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1506 UNIVERSITÀ DEGLI STUDI DI URBINO CARLO BO
DISB DIPARTIMENTO DI SCIENZE BIOMOLECOLARI

UNIVERSITÀ DEL SALENTO

Superparamagnetic nanoparticles for the inclusion into Red Blood Cells and MRI contrast agents.

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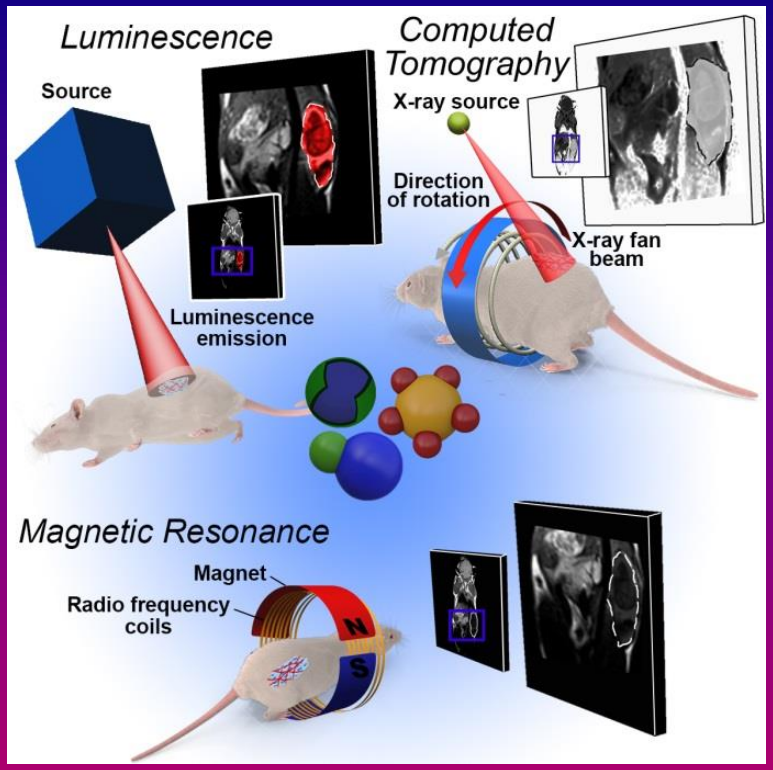
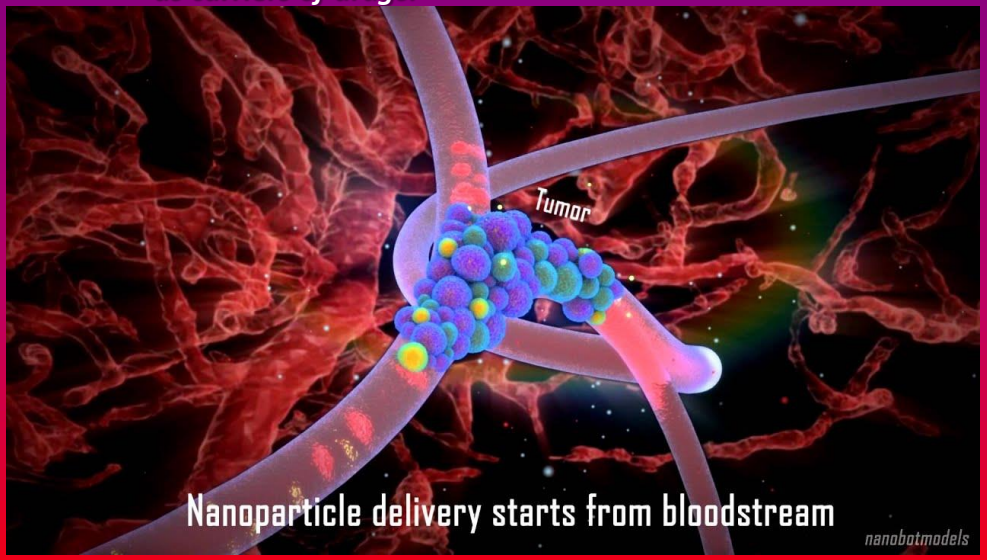
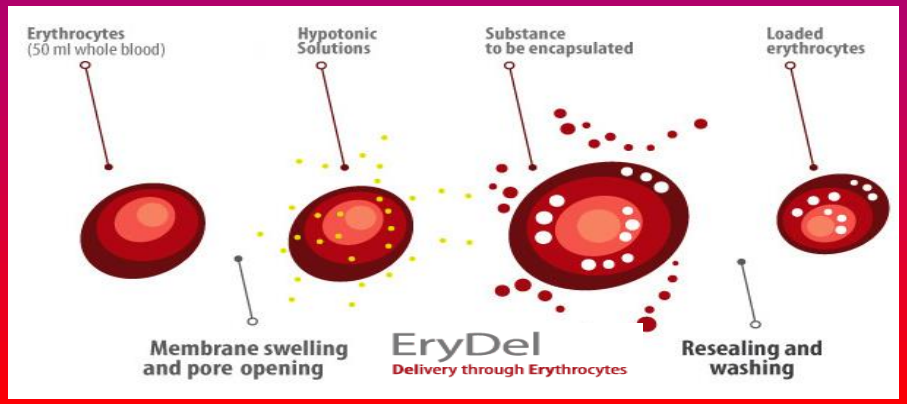
SPIONs and their application in nanomedicine.

