IECBM 2022
The 2nd International Electronic Conference on Biomolecules:
BIOMACROMOLECULES AND THE MODERN WORLD CHALLENGES
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Formulation and characterization of a methacrylated chitosan topical treatment with dispersed magnetite nanoparticles functionalized with hydrophobic drugs encapsulated in liposomes

GINIB | Grupo de Investigación en Nanobiomateriales, Ingeniería Celular y Bioimpresión

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Professor

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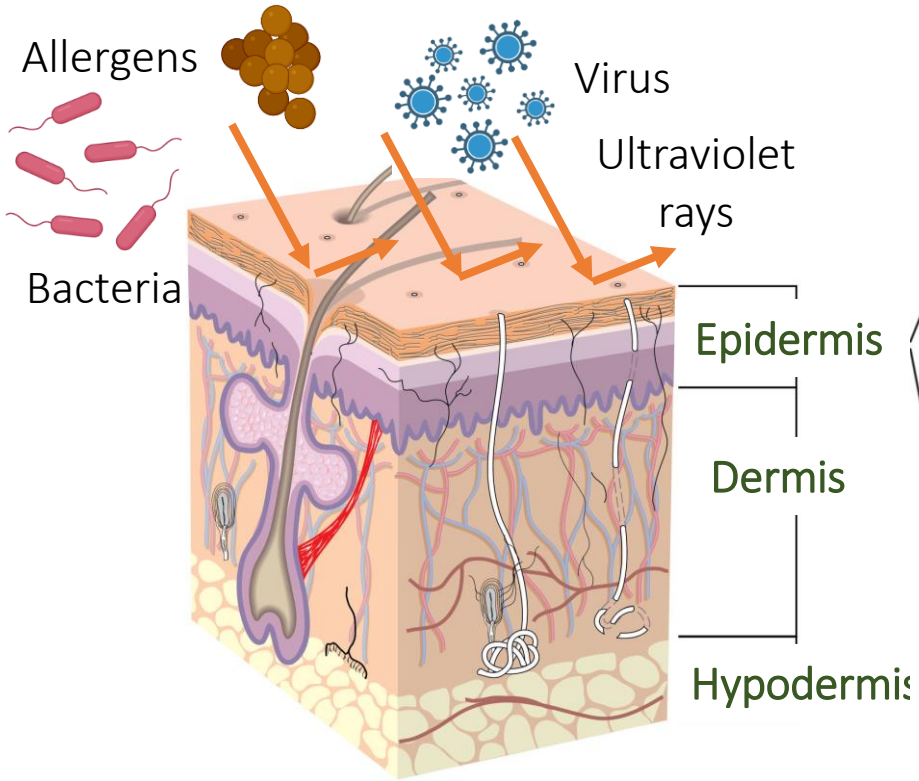
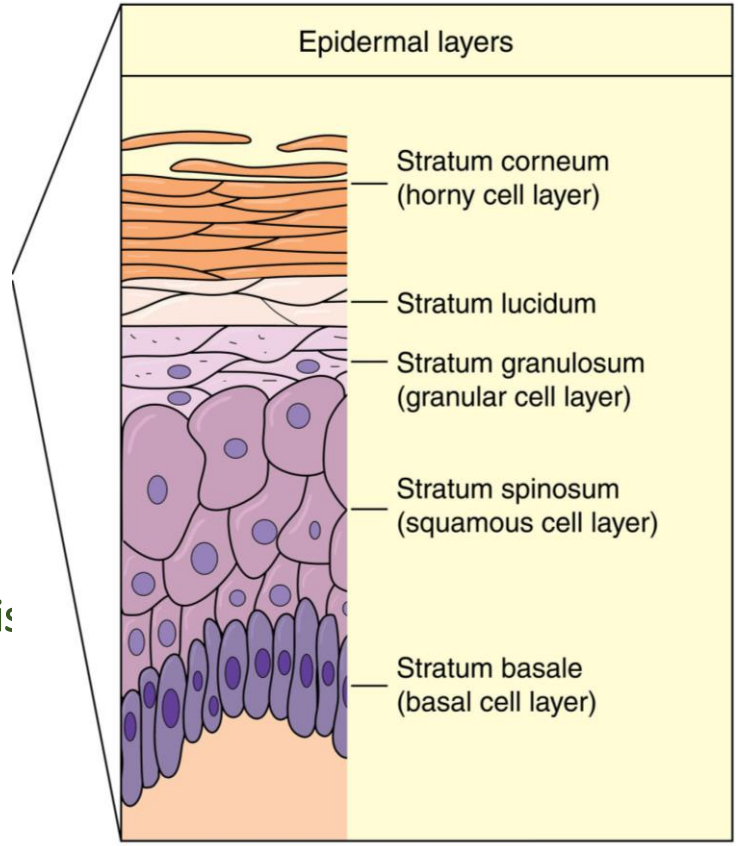
Skin and drug administration

