Imaging
Transmission Electron Microscopy images of mesoporous silica nanoparticles. TEM images verify DLS particle size in the range of 40 – 60 nm.



Nitrogen Adsorption

Figure 6. Pore size determination
Isothermal curve of the control mesoporous nanoparticles to determine pore sizes.





Hydrogels characterization

Both amplitude sweep and frequency sweep measurements were performed following crosslinking of the hydrogel directly on the rheometer plate. Before starting the analysis, the solution was irradiated for one minute from all sides with a UV light to form the gel.

Amplitude sweep: γ0 = 0,01 ; γf = 10 ; f = 1 Hz ; T = 25°C ; Gap = 1mm

Frequency sweep: γ0 = 0,05 ; fi = 1 Hz ; ff = 100 Hz ; T = 25°C ; Gap = 1 mm

Figure 1. PEGMA hydrogels

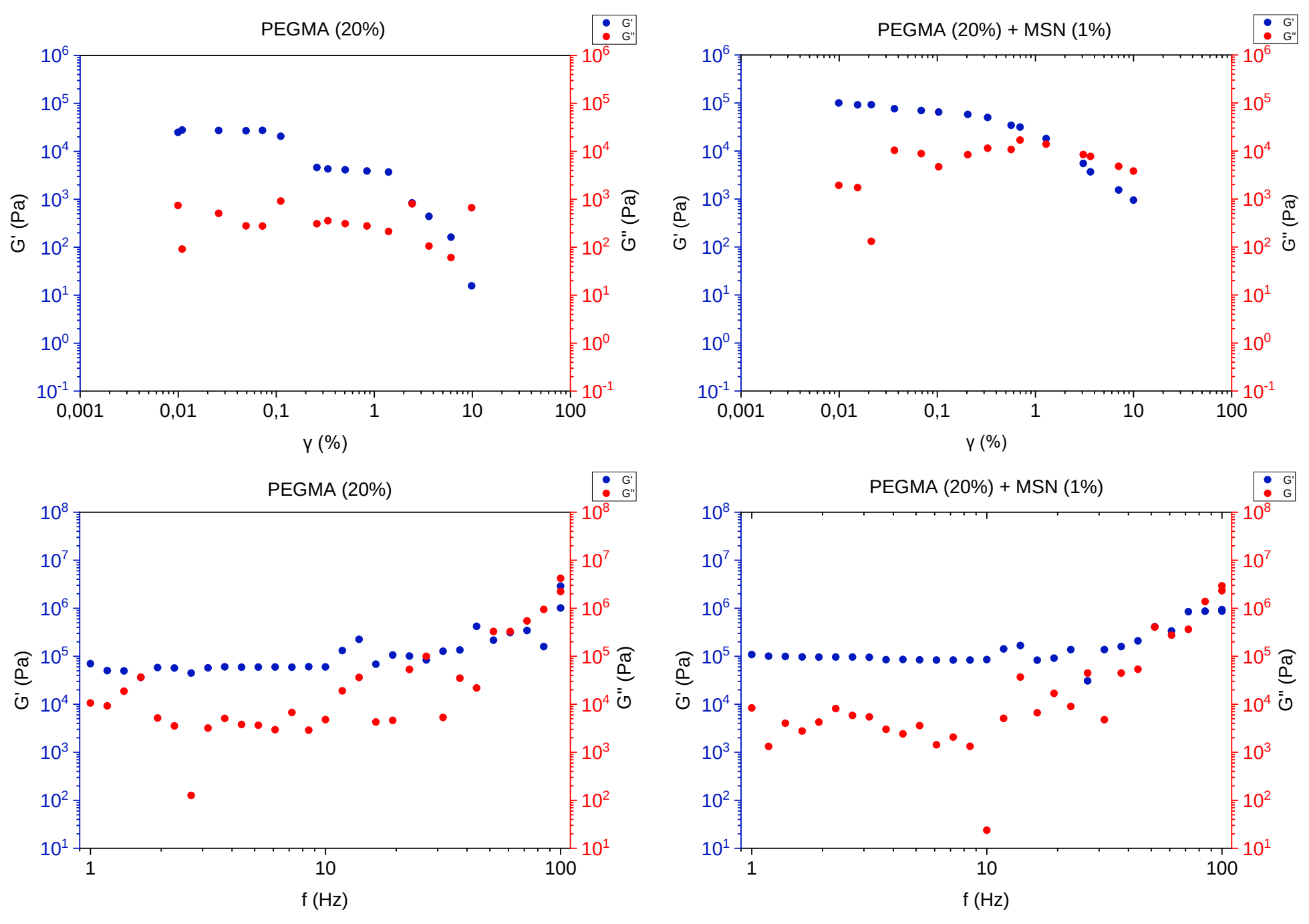


Figure 2. Storage modulus comparison
PEGMA hydrogels (20%) with and without nanoparticles show different G' values.

