

MAGNETOLIPOGELS: A MIXED STRATEGY FOR CONTROLLED DRUG RELEASE

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ABSTRACT

Why combining **hydrogels** and **lipid-containing magnetic systems**?

- Hydrogels provide **structural support** of the components
- Combine properties of **hydrogels** and **magnetic nanoparticles** [1,2]
- The presence of lipid-containing systems provides **hydrophobic reservoirs**
- Coating with **lipids** can **improve stability** of the nanoparticles

What is the here developed **magnetolipogel concept**?

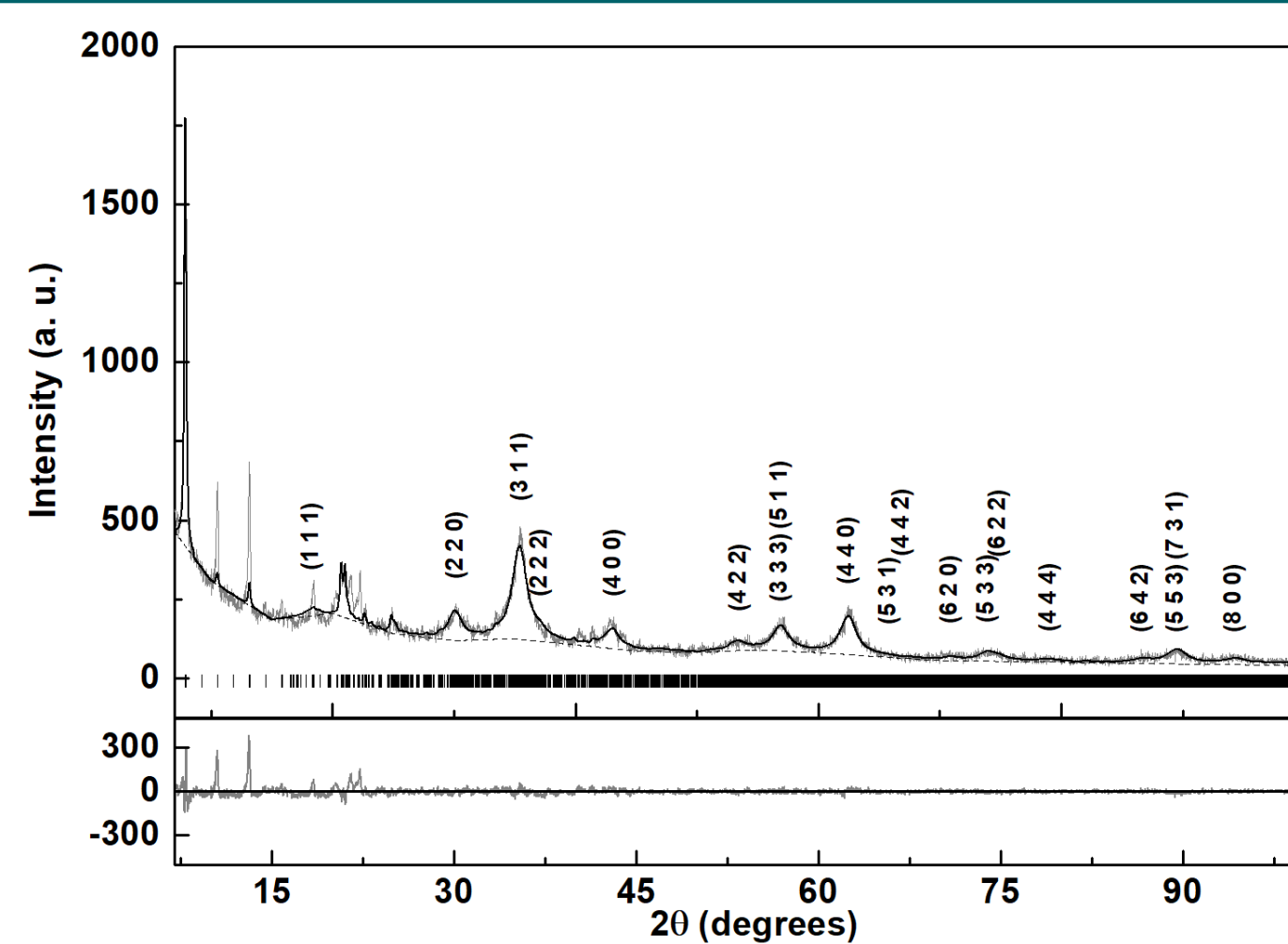
- A **Methionine** residue that favours **self-assembly** through hydrophobic collapse
- Dehydropeptides** that display improved **proteolytic stability**
- Lauric acid-coated** manganese ferrite nanoparticles to favour **colloidal stability**

Which is the **proof-of-concept**?