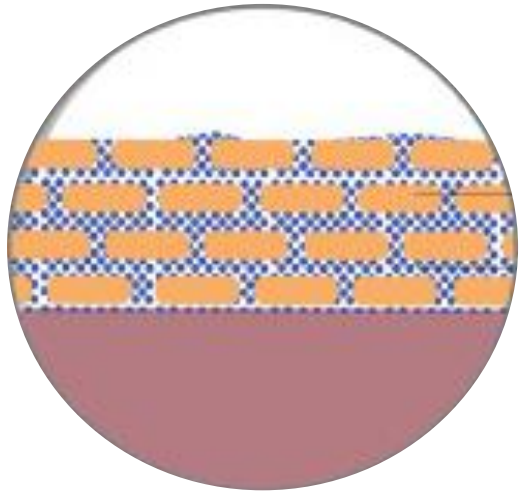
Skin and its structure





The body's largest organ and first contact with the outside world

Break – Mortar wall



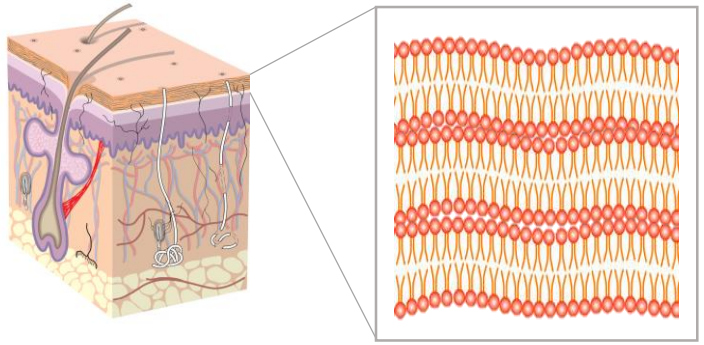
Barrier, not only against pathogens, but also **against hydrophilic molecules and drugs.**

[1] Transdermal and Topical Drug Administration in the Treatment of PainMolecules. DOI: 10.3390/molecules23030681 PMCID: PMC6017304PMID: 29562618
[2]J. Lai-Cheong and J. McGrath, "Structure and function of skin, hair and nails",. DOI:10.1016/j.mpmed.2021.03.001
[3] Emerging Nanotechnologies in Immunology. DOI: https://doi.org/10.1016/B978-0-323-40016-9.00003-8

Skin and drug administration

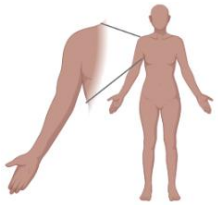
Challenges

Difficult to penetrate the **selective barrier structures** of the skin



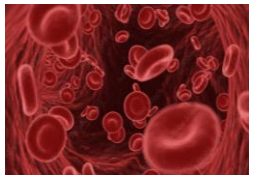
- Permeability to **lipophilic compounds**
- Impermeability to **hydrophilic compounds**
- Some drugs may be less permeable through the skin due to their size and penetrability.

Advantages

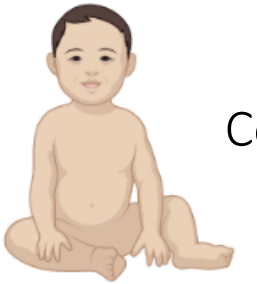


Concentrating the active agents

Avoids hepatic metabolism



Reducing systemic side effects



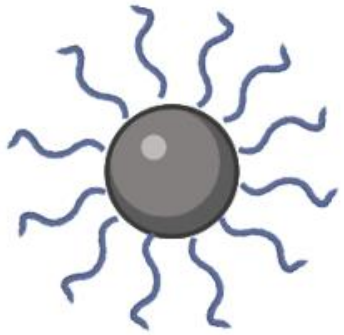
Comfortable for the patient

Provides sustained administration over long periods of time

[4] "Application of the human stratum corneum lipid-based mimetic model in assessment of drug-loaded nanoparticles for skin administration", International Journal of Pharmaceutics, DOI: 10.1016/j.ijpharm.2020.119960.
[5] T. Moniz, S. Costa Lima and S. Reis, "Application of the human stratum corneum lipid-based mimetic model in assessment of drug-loaded nanoparticles for skin administration", International Journal of Pharmaceutics, vol. 591, p. 119960, 2020. Available: 10.1016/j.ijpharm.2020.119960.

Approach: Bio and nano-material for drug delivery

Functionalized magnetite nanoparticles



Higher number of active molecules per unit mass

- Biocompatible
- Biodegradable
- Biologically inert

[6] J. Perez et all. Cell-Penetrating And Antibacterial BUF-II Nanobioconjugates: Enhanced Potency Via Immobilization On Polyetheramine-Modified Magnetite Nanoparticles. DOI: https://doi.org/10.2147/IJN.S224286
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[8] M. Cuellar et all. Novel BUF2-magnetite nanobioconjugates with cell-penetrating abilities. DOI: https://doi.org/10.2147/IJN.S188074

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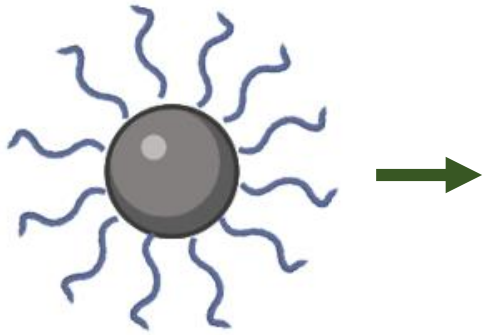

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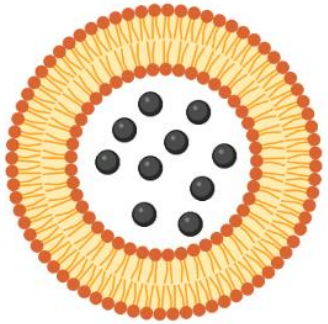
Magnetoliposomes

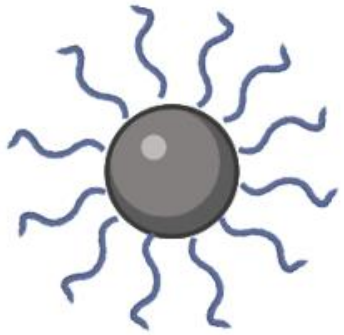


- **Facilitate the penetration of physiological barriers**
- Increase the solubility of drugs
- Low toxicity