The application of nanotechnology in cancer diagnosis is an emerging field. A non-invasive diagnosis in patients can be achieved using in vivo imaging techniques which are powerful tools for visualizing the abnormal state of the body and for monitoring biological situations at the target site.

Magnetic nanoparticles have high potential in nanomedicine as theranostic agents, because of their magnetic properties, crystal structure, high surface area, and low toxicity. The research activity consists of the inclusion of synthetic magnetic nanoparticles into living red blood cells (RBCs) for the development of a multifunctional system, active both as diagnostic, or therapeutic, agent and as carriers of drugs.







Riccardo Di Corato et al. **Appl. Mater. Interfaces,** 10 (2018): 20271-20280.

Antonelli A. et al. **Nanomedicine,** 6 (2011): 211-223.

Magnetic NPs: proposed synthetic approaches

Hydrothermal synthesis (directly water-dispersable NPs)

Co-precipitation method: Iron Oxide NPs (γ-Fe_2O_3) and doped ferrites.

Thermal Decomposition Synthesis (organic solvents-dispersable NPs)
→ to be transferred in water.

Multi-domain Au-Fe_3O_4 (dumbell-like NPs).

Magnetic Heterostructers

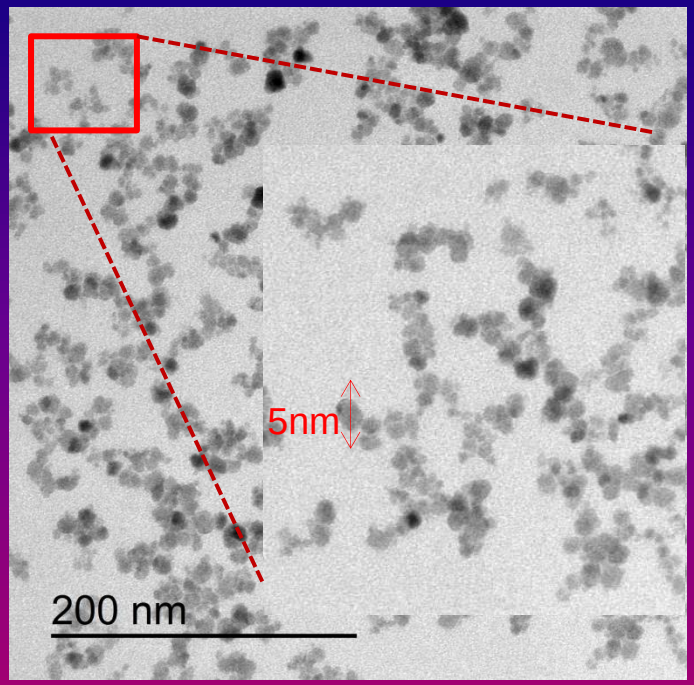
Zinc/Manganese-Ferrite NPs

Superparamagnetic doped-ferrite and iron oxide nanoparticles were obtained by different synthetic approaches; moreover, a biomimetic coating based on non-modified dextran was grafted to nanoparticles surface for ensuring optimal stability and low toxicity for subsequent inclusion in RBCs.

To improve the characteristics of the NPs, it was used an alternative material based on the dopping of iron oxide with zinc and manganese.