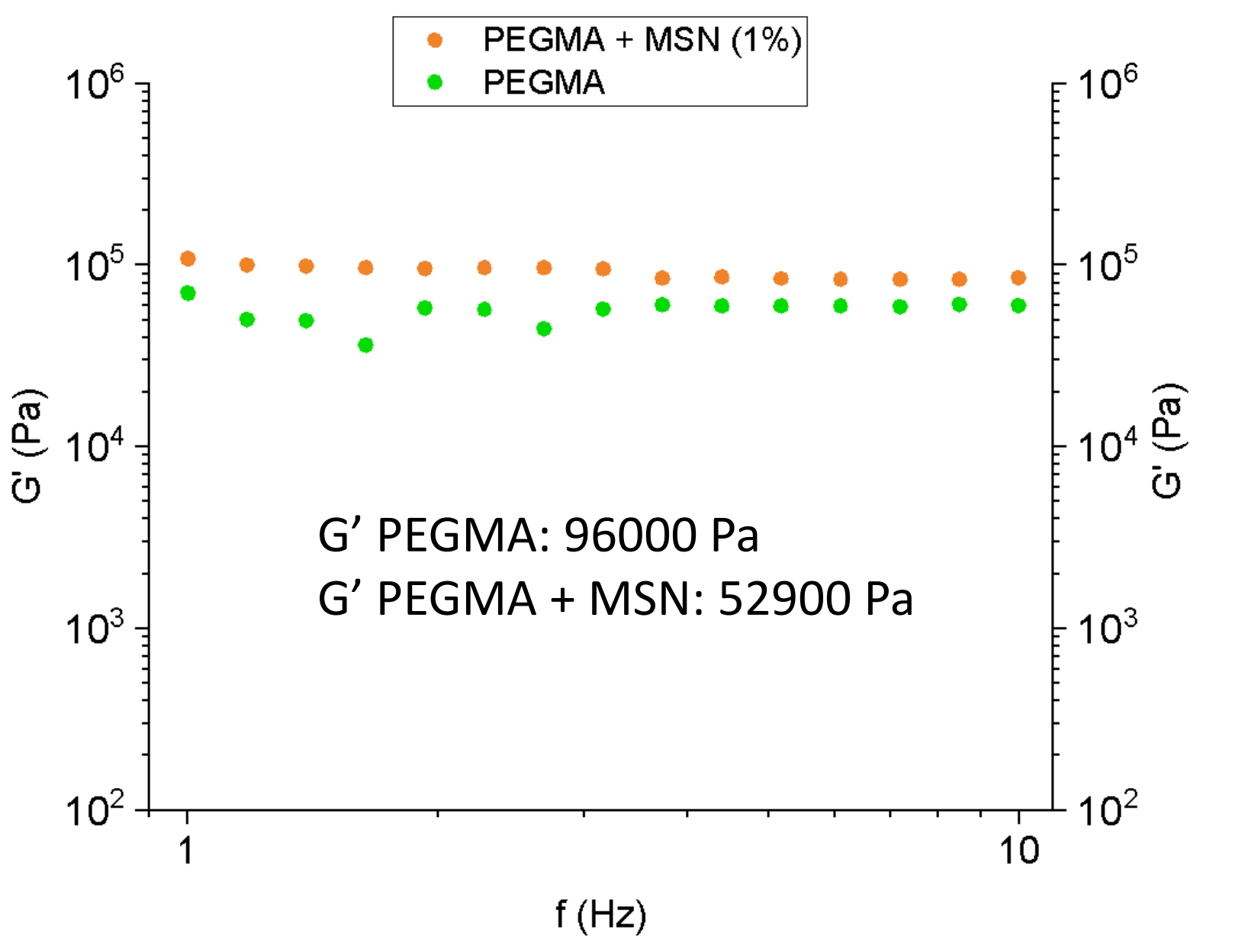



Figure 3

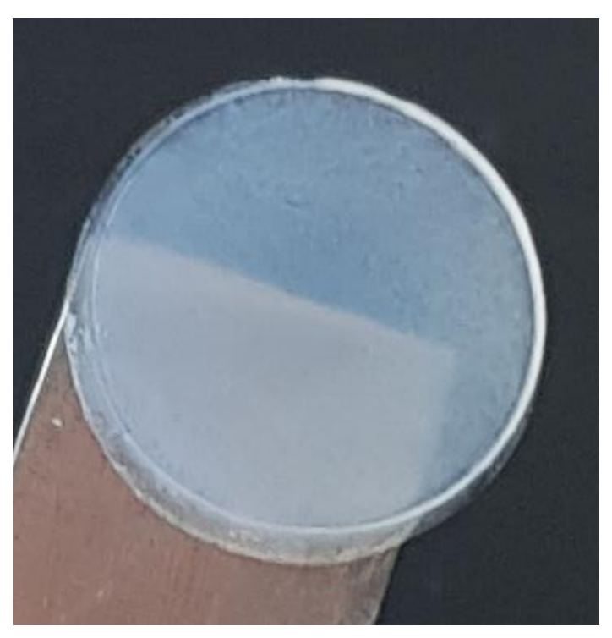


Figure 4

Figure 3.
PEGMA hydrogel

Figure 4.
PEGMA hydrogel + MSN (1%)

The presence of the nanoparticles in the hydrogel changes the transparency of the material, as shown in the images.