[9] C. E-Torres et all. Microfluidic Synthesis and Purification of Magnetoliposomes for Potential Applications in the Gastrointestinal Delivery of Difficult-to-Transport Drugs. DOI: https://doi.org/10.3390/pharmaceutics14020315
[10] S. C. Gomez et all. Design and Manufacture of a Low-Cost Microfluidic System for the Synthesis of Giant Liposomes for the Encapsulation of Yeast Homologues: Applications in the Screening of Membrane-Active Peptide Libraries. DOI: https://doi.org/10.3390/mi12111377

Approach: Bio and nano-material for drug delivery

Functionalized magnetite nanoparticles



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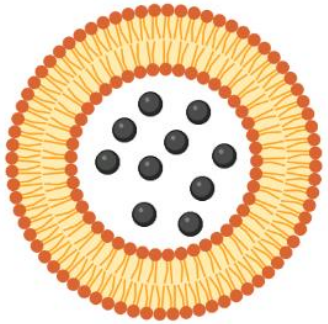
Magnetoliposomes



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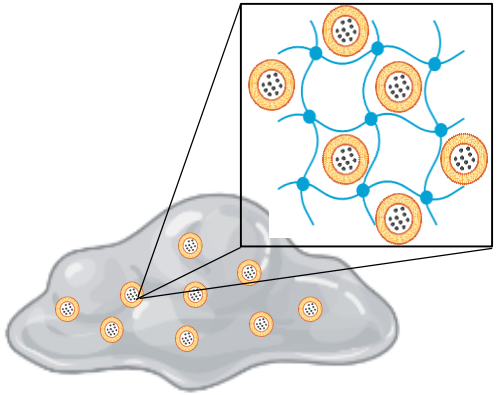
Methacrylated chitosan hydrogel



Good permeability, biocompatibility, flexibility and viscoelasticity

Topical treatment

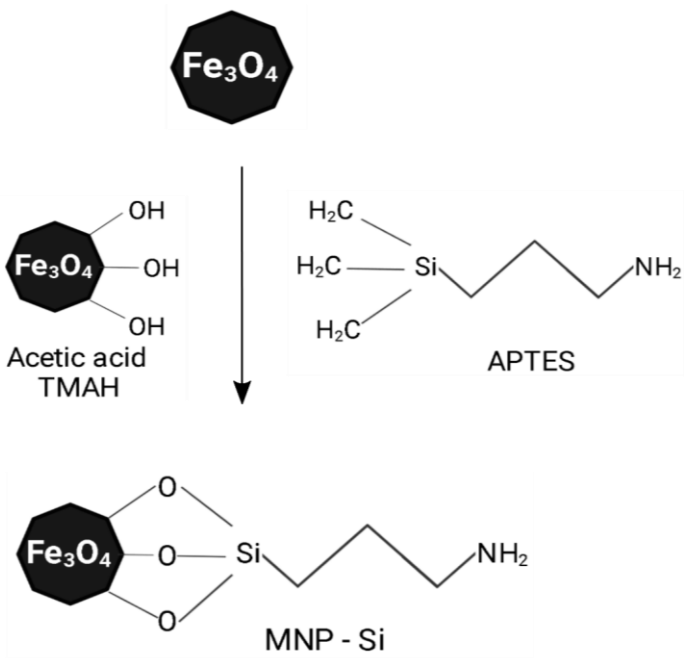
[10] D. Cespedes, "Novel photo- and thermo- responsive nanocomposite hydrogels based on functionalized rGO and modified SIS/Chitosan polymers for localized treatment of malignant cutaneous melanoma". DOI: doi: 10.3389/fbioe.
[11] J A. Serna. Recent Advances on Stimuli-Responsive Hydrogels Based on Tissue-Derived ECMs and Their Components: Towards Improving Functionality for Tissue Engineering and Controlled Drug Delivery. DOI: https://doi.org/10.3390/polym13193263