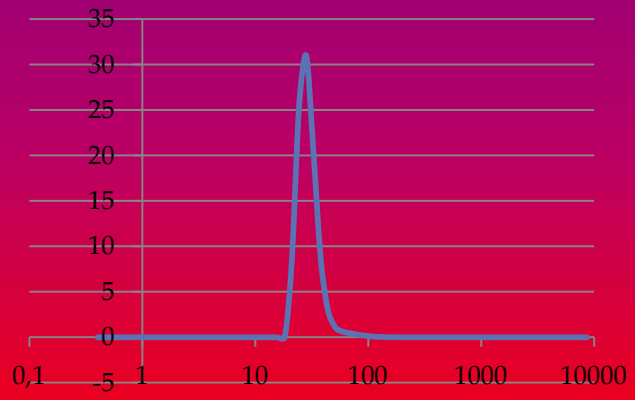
Massart R et al. **Magnetics, IEEE Transactions on** 1981**.** 17(2) 1247-1248.

Synthesis by Co-Precipitation (Iron Oxide NPs).



The NPs are precipitated from an aqueous solution containing a mixture of iron salts by adding ammonium hydroxide by drop-wise at different temperatures. Since the NPs are nude and therfore not stable in aqueous solution, sodium citrate was used to cover the surface with a biocompatible agent and to make them stable.

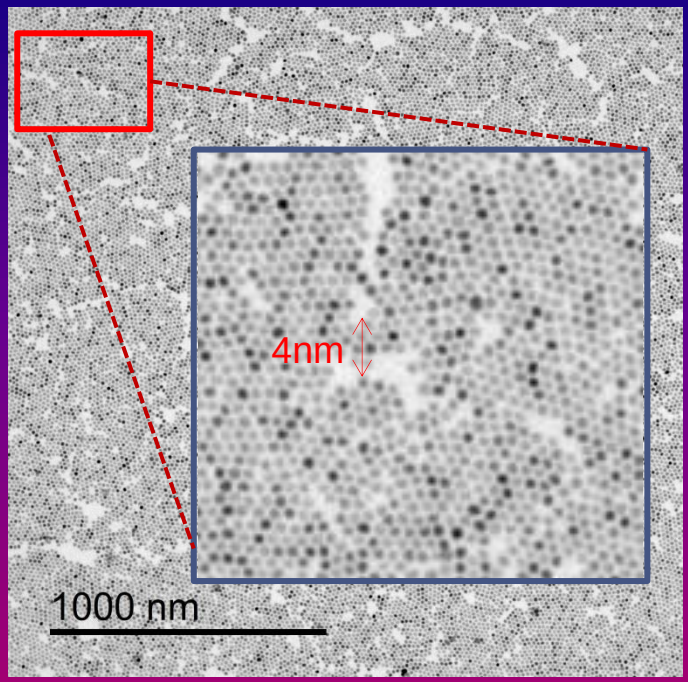
Organic iron compounds like ferric acetylacetonate and iron oleate are decomposed at high tempereature inside the non-polar boiling solvent with a presence of capping agents. The size of the NPs is obtained due to feature of the nucleation and growth mechanism.

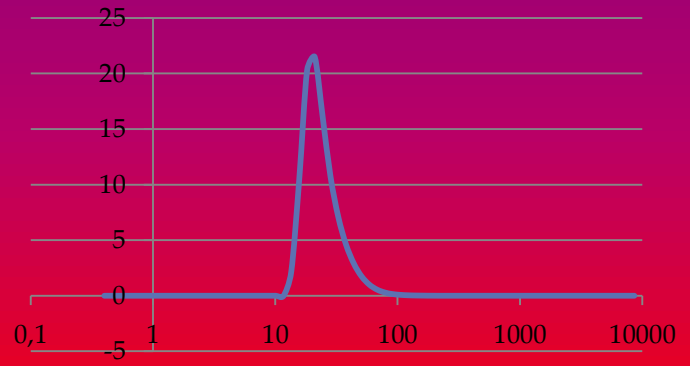


		Size (d.nm):	% Number:	St Dev (d.nm)
Z-Average (d.nm): 66,40	Peak 1:	31,40	100,0	10,84
PdI: 0,191	Peak 2:	0,000	0,0	0,000
Intercept: 0,926	Peak 3:	0,000	0,0	0,000

