CHITOSAN-COATED IRON OXIDE NANOPARTICLES AS PROMISING NANOCARRIERS FOR GALLIC ACID TARGETED DELIVERY

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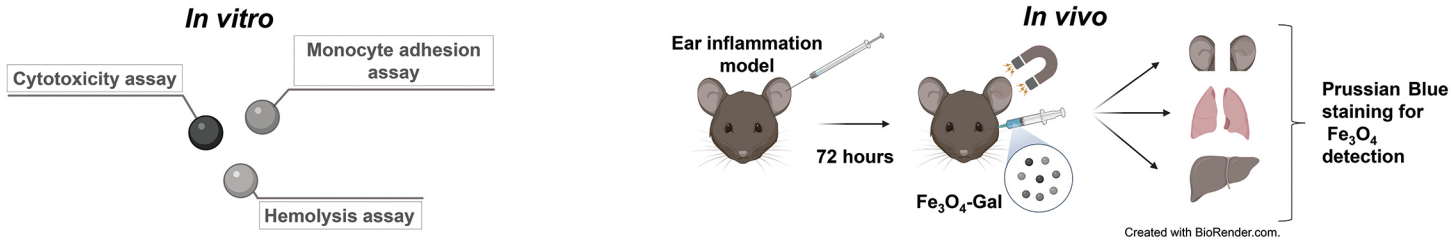
INTRODUCTION

Chronic inflammation is a common factor in various diseases, including cardiovascular diseases (CVD). Polyphenols are known to have multiple beneficial effects, such as anti-inflammatory, anti-oxidant, anti-fibrotic, and anti-aging properties, but their low bioavailability prevents them from being used as therapeutic agents [1,2]. To overcome this limitation, we designed chitosan-coated iron oxide nanoparticles (Fe_3O_4) as nanocarriers for gallic acid (Fe_3O_4-Gal) targeted delivery to areas of inflammation via an external magnet.

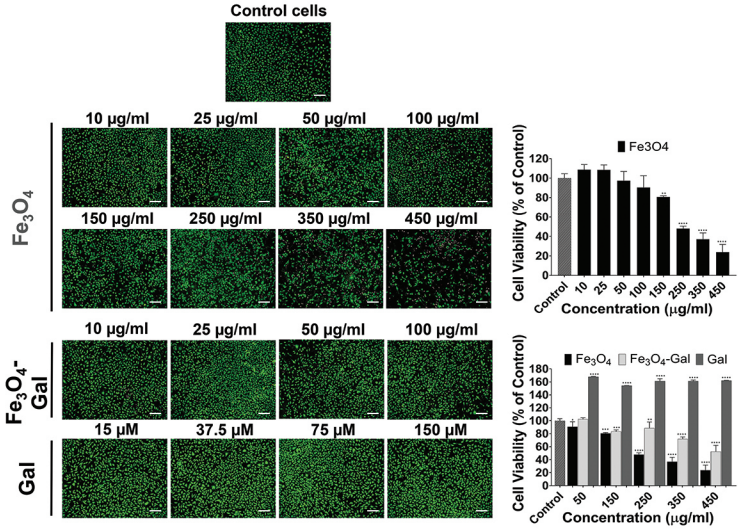
MATERIALS AND METHODS

Fe_3O_4-Gal were biologically characterized by investigating their cytotoxicity on EA.hy926 cell line, their ability to inhibit THP-1 monocyte adhesion to endothelial cells EA.hy926, as well as their biocompatibility via hemolysis assay. We also investigated the biodistribution of intravenously administered Fe_3O_4-Gal in a localized ear inflammation model after attracting the particles to the inflamed site with an external magnet.