Nanoparticle Synthesis and functionalization

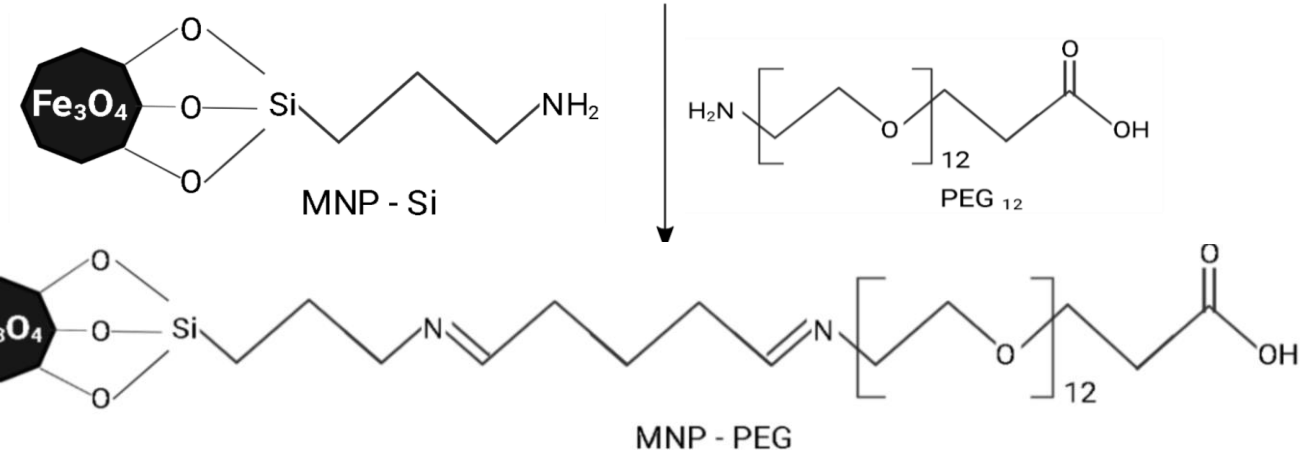
1 Synthesis of MNPs

$$Fe^{2+} + 2Fe^{3+} + 8OH^- \rightarrow Fe_3O_4 + 4H_2O$$

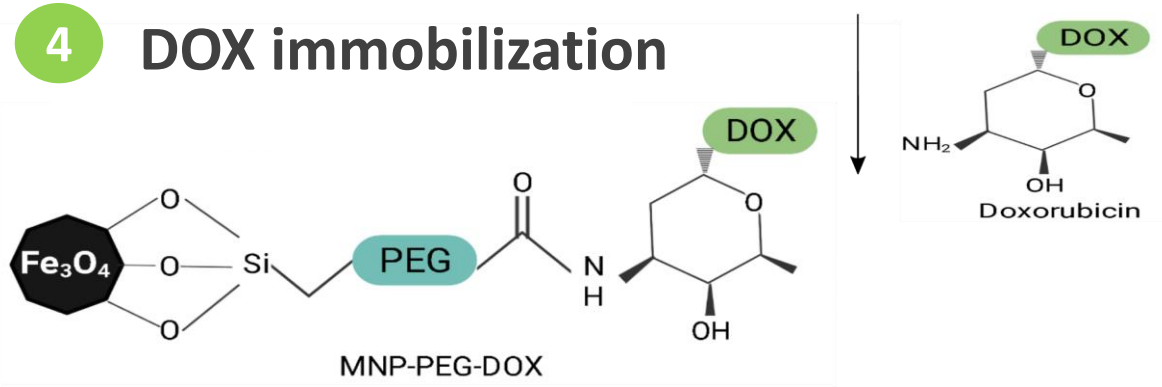
2 Funcionalization of MNPs



3 PEG immobilization



4 DOX immobilization



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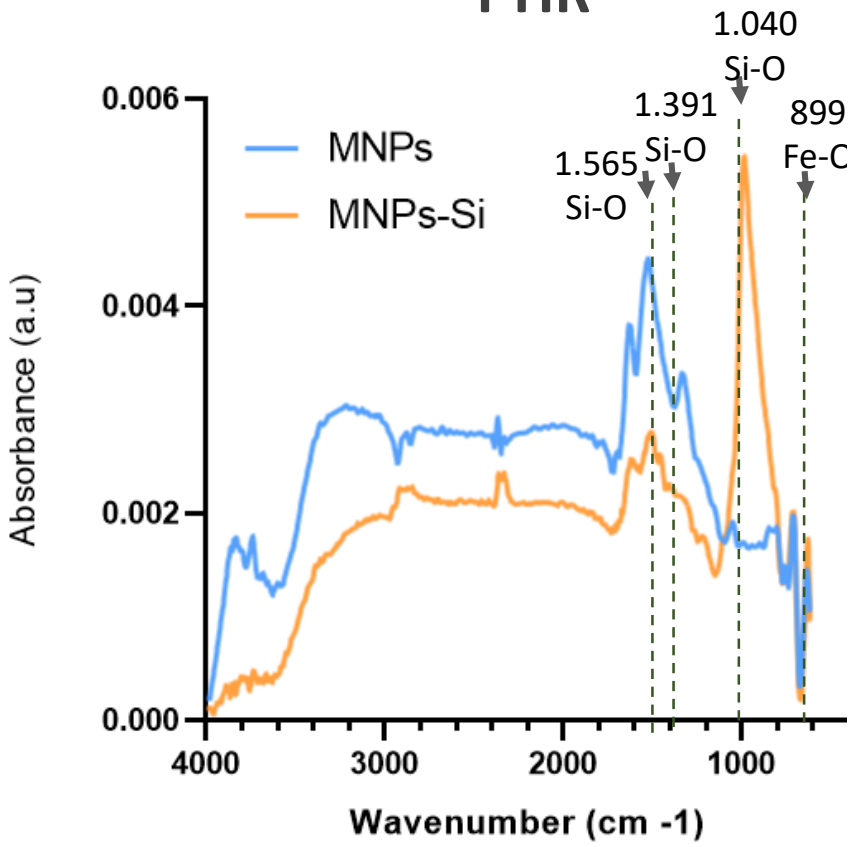
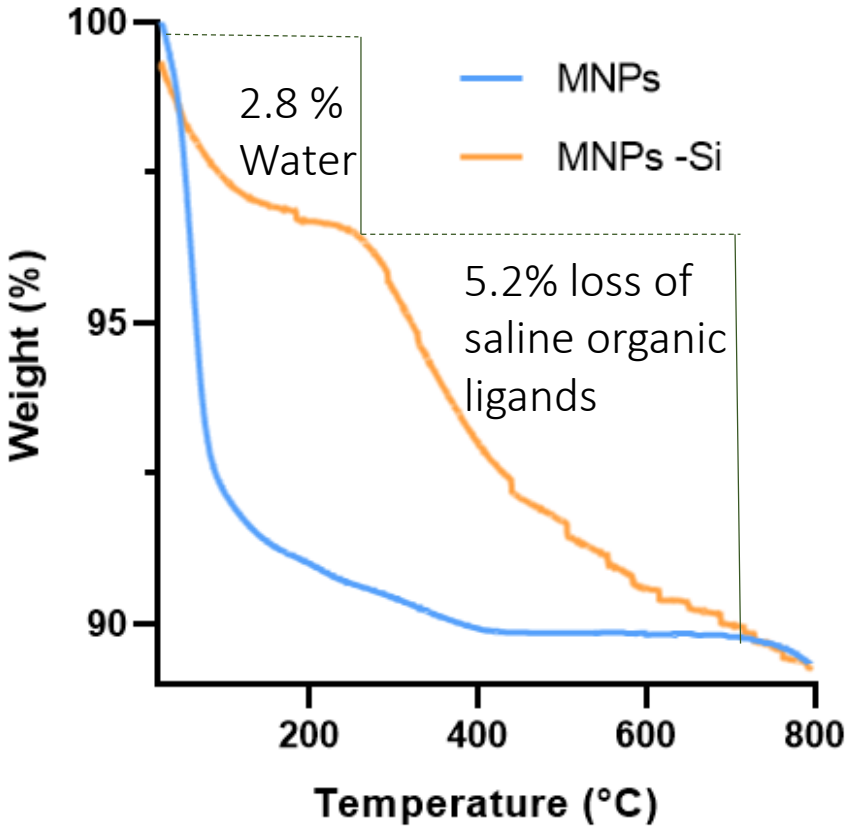
Nanoparticle Characterization