Result quality : Good

Synthesis by thermal decomposition (Zinc/Manganese-Ferrite NPs)



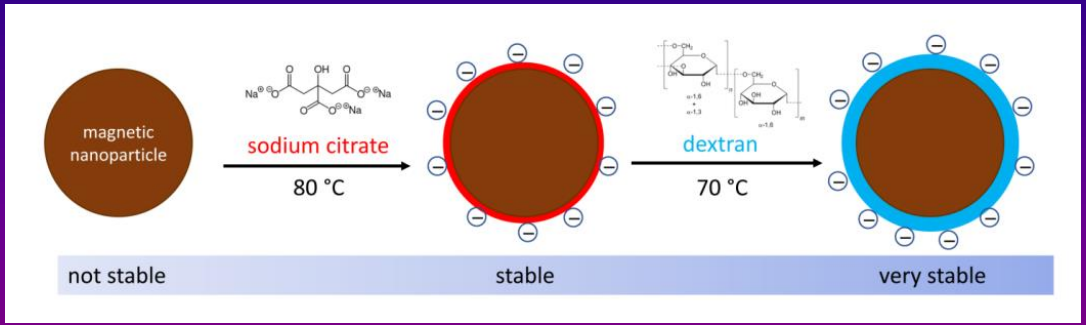


		Size (d.nm):	% Number:	St Dev (d.nm):
Z-Average (d.nm): 170,2	Peak 1:	40,88	100,0	15,34
PdI: 0,663	Peak 2:	0,000	0,0	0,000
Intercept: 0,540	Peak 3:	0,000	0,0	0,000

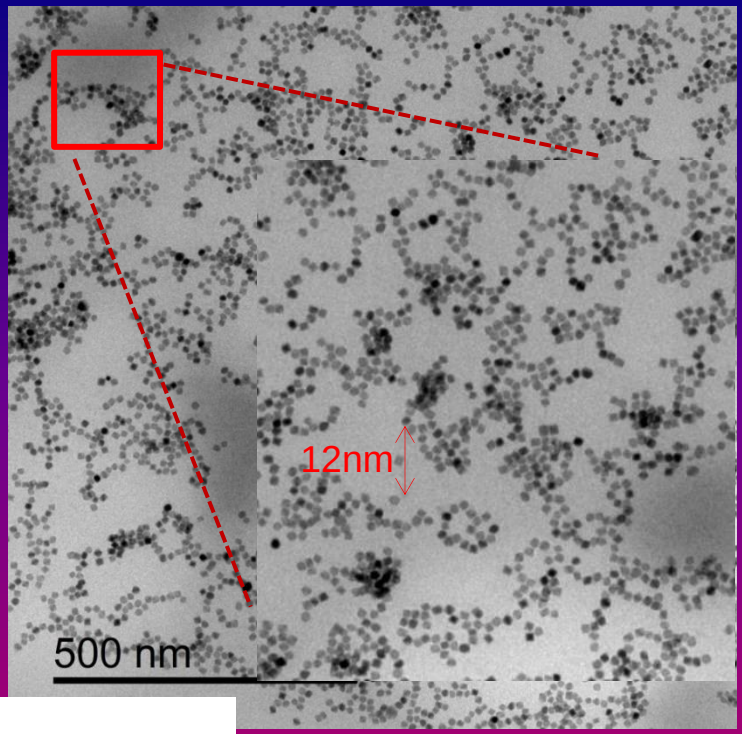
Result quality : Refer to quality report

Dextran Coated NPs.

