IMAGINENANO 2020 ONLINE

SEPT 29 – OCT 01, 2020

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DEVELOPMENT OF MAGNETIC NANOCARRIERS FOR ENHANCED ANTICANCER POTENTIAL OF LACTOFERRIN

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INTRODUCTION AND OBJECTIVES

What is the problem?

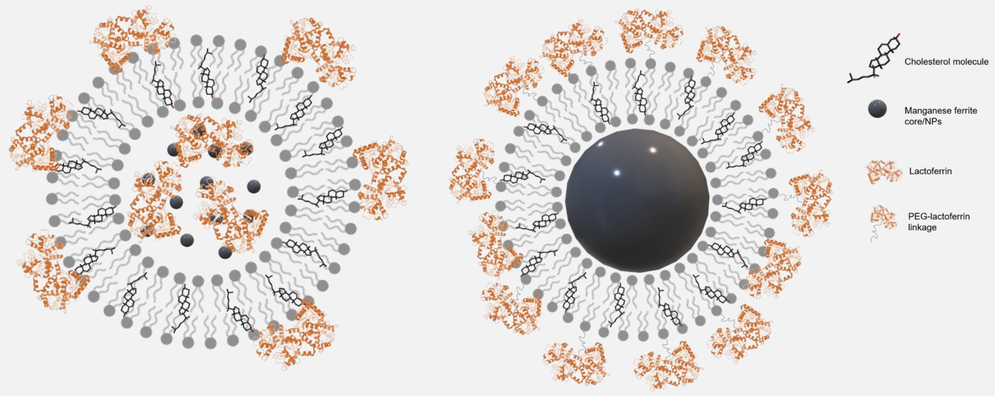
- Lactoferrin administration faces several problems regarding its bioavailability and pharmacokinetics

Possible solution

- Development of efficient nanocarriers such as **magnetoliposomes** [1]
- **Lactoferrin** is an iron-binding glycoprotein with **anticancer activity** for breast cancer cells [2]
- Incorporation of lactoferrin in magnetoliposomes is a possible way to enhance the biological activity of this protein

What is the aim of this work?

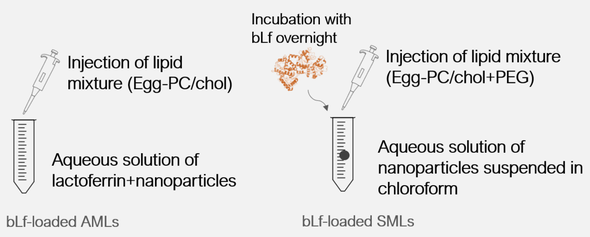
- Development of **bovine lactoferrin (bLf)-loaded magnetoliposomes**
- **Selective targeting** and **accumulation** of lactoferrin in tumor sites
- Enhancement of lactoferrin's anticancer activity



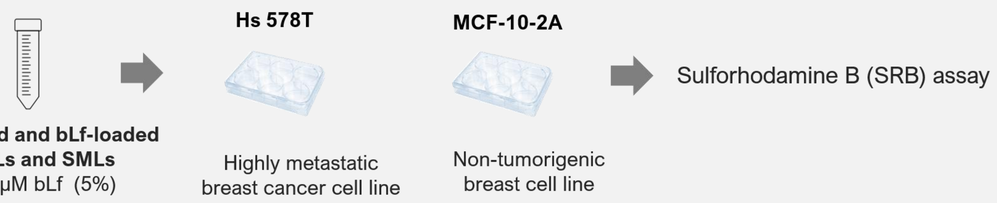
METHODS

Development of bLf-loaded magnetoliposomes

- Synthesis of $MnFe_2O_4$ magnetic nanoparticles by co-precipitation method
- Formation of the lipid bilayers by ethanolic injection (AMLs) or successive addition of lipid layers over nanoparticle aggregates (SMLs)