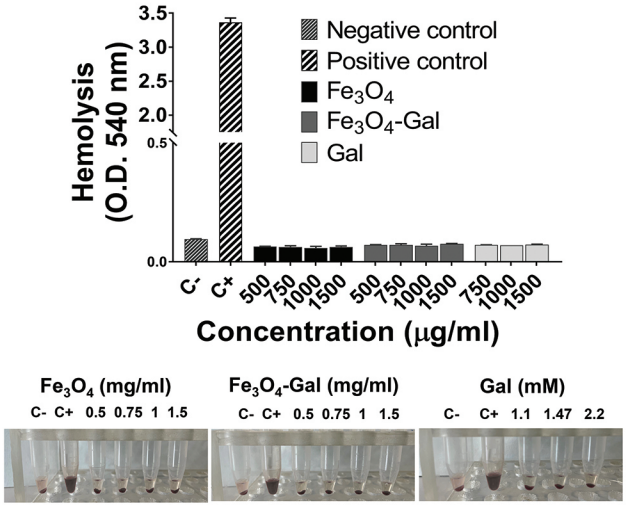


RESULTS

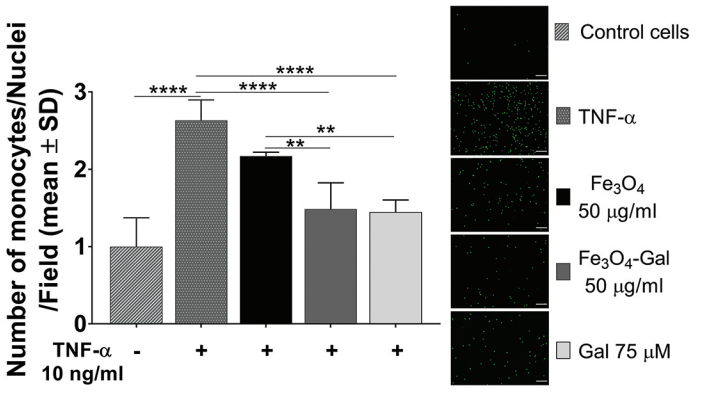
1. *In vitro* cytotoxicity evaluation of Fe_3O_4-Gal



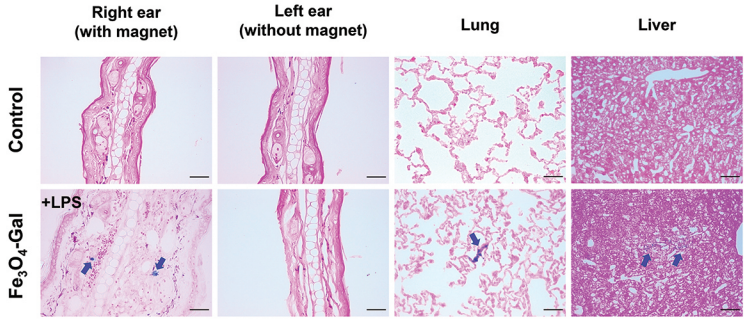
3. Hemocompatibility of Fe_3O_4-Gal



2. Monocyte adhesion assay



4. *In vivo* biodistribution of Fe_3O_4-Gal



Histological analysis of Fe_3O_4-Gal biodistribution in a C57BL/6 animal model after intravenous administration of 1 mg magnetic nanoparticles. Right ears were injected with 20 µg LPS 72 hours prior to induce inflammation, and were subjected to a magnetic field upon Fe_3O_4-Gal administration.
Scale Bar: 50 µm

CONCLUSION

The chitosan-coated polyphenol-loaded Fe_3O_4 nanoparticles tested in this study do not significantly induce cytotoxicity up to 100 µg/ml and have an anti-inflammatory effect *in vitro* by inhibiting THP-1 monocyte adhesion to EC. We found that even at higher iron concentrations, Fe_3O_4-Gal did not lyse erythrocytes, demonstrating good biocompatibility, as evidenced by the administration and subsequent localization of magnetic nanoparticles in the right ear after being directed by the applied magnetic field. Our findings suggest that Fe_3O_4 nanoparticles could be promising carriers for delivering low bioavailable compounds such as gallic acid to specific sites of interest.

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References:
1. Bejarano J, Navarro-Marquez M, Morales-Zavala F, Morales J, Garcia-Carvajal I, Araya-Fuentes E, et al. (2018). Nanoparticles for diagnosis and therapy of atherosclerosis and myocardial infarction: evolution toward prospective theranostic approaches. Theranostics, 8.
2. Tangney C.C, Rasmussen H.E (2013). Polyphenols, inflammation, and cardiovascular disease. Current atherosclerosis reports, 15(5).