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Comparative toxicological and histological evaluation of polymer-encapsulated, amine-functionalized iron-based MRI contrast materials

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Introduction

Iron-based nanoparticles are widely investigated as MRI contrast agents, yet their translational advancement is often limited by insufficiently standardized in vivo safety assessments across different ferrite compositions and synthesis strategies. In particular, comparative histological data linking synthesis route, surface chemistry, and biodistribution remain scarce. This study presents a systematic toxicological and histopathological evaluation of polymer-encapsulated, amine-functionalized ferrite nanoparticles to assess their in vivo safety profile under comparable experimental conditions.

Methods

$ZnFe_2O_4$-NH_2, $CuFe_2O_4$-NH_2, and Prussian blue–coated $MnFe_2O_4$-NH_2 nanoparticles were synthesized using conventional reflux and microwave-assisted solvothermal methods and stabilized with polyvinylpyrrolidone for reproducible aqueous redispersibility. In vitro cytotoxicity was evaluated using the Alamar Blue assay in HEK293 cells, with culture medium and distilled water serving as control and negative control, respectively. In vivo histological assessment was performed in C57BL/6 mice (n = 4 per nanoparticle type per synthesis route) at 4 h, 1, 2, and 4 weeks

following systemic administration. Liver, spleen, kidney, and lung tissues were harvested and analyzed using hematoxylin–eosin staining, Perls' Prussian blue staining, and native microscopy.

Results/Discussion

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. Perls' Prussian blue staining confirmed predominant hepatic and splenic accumulation for all nanoparticle systems, consistent with reticuloendothelial system uptake, while non-target organs displayed preserved tissue architecture and absence of pathological iron deposition. Native microscopy supported the lack of pigment accumulation or structural abnormalities outside clearance organs. Importantly, although ferrite composition and synthesis route influenced biodistribution patterns, no adverse histological effects were observed, indicating that these parameters modulate in vivo fate without compromising tissue safety.

Conclusion

This comparative toxicological and histological analysis demonstrates that polymer-encapsulated, amine-functionalized ferrite nanoparticles exhibit favorable in vivo safety profiles across compositions and synthesis routes. The results provide robust preclinical evidence supporting their continued development as MRI contrast materials with predictable biodistribution and histological compatibility.

Novelty

First integrative, time-resolved histological comparison of multiple ferrite MRI contrast materials across synthesis routes.

Impact

Provides standardized preclinical safety evidence supporting translational development of iron-based MRI contrast agents.

Disclosure

Neither I nor any of my co-authors have any financial interests or relationships to disclose in relation to the subject of this presentation.

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Keyword
MRI contrast agents, ferrite nanoparticles, toxicology, histology, biodistribution