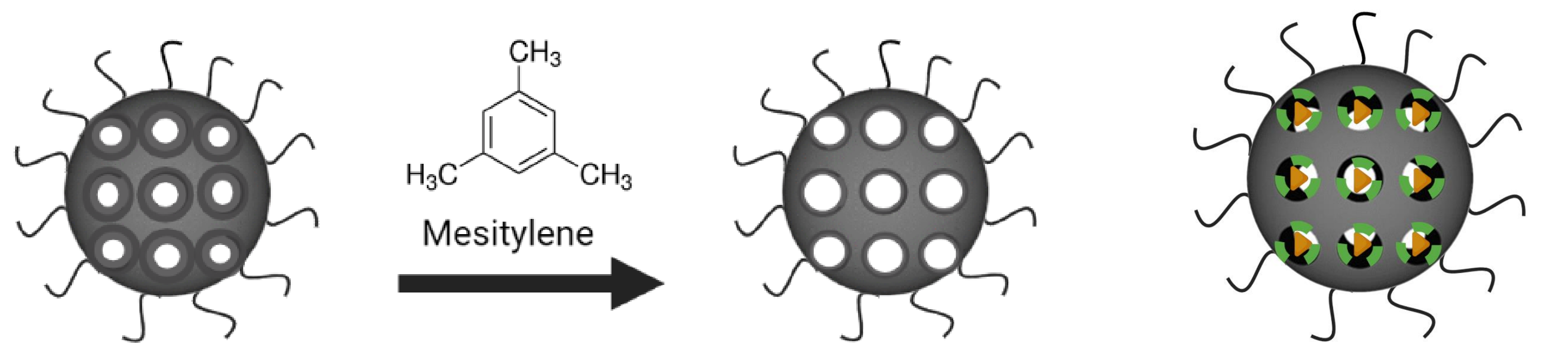
Conclusions

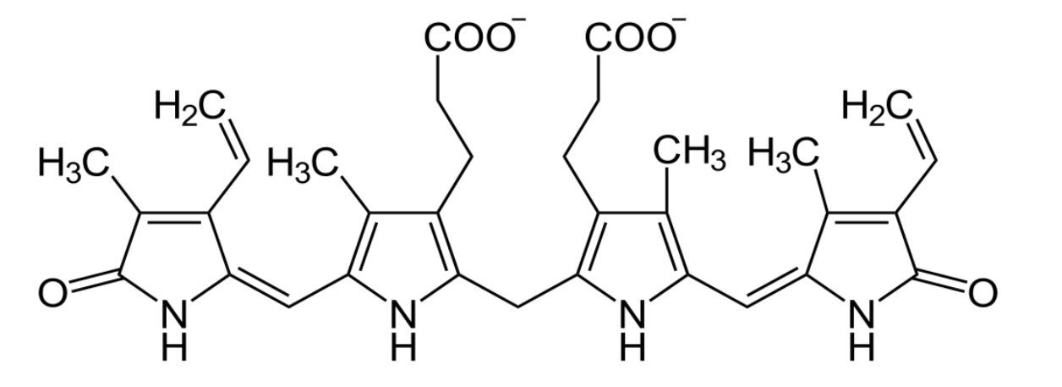
- Silica based mesoporous nanoparticles with acryloxypropyl group on the surface have been synthetized. Using CTAB as surfactant the maximum pore size obtainable is 2-3 nm.
- Hybrid material composed of hydrogel and nanoparticles were crosslinked together and the effect of the nanoparticles crosslinking has been studied. The presence of nanoparticles inside the hydrogel has shown an increase in the stiffness of the material, as it can be seen from the value of G' which is higher for the hydrogel with the nanoparticles.

Future Directions

- Create nanoparticles with enlarged pores size keeping the already synthesized nanoparticles at 160 °C for 3 days in the presence of Mesitylene (1,3,5-Trimethylbenzene).[3]
- Find a functionalization for the pores internal surface: the idea is to use amino groups for electrostatic interactions with the two carboxilyc acid of Bilirubin. Bilirubin has been chosen because it is an orange compound present in the blood that, thanks to its natural color, can be easily observed.
- Investigate the bilirubin entrapment inside the mesoporous nanoparticles.
- Investigate nanoparticle retention into the hydrogel.
- Conduct a study flowing a bilirubin solution through the hydrogel to quantify entrapment.

Amino group
Bilirubin





References: [1] VAN GELDER, Maaike K., et al. Urea removal strategies for dialysate regeneration in a wearable artificial kidney. Biomaterials, 2020, 234: 119735. [2] PIANTANIDA, E., et al. Nanocomposite hyaluronic acid-based hydrogel for the treatment of esophageal fistulas. Materials Today Bio, 2021, 10: 100109. [3] Mike Dentinger. Breakable silica nanoparticles for the in vitro and in vivo delivery of biomolecules. Other. Université de Strasbourg, 2018. English. NNT : 2018STRAF057ff. tel-03270816f

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