FTIR



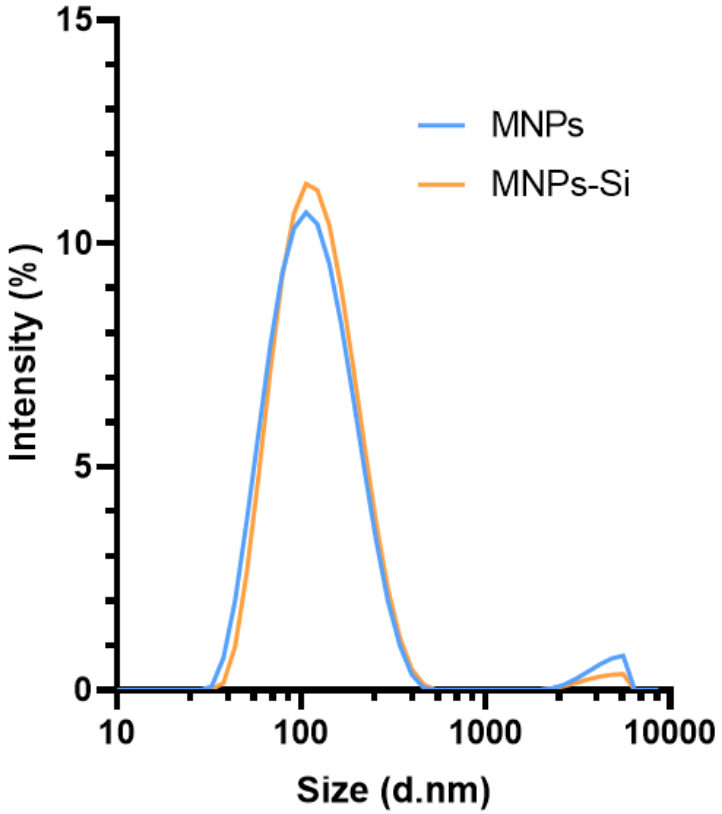
Presence of functional groups and bonds showing correct surface functionalization

TGA



MNPs: Single 10% mass loss zone corresponding to water loss

Size



Average particle size of 100 nm

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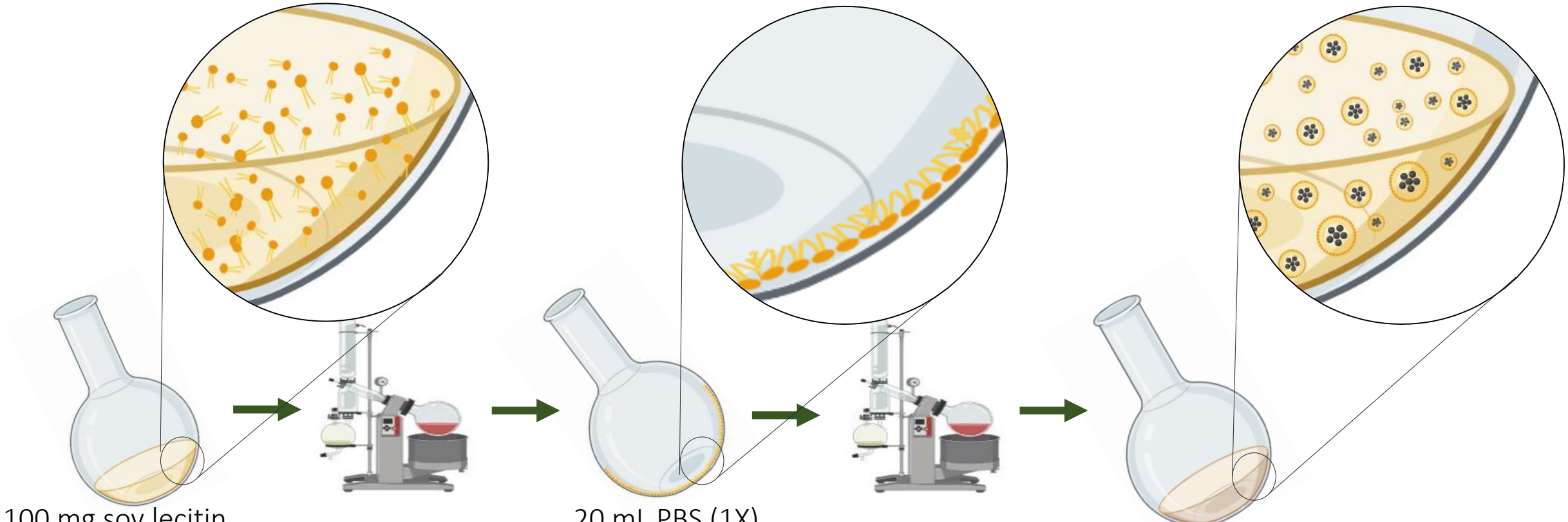
Liposomes synthesis