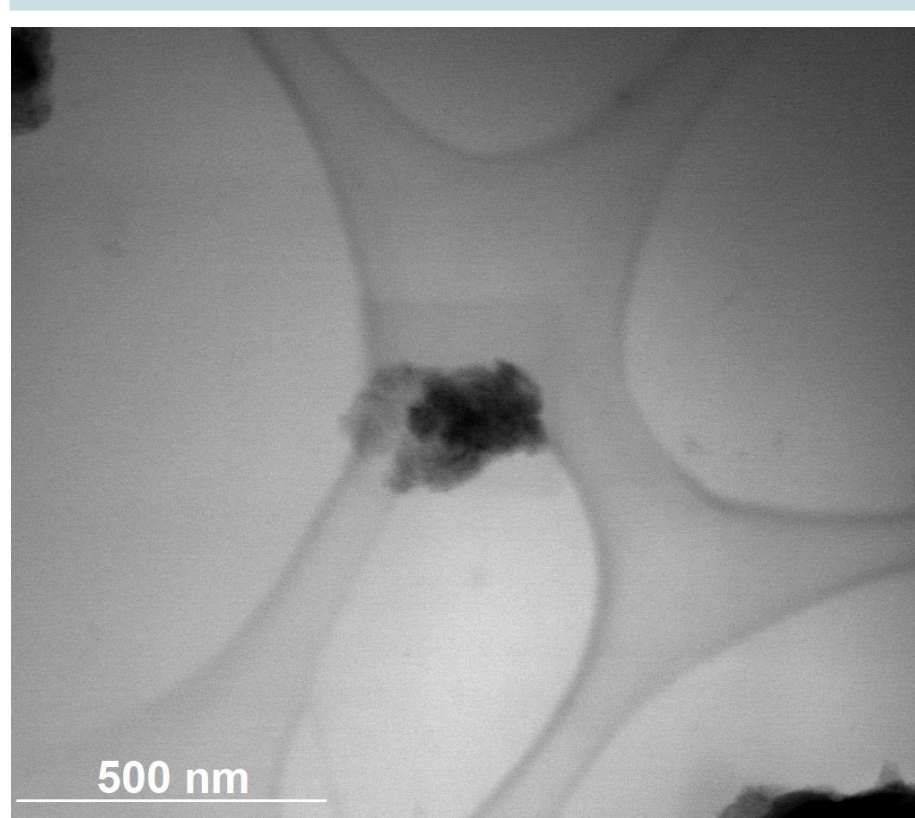
- Improve the encapsulation of hydrophobic drugs
- Tuneable** and reproducible doxorubicin release