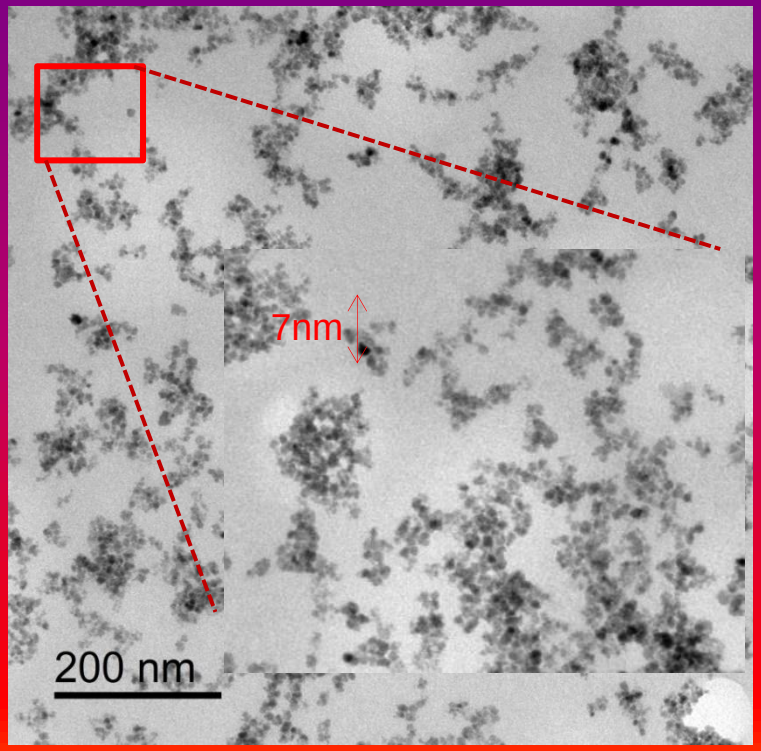
In order to obtain nanoparticles suspension stable in physiological condition, a layer of dextran was applied to previously obtained NPs.

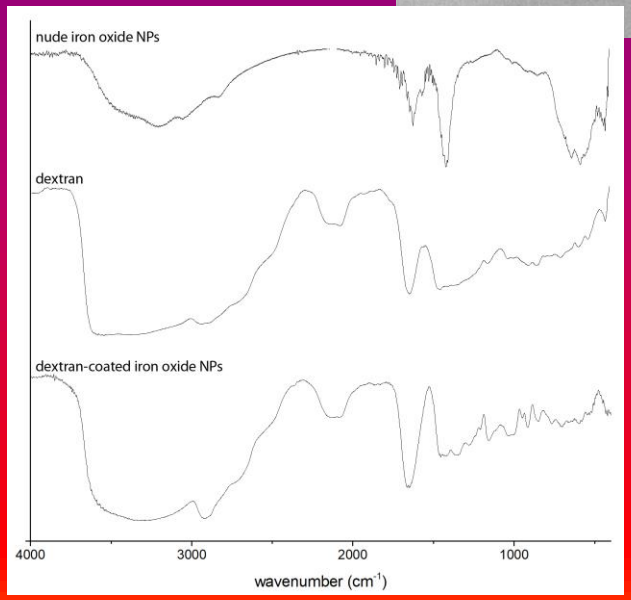


Thermal decomposition method.



Co-precipitation method.