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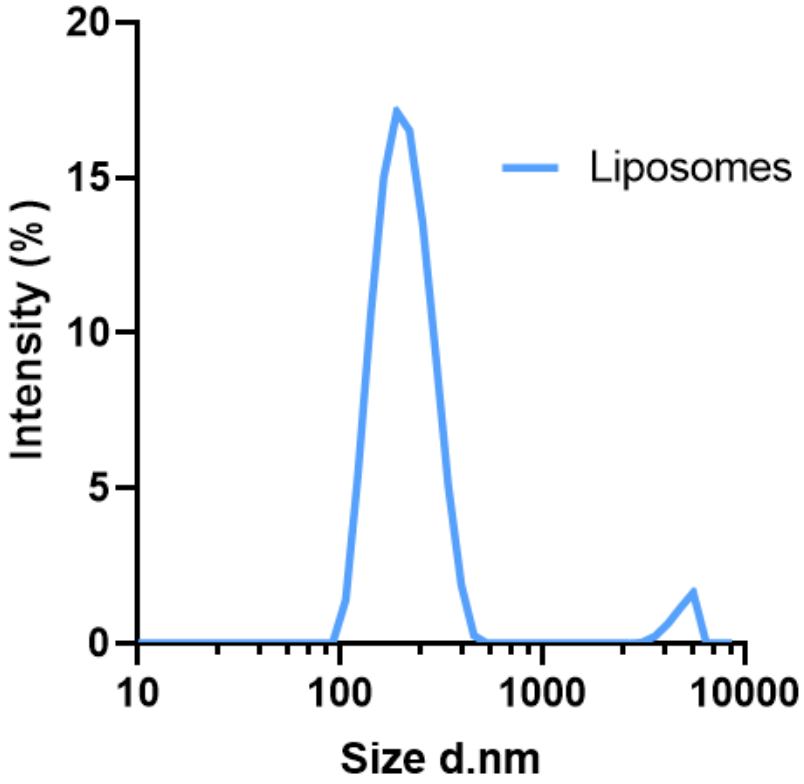
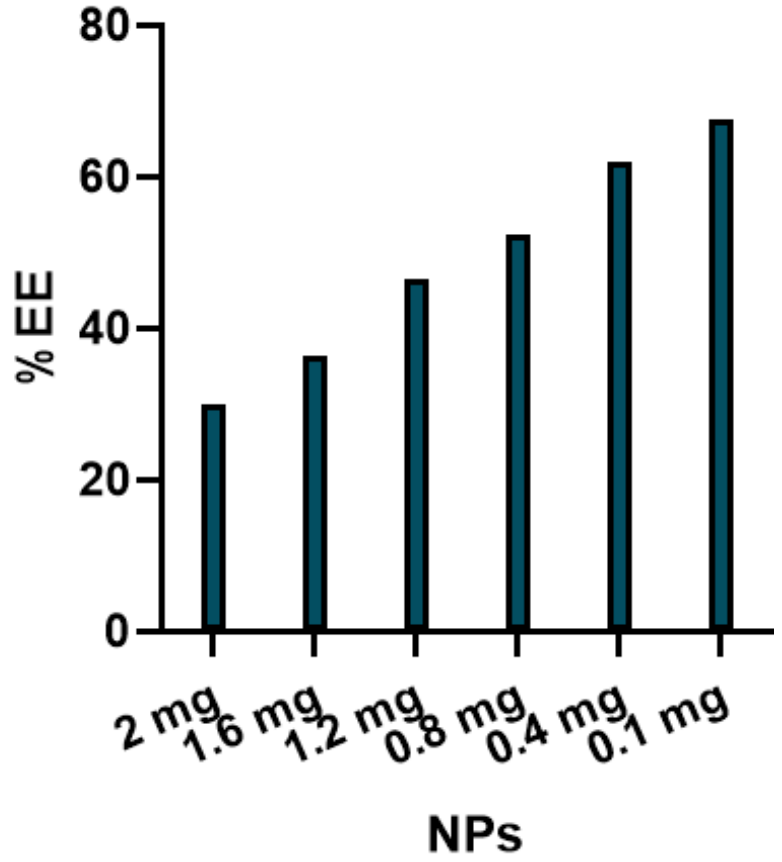
Liposomes characterization

Size



Average size of 208.9 nm and IDP: 0.203 were obtained. They have monodisperse liposomes.