MAGNETIC NANOPARTICLES

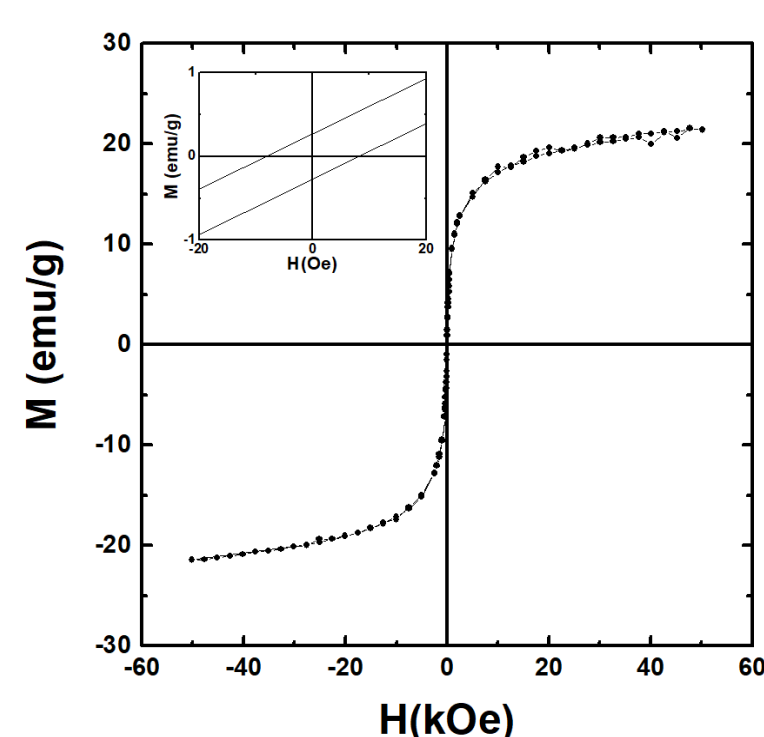
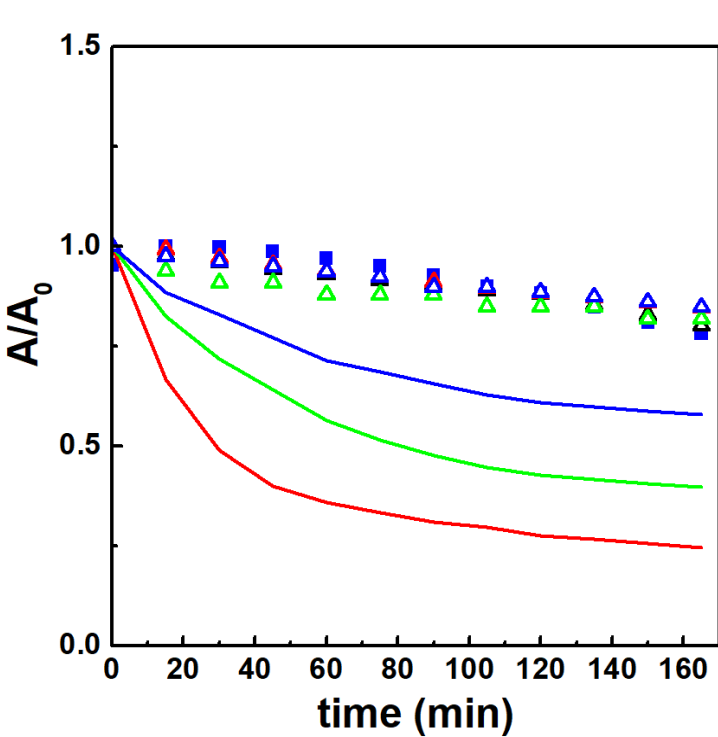
1



- MnFe₂O₄ phase 4.3 nm
- Display **ordered lauric acid** molecules at the **surface**



- Superparamagnetic**
 - 8.9 ± 2.1 nm (M_s/M_i: 0.01 M_s: 21.4 emu/g)
- Colloidal stability**
 - Slower sedimentation than bare nanoparticles
 - Concentration-independent sedimentation in the require range

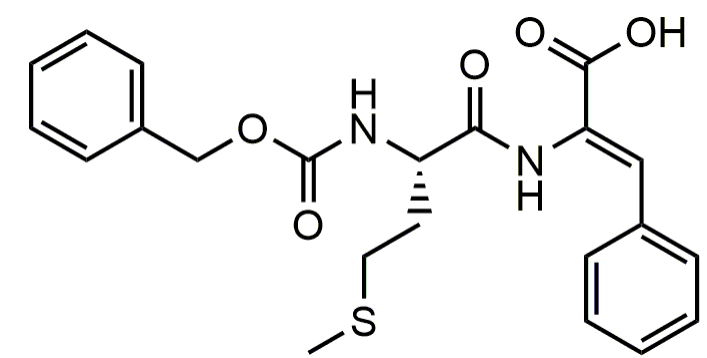


Sedimentation: lipid-coated (triangles) and bare (line) MnFe₂O₄ nanoparticles at 0.2 wt% (black), 0.1 wt% (red), 0.05 wt% (green) and 0.025 wt% (blue)