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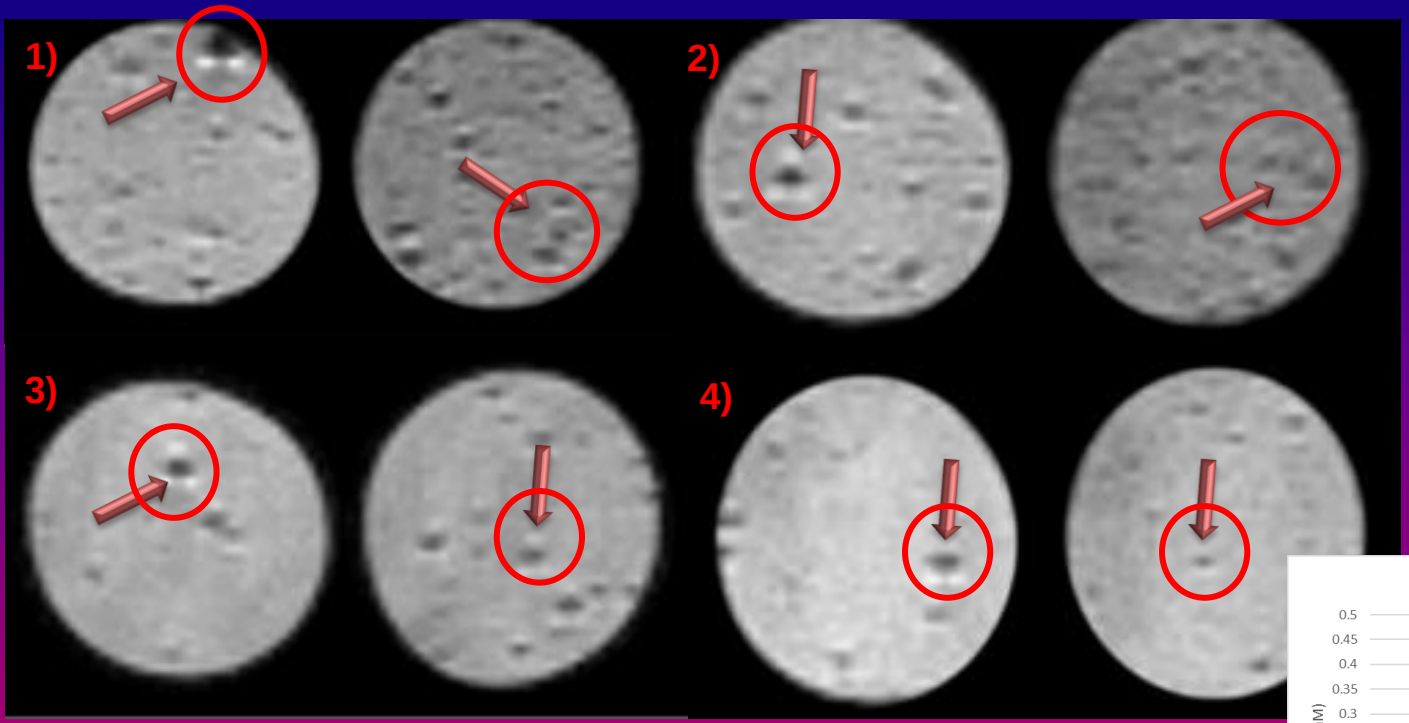
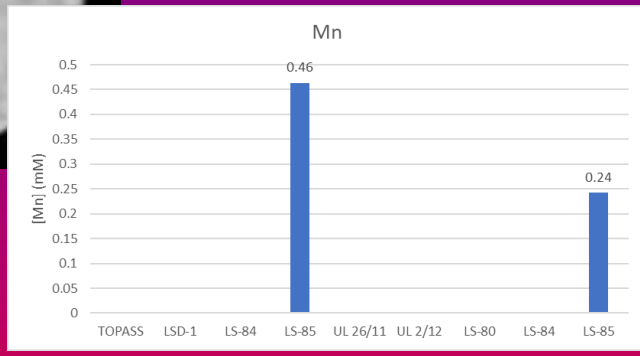
Inclusion into Red Blood Cells, charactherization.

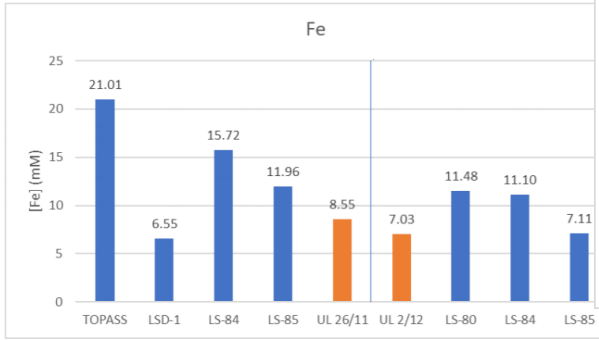


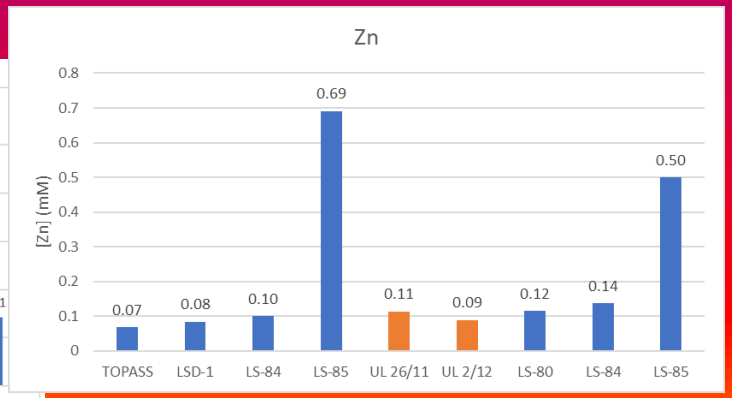
1) Dextran Coated Iron Oxide NPs.
2) Zinc/Manganese Ferrite NPs by Co-precipitation method.
3) Zinc/Manganese Ferrite NPs by Thermal Decomposition method.
4) Commercial NPs.