Encapsulation efficiency (%EE)

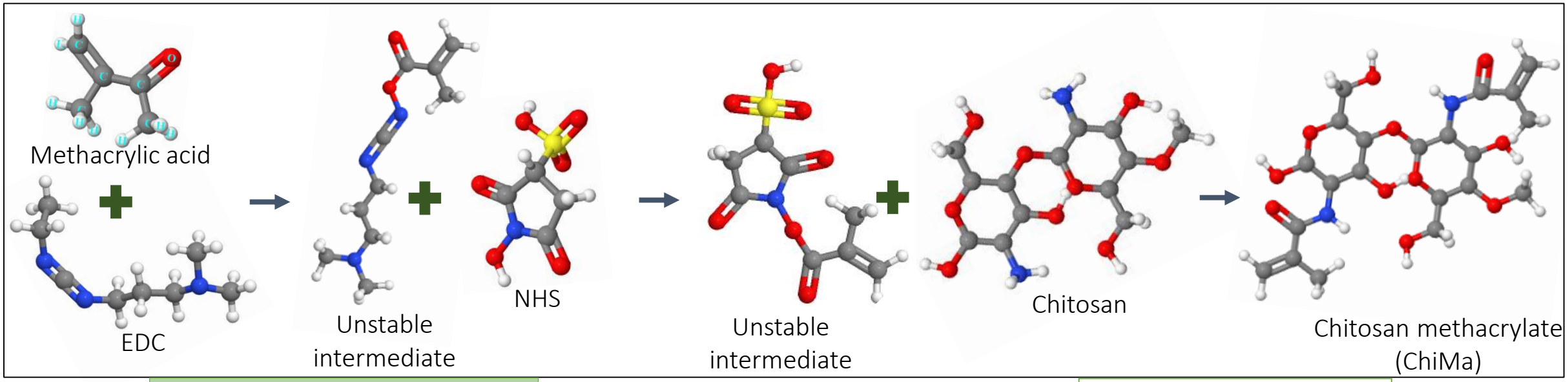


The %EE was obtained by applying the following equation

$$\%EE = \frac{I_f - I_I}{I_f}$$

The %EE obtained was 67.5% for a concentration of 0.1 mg/mL NPs.

ChiMa hydrogels syntesis



Chitosan methacrylation

MA(1:1)
EDC (1:2)
NHS (1:4)

Chitosan (3 %v/v)
(0.17M)acetic acid

600 RPM
60°c 24 H

Dialysis 48 H

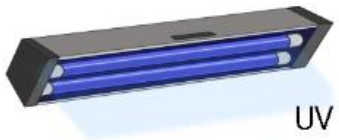
Lyophilize

Photocrosslinking

Riboflavin
(1% w/v)

ChiMa (3% v/v)
Acetic acid (0.17 M)

1000 rpm 1 min



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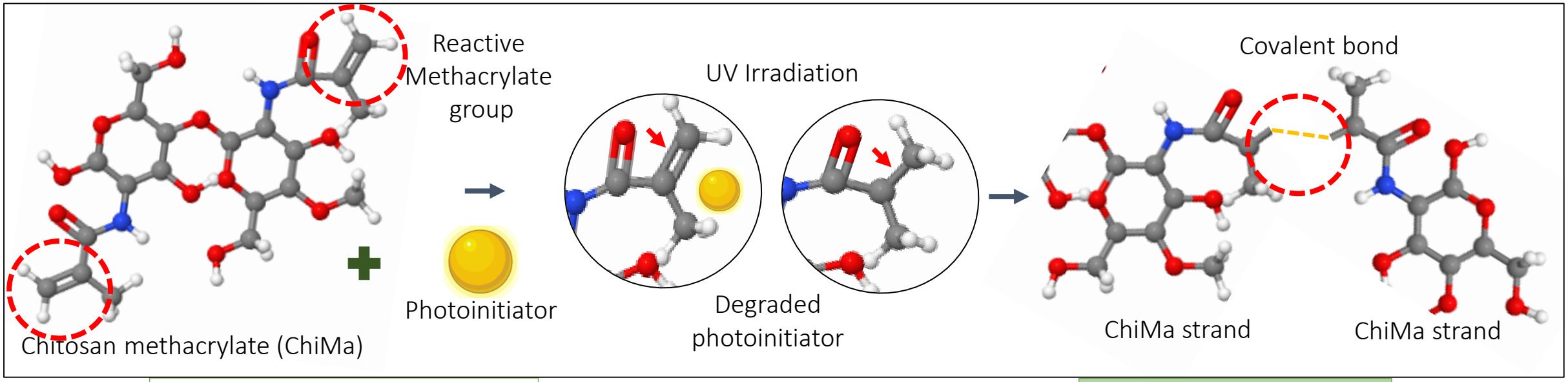
ChiMa hydrogels synthesis



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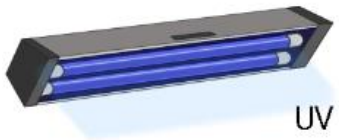