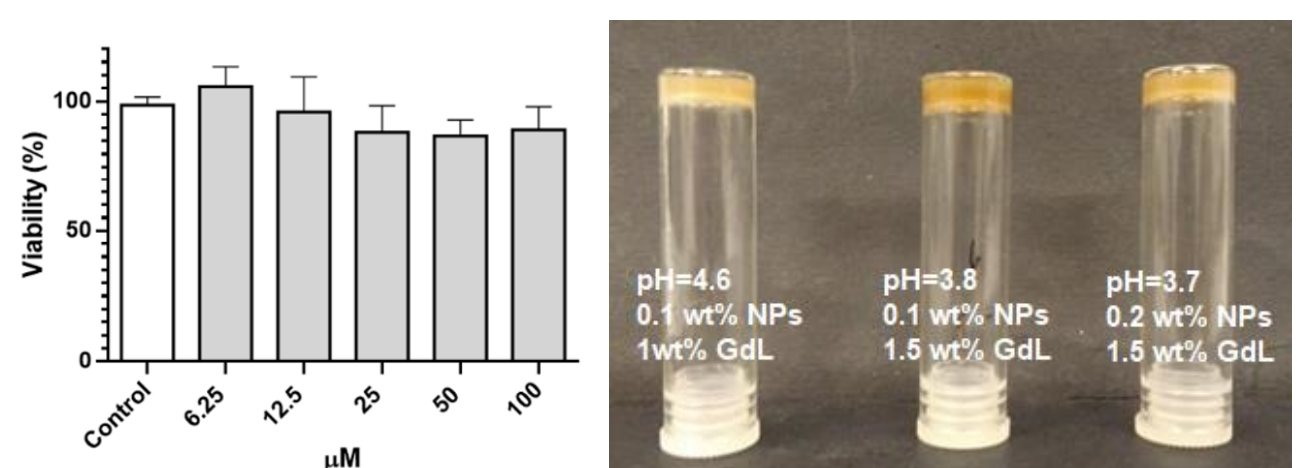
MAGNETOGELS DEVELOPMENT

2

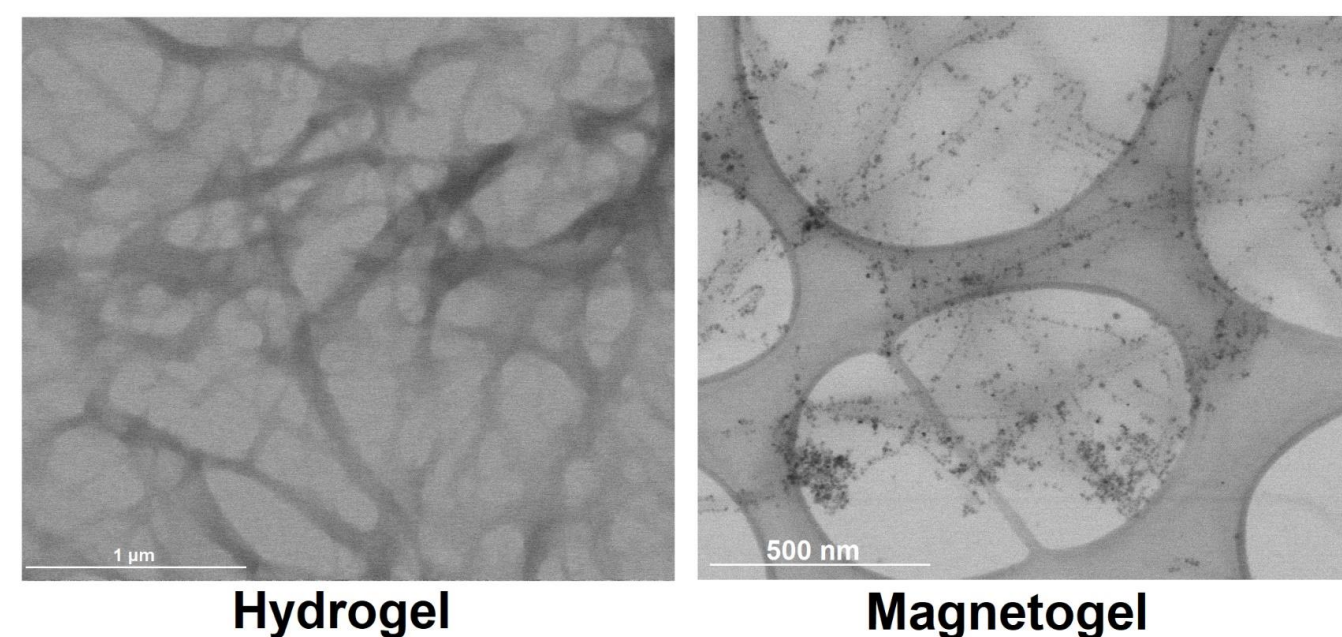
CGC = 0.1 wt%
pKa ~ 3.5
Gelation pH ~ 5.5



