COMPARATIVE TOXICOLOGICAL AND HISTOLOGICAL EVALUATION OF POLYMER-ENCAPSULATED, AMINE-FUNCTIONALIZED IRON-BASED MRI CONTRAST MATERIALS

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BACKGROUND: Superparamagnetic ferrite nanoparticles (NPs) are promising alternatives to conventional MRI contrast agents due to their favorable biocompatibility and tissue specificity. Among iron-based NPs, Zn- and Cu-doped ferrites are of particular interest for biomedical applications. Understanding their in vivo distribution and tissue response is essential for their safe development as next-generation contrast agents.

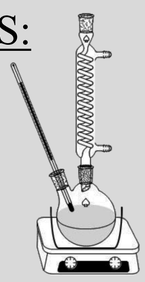
OBJECTIVES:

- To synthesize and surface-functionalize iron-based ferrite nanoparticles ($ZnFe_2O_4$-NH_2 and $CuFe_2O_4$-NH_2).
- To evaluate their biodistribution and histopathological effects in vivo using ex vivo liver, spleen, and kidney tissue samples at different post-injection time points.

MATERIALS & METHODS:

1

Ferrite precursors:
$Fe(NO_3)_3$
and
$Me(NO_3)_2$
Where Me = $metal^{2+}$

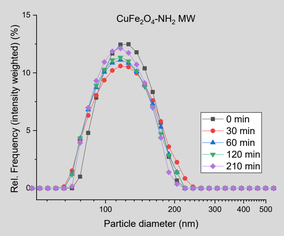


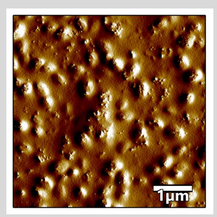
Reflux Synthesis: 12 h

MW Synthesis: 4 mins

2

In vitro





Complete characterization of the NPs, including HR-TEM, FTIR, XRD, AFM and DLS

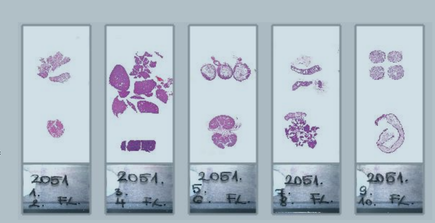
3

In vivo

In vitro magnetic characterization and in vivo biodistribution with 3T MRI system