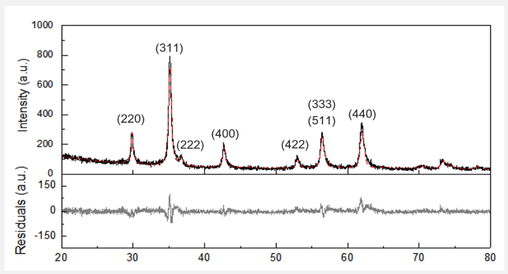


In vitro cytotoxicity studies



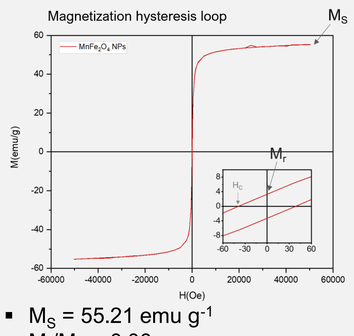
RESULTS

X-RAY DIFFRACTION



- $MnFe_2O_4$ nanoparticles with **14.5** nm

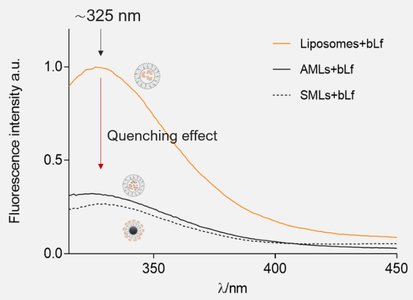
MAGNETIC MEASUREMENTS



- M_S = 55.21 emu g^{-1}
- M_r/M_S = 0.06

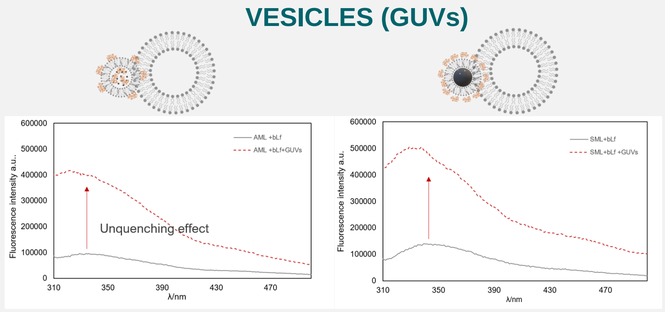
✓ **Superparamagnetic behavior**

INCORPORATION OF LACTOFERRIN IN MAGNETOLIPOSOMES



✓ **bLf is present in AMLs and SMLs**

INTERACTION WITH GIANT UNILAMELLAR VESICLES (GUVs)



✓ **Fusion with GUVs occurs for both bLf-loaded AMLs and SMLs**

RESULTS

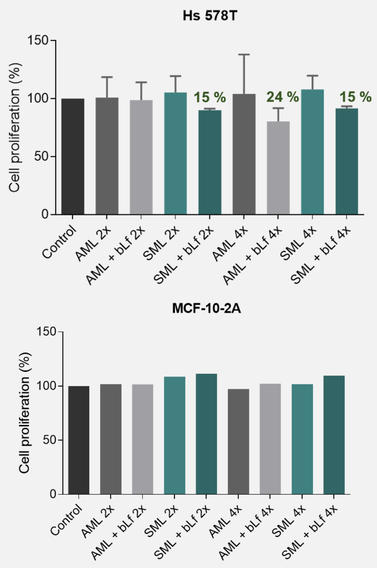
ENCAPSULATION EFFICIENCY (%)

62 ± 8 % **44 ± 20 %**

SIZE AND ZETA POTENTIAL

	Hydrodynamic size ± SD (nm)	**Zeta potential** ± SD (mV)
AML	92 ± 11	-15.3 ± 2
AML+ bLf	148 ± 23	-10.9 ± 0.9
SML	107 ± 16	-21.4 ± 3
SML+ bLf	164 ± 31	-2.1 ± 0.8

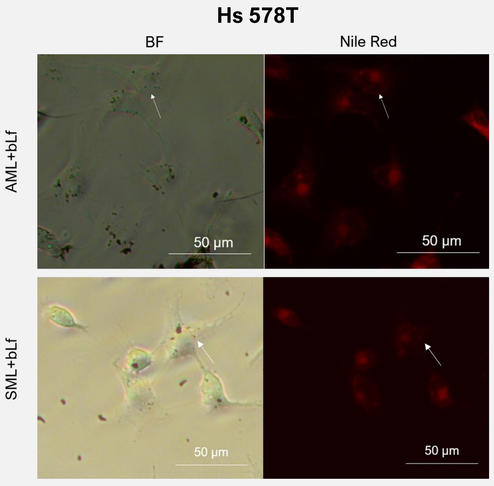
IN VITRO CYTOTOXICITY



✓ **Cytotoxic effect in Hs 578T cells was low**

✓ **Both bLf-loaded AMLs and SMLs are cytocompatible for non-tumorigenic breast cells**

CELLULAR INTERNALIZATION



✓ **Both bLf-loaded AMLs and SMLs are internalized in Hs 578T cells**

CONCLUSIONS

- Manganese ferrite nanoparticles have **superparamagnetic behaviour** → **Suitable for magnetic drug targeting**
- Fluorescence measurements
- DLS
- ELS → **bLf incorporation is confirmed for both AMLs and SMLs**
- Encapsulation of bLf is probably the best way to incorporate bLf
- Fluorescence microscopy images demonstrated internalization of magnetoliposomes in both cell lines
- bLf-loaded magnetoliposomes are cytocompatible for MCF-10-2A cells
- **Magnetoliposomes are promising nanocarriers for proteins like lactoferrin**

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REFERENCES

[1] B. Cardoso, I.S.R. Rio, A.R.O. Rodrigues, F.C.T. Fernandes, B.G. Almeida, A. Pires, A.M. Pereira, J.P. Araújo, E.M.S. Castanheira and P.J.G Coutinho, *Royal Society Open Science*, 5 (2018) 181017.
[2] C.S. Pereira, J.P. Guedes, M. Gonçalves, L. Loureiro, L. Castro, H. Gerós, L.R. Rodrigues, and M. Côrte-Real, *Oncotarget*, 38 (2016) 62144-62158.

AKNOWLEDGEMENTS

This work was supported by Fundação para a Ciência e a Tecnologia (FCT) under the Strategic Funding of "Centre of Physics of Minho and Porto Universities (CF-UM-UP)" and the research project PTDC/QUI-QFI/28020/2017 (POCI-01-0145-FEDER-028020) "MagLiDUo: Magnetoliposomes for Dual Cancer Therapy", also funded by FEDER, Compete2020 and Portugal2020.

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