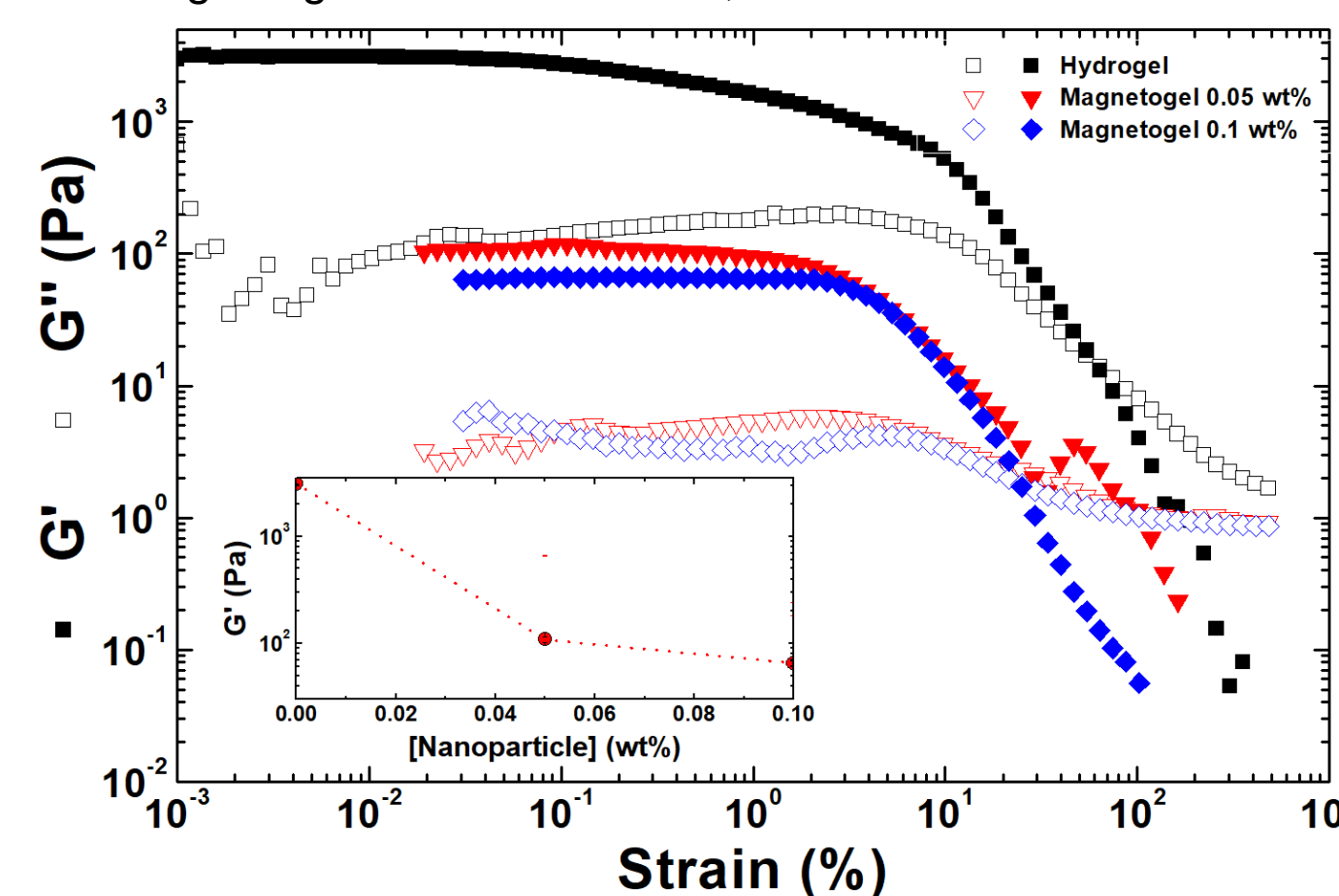
Preparation through addition of **glucono-δ-lactone** (GdL) to a basic solution



- Cytocompatible** minimalist hydrogelator
- Gels at **low** hydrogelator concentration (**0.5 wt%**)
- The **nanoparticles adsorb** to the **fibres**
- Suitable** for application in **soft tissues**



Fibres cross-section:
Hydrogel: 104.6 ± 24.5 nm; 36.2 ± 11.9 nm
Magnetogels: 48.4 ± 13.8 nm; 21.3 ± 3.4 nm