4

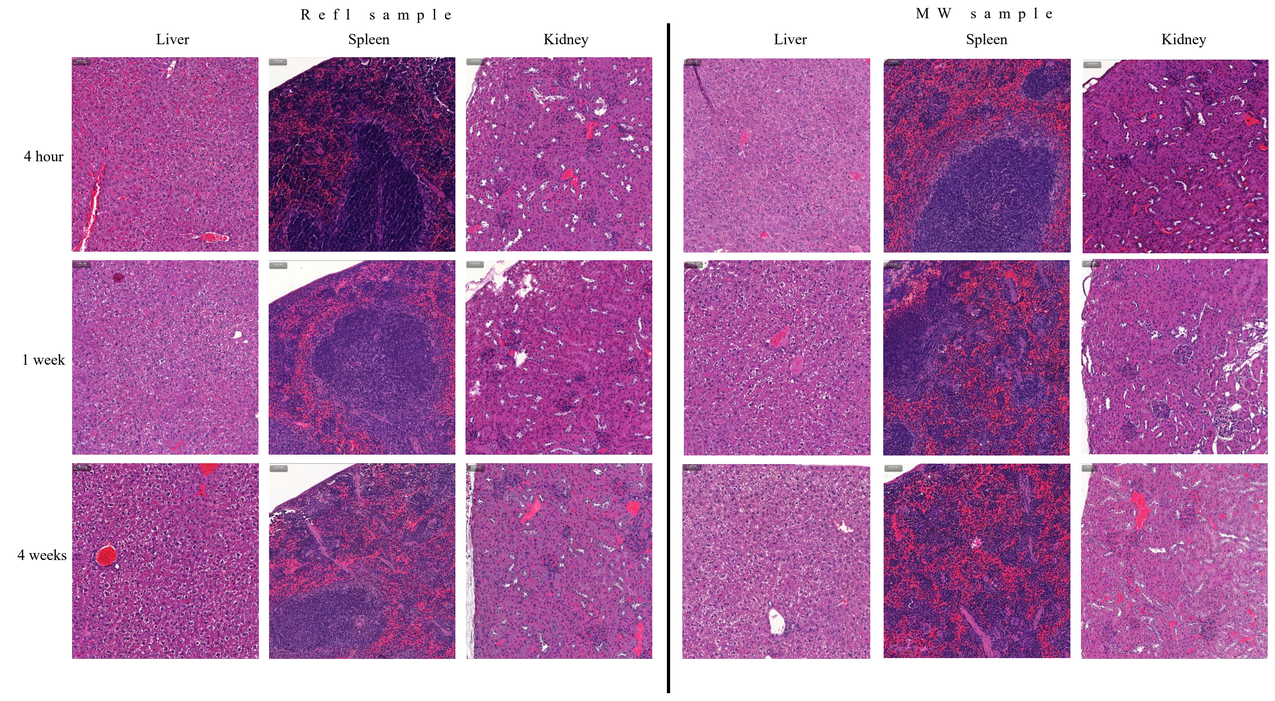
Ex vivo



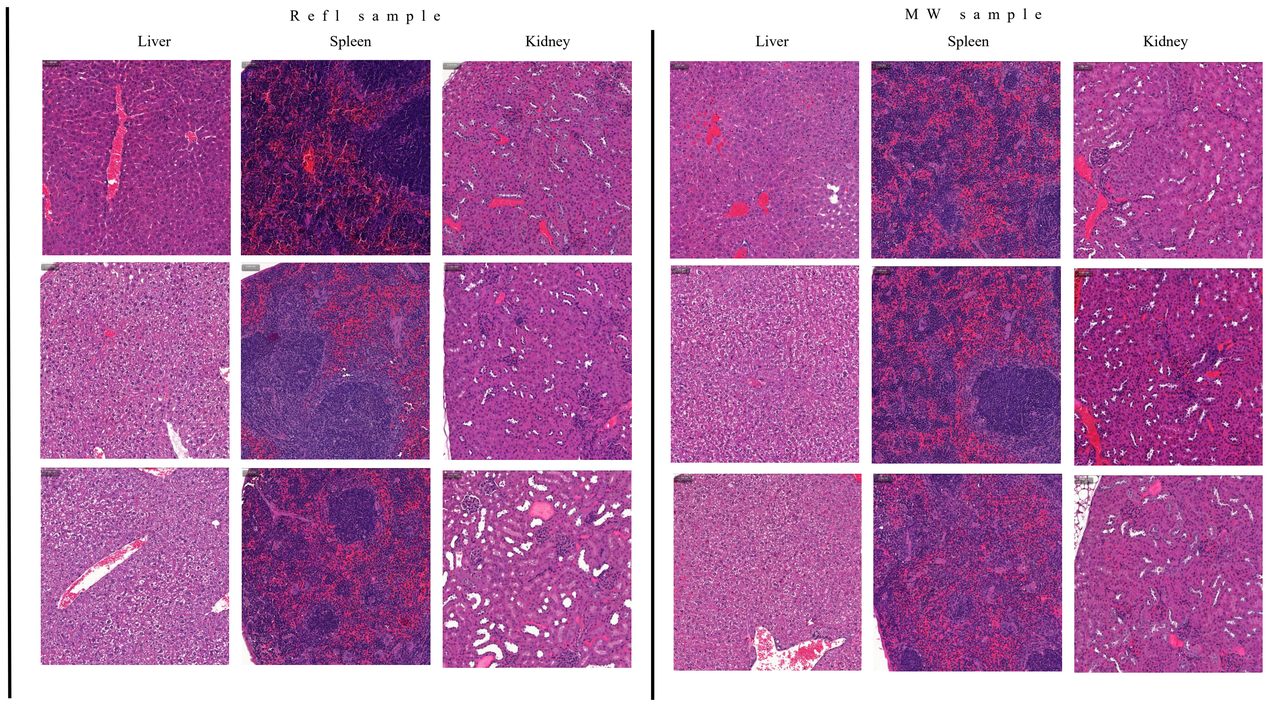
Ex vivo characterization after a pre-determined time, post injection