UV

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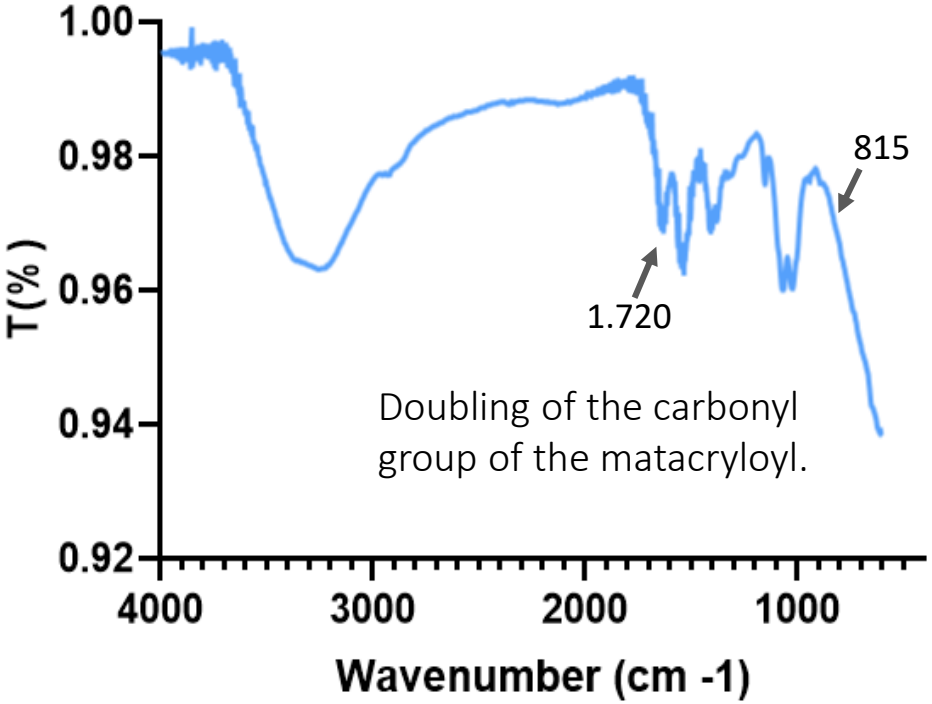
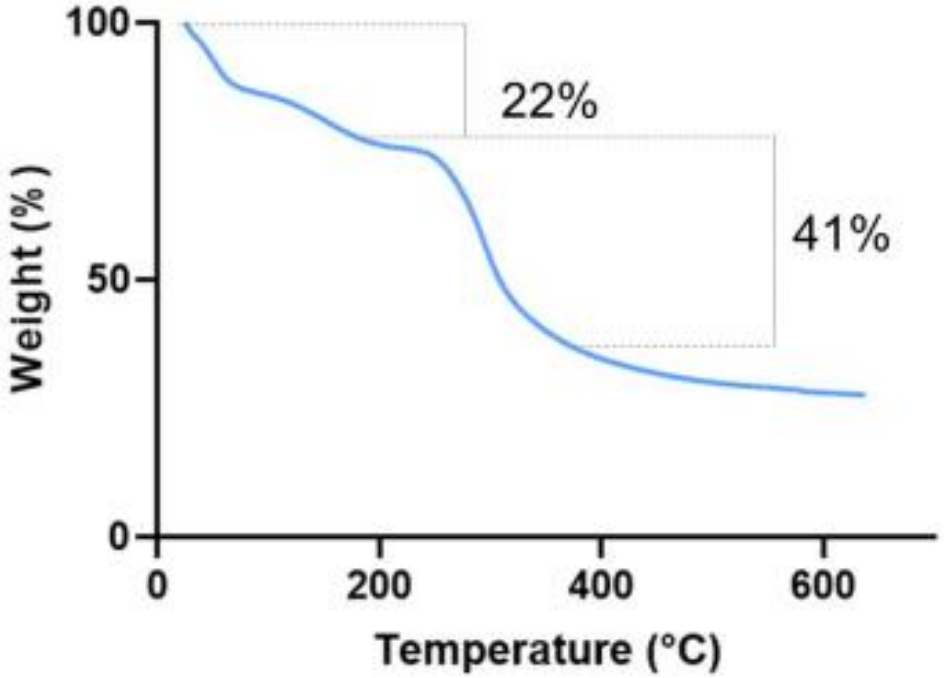
ChiMa hydrogels characterization

FTIR



The correct addition of methacryloyl groups to chitosan is validated.

TGA



Two mass loss zones

- Zone1: 22% water evaporation.
- Zone2: 41% polymer degradation

Viscosity

Hydrogels viscosity = 156 cP

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Clonclusions

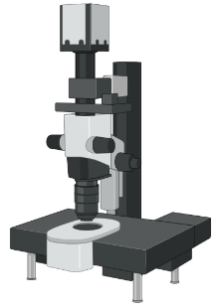
MNPs-Si of 100 nm were obtained. Their correct functionalization was validated by the presence of FTIR bands at **1040 cm^{-1}, 1391 cm^{-1}, 1653cm^{-1}**, corresponding to stretching vibrations of **Si-O groups**.

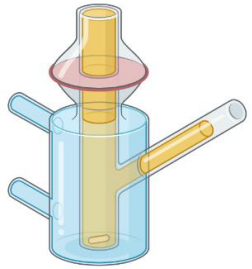
Magnetoliposomes with a hydrodynamic diameter of 208 nm and PDI of 0.23% were obtained.

The correct methacrylation of chitosan was performed as evidenced by **stretching bands of the carbonyl groups of the metacryloyl** at **1720 cm^{-1} and 815 cm^{-1}.**

Future work

Validation of liposome dispersion by microscopy

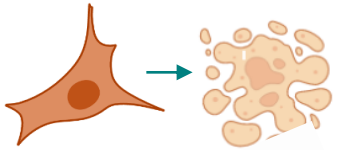


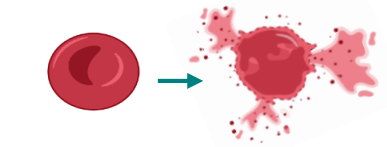


Diffusion test with franz cell

Biological characterization

- Cytotoxicity
- Hemocompatiblity
- Platelet aggregation





Thank you!

GINIB | **G**rupo de **I**nvestigación en **N**anobiomateriales, **I**ngeniería Celular y **B**ioimpresión

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