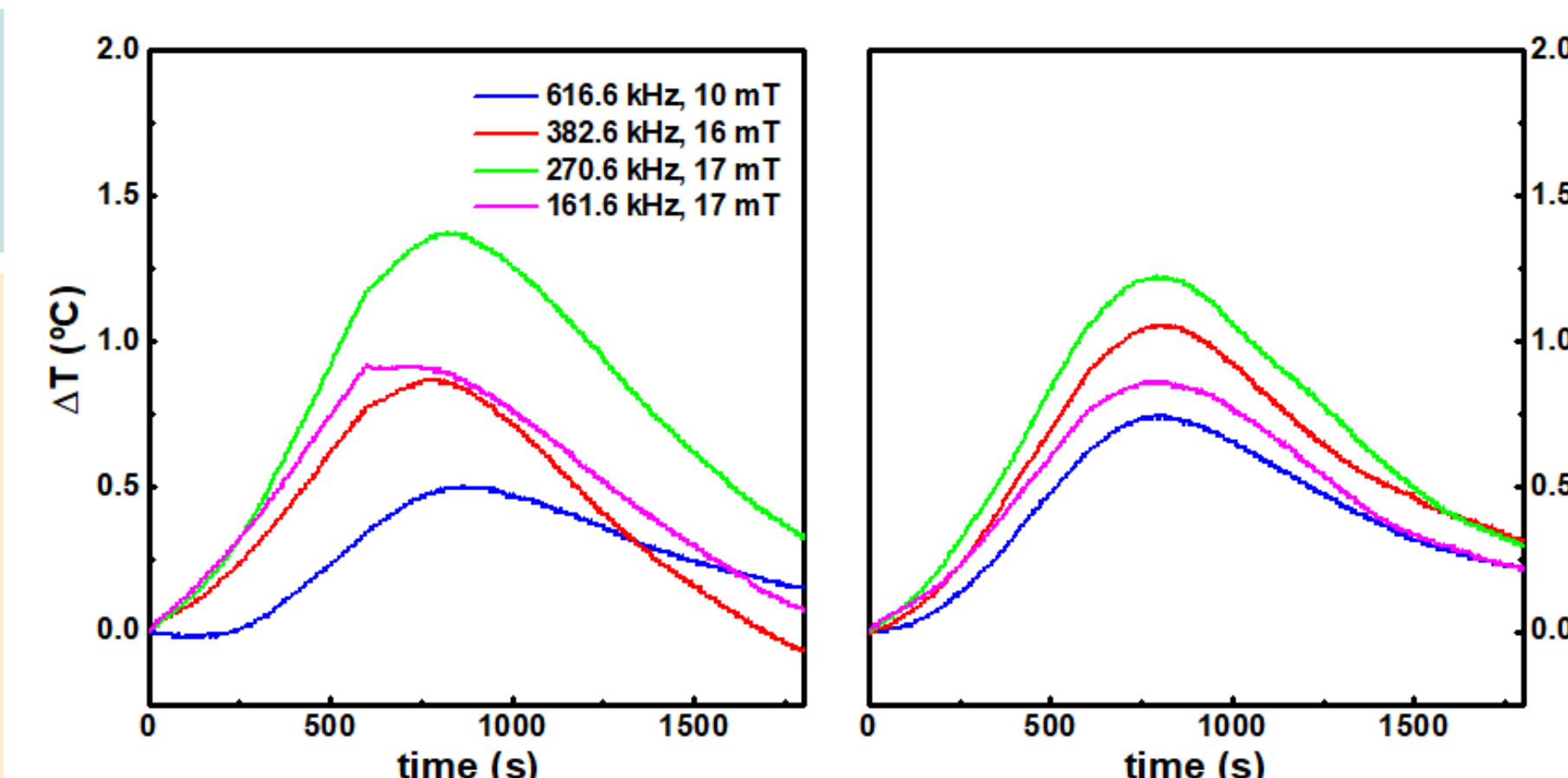
Shear elastic modulus 3 kPa
Soft tissues elastic modulus: 0.1 kPa to 100 kPa

MAGNETIC HYPERTHERMIA

3

Below threshold limit of $H_0 f \leq 5 \times 10^9 \text{ A m}^{-1} \text{ s}^{-1}$

- Heating effect is **reproducible in gels**
- Encapsulation did **not** affect heating
- The heating is **reversible**