RESULTS:

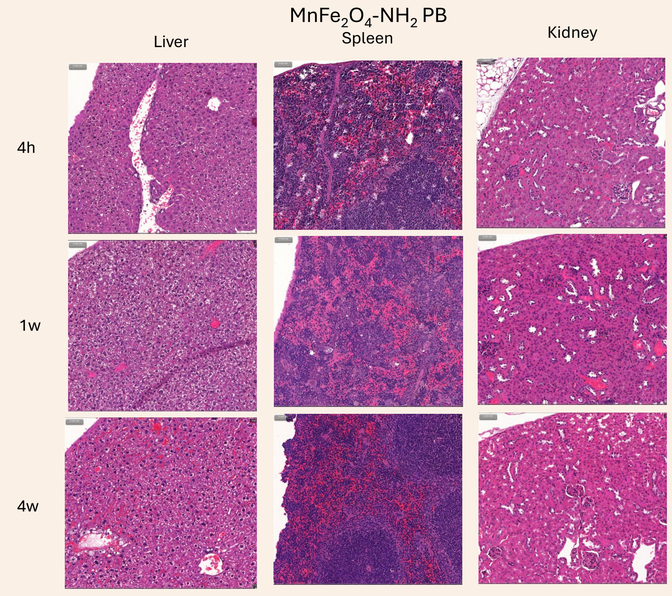
$ZnFe_2O_4$ particles



$CuFe_2O_4$ particles



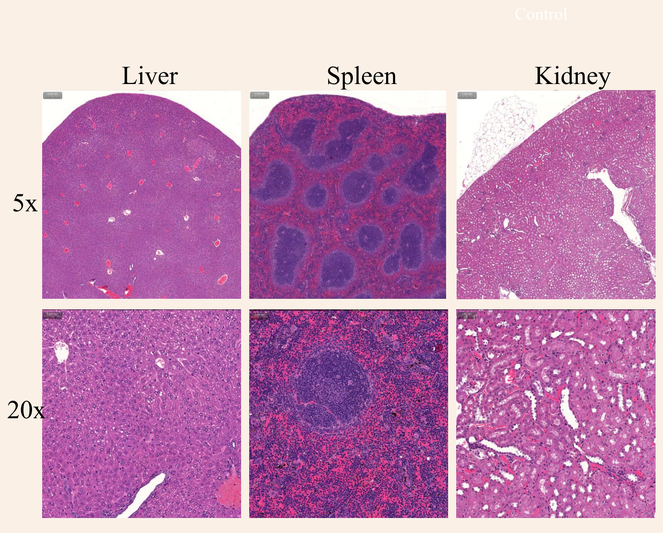
In case of both Zn- and Cu- samples, the samples nanoparticles prepared by MW synthesis showed reduced initial uptake in liver and spleen (4 h), with no notable renal accumulation. By 4 weeks, clearance was evident, indicating improved biodistribution and elimination compared to reflux-synthesized counterparts.



All nanoparticle formulations demonstrated concentration-dependent but acceptable in vitro biocompatibility, with Prussian blue–coated $MnFe_2O_4$-NH_2 exhibiting the lowest cytotoxic response. Histological analysis revealed no evidence of acute or delayed inflammation, necrosis, or tissue damage in any examined organ across all time points.

CONTROL

Control tissue samples were conducted witout NP injection, in healthy mice



CONCLUSION:

Our results demonstrate that polymer-stabilized, amine-functionalized iron-oxide nanoparticles can be synthesized reproducibly by both conventional reflux and microwave-assisted methods. Histological evaluation in mice confirmed biocompatibility, with organ distribution consistent with reticuloendothelial system (RES) uptake. Microwave-synthesized samples exhibited reduced early accumulation in liver and spleen (4 h) and no detectable renal deposition, with evidence of clearance after 4 weeks. These findings suggest that synthesis route strongly influences in vivo fate, with microwave methods offering potential advantages for biodistribution and clearance.

Preliminary, unpublished results (manuscript in preparation)

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