Through MRI measurements an increase in T2 due to iron nanoparticles inside the cells was revealed.

Considerate the concentration of ferrous into the cells, from the analysis of transmission electron microscopy reveals that the nanoparticles are slightly into red blood cells. A preliminary result is that the coating with dextran is more efficacy and provides a major stability respect the coating with citrate.



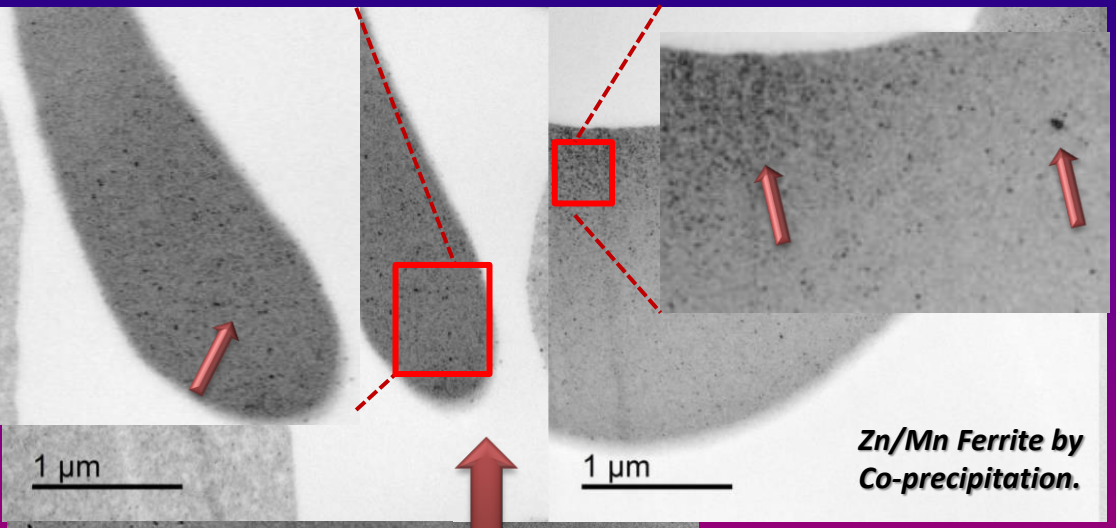




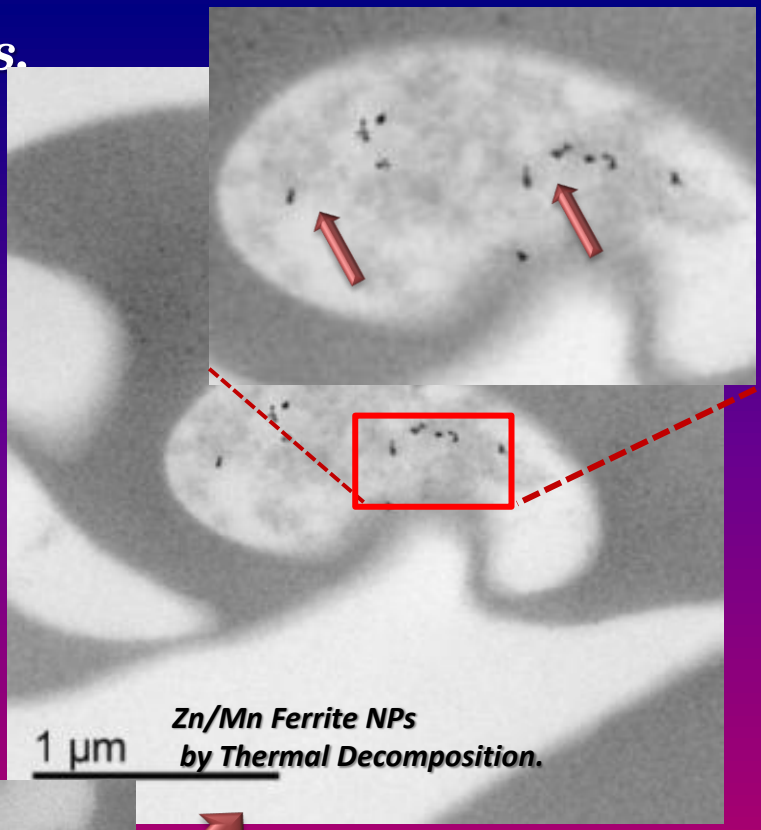
In the image we can see that by co-precipitation method the nanoparticles are not aggregated and mostly of them are inside the cells instead external of the RBCs. By Thermal Decomposition method nanocubes with the size of 12 nm are observed inside the cells but also external cells but in this case we have considerate the concentration of ferrous wich was rather low.