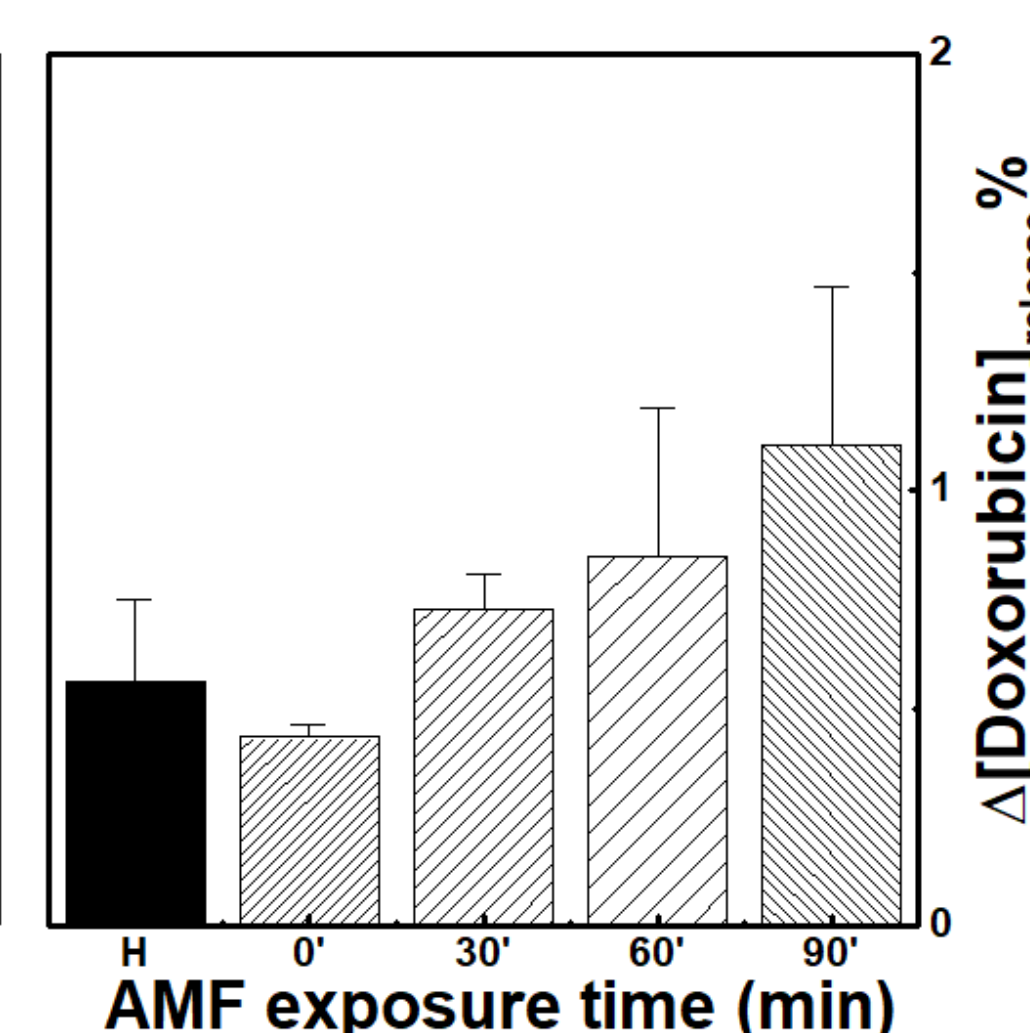
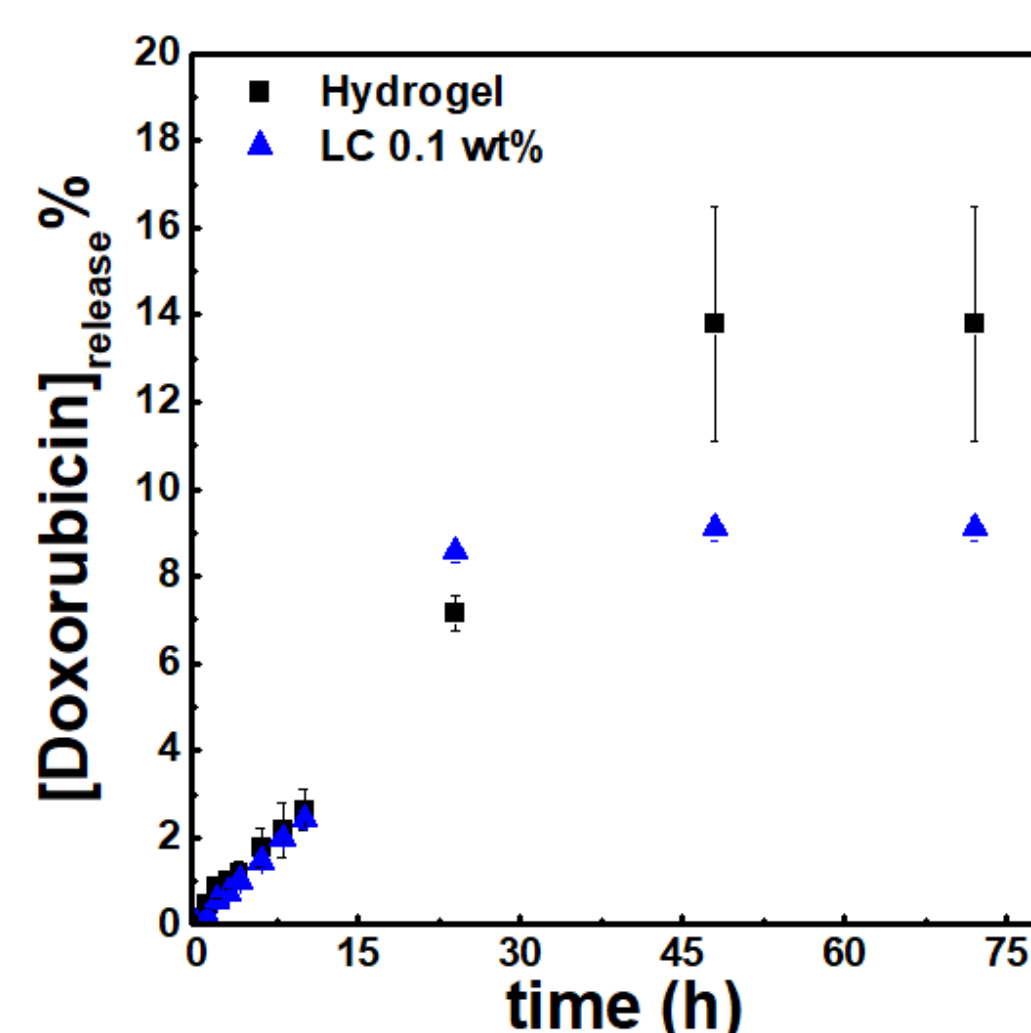


Left: Aqueous nanoparticle solution (0.1 wt%)
Right: Magnetic gels (0.1 wt% NPs; 0.5 wt% Hydrogel; 1 wt% GdL)

DRUG RELEASE

4

Release of doxorubicin



H: hydrogel 0.5 wt%
LC: magnetogel 0.5 wt% (1 wt% GdL; 0.1 wt% NPs)

Left: Drug release profile
Right: Comparison of the magnetogel release when an AMF is applied for 30, 60 and 90 min between t=4 h and t=6 h

Without AMF:

- Hydrogel displays **larger doxorubicin release** than the magnetogel

With AMF:

- Release was **enhanced** in magnetogels containing **lipid-coated NPs**

- Controlled** doxorubicin release
- Lipid-coated NPs** induce **enhanced release** upon application of **AMF**

CONCLUSIONS

Materials concept

- Lauric acid** stabilized manganese ferrite nanoparticles
- Supramolecular magnetogels** containing lipid-coated nanoparticles
- Gels with **nanoparticles adsorbed** to the fibres
- Suitable properties** for biomedical applications in **soft tissues**

Proof-of-concept

- Gels magnetic **hyperthermia** is **reproducible** and **reversible**
- Hydrogels and magnetogels matrices ensure **controlled drug release**
- Lipid-coated nanoparticles **hampered release** of doxorubicin
- Drug release** was **enhanced** upon application of **alternating magnetic field**

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REFERENCES

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- S.R.S. Veloso, C. Magalhães, A.R.O. Rodrigues, H. Vilaça, M.J.R.P. Queiroz, J.A. Martins, P.J.G. Coutinho, P.M.T. Ferreira, E.M.S. Castanheira, *Phys. Chem. Chem. Phys.* 21 (2019) 10377-10390.

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