Encapsulation of magnetic NPs into RBCs.

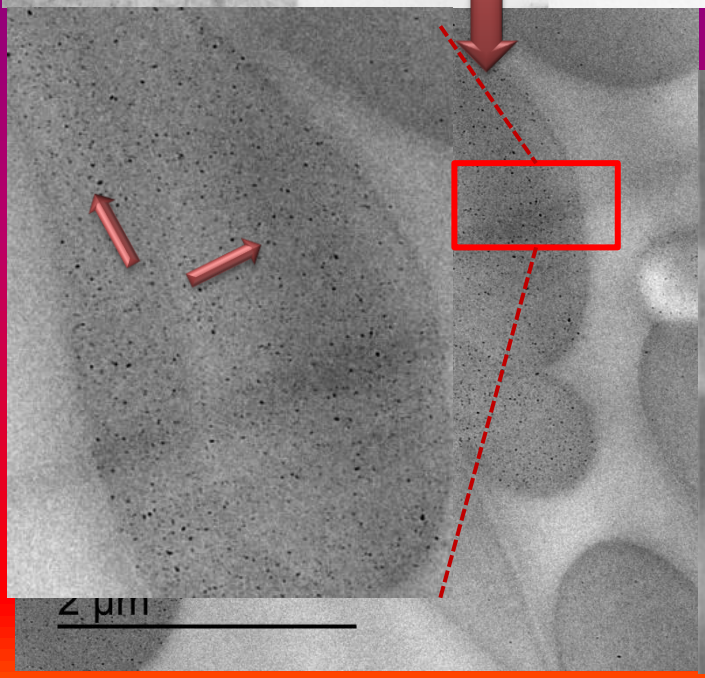
The microscope analysis revealed that the nanoparticles were slightly inside the cells.

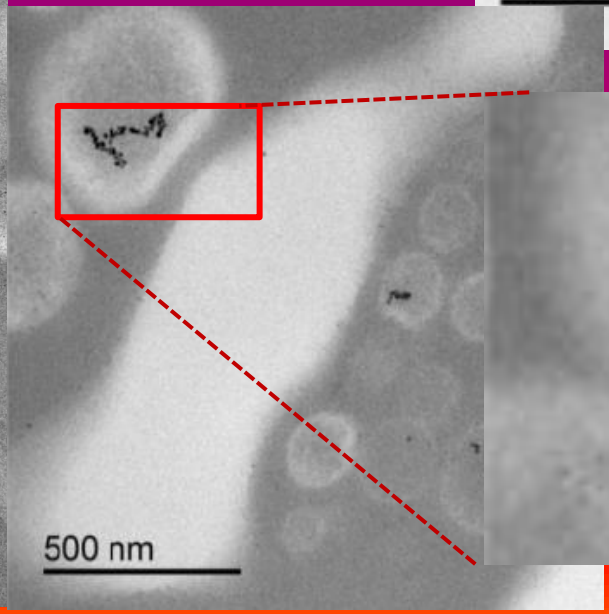


Zn/Mn Ferrite by Co-precipitation.



Zn/Mn Ferrite NPs by Thermal Decomposition.





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Conclusions...

Iron Oxide nanoparticles and zinc/manganese ferrite nanoparticles were obtained with good polydispersity, narrow size and efficient response to magnetic fields.

The RBCs-inclusion test inside the red blood cells revealed that the NPs interacted with the red blood cells.

...and future perspectives

Different types of colloids will be synthesized with the aim to obtain NPs :

- **With dimensions such as not to interfere with the process of inclusion into RBCs.**
- **With superparamagnetic behaviour.**

Will be evaluated:

- *The magnetization.*
- *The performance in Hypertermia , MPI and SQUID (Superconducting Quantum Interference Devices).*

Thank you for your attention !