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38. DEVELOPMENT OF MAGNETIC NANOSYSTEMS WITH POTENTIAL FOR THE TREATMENT OF INNER EAR PATHOLOGIES

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Hearing loss (HL) affects more than 5% of the global population, and projections suggest it could impact up to 50% of young individuals in the coming years. Most cases of HL are associated with local inflammation. Current treatments for HL are limited due to the inner ear's protective barriers, with intratympanic (ITT) administration being the most efficient method for drug delivery. However, the round window membrane (RWM) still poses a significant barrier for most drugs.

Our research focuses on overcoming this limitation through the implementation of nanotechnology. We propose the ITT injection of magnetic nanoparticles (MNPs) loaded with Diclofenac (Dfc), followed by their guidance to the inner ear via the RWM using an external magnetic field (EMF). Previously, we developed iron-oxide MNPs coated with folic acid (FA). This work aims to formulate MNPs loaded with Dfc, MPNs@FA.Dfc. The loading process was optimized for the physical adsorption of Dfc via weak interactions. Thus, Dfc can be easily released in the perilymph, which is the inner ear's target fluid. Drug loading capability and efficiency as well as the release kinetics were quantified by HPLC. Hydrodynamic diameter, Z potential and iron content estimation served to evaluate the influence of Dfc loading on these properties. Additionally, the FA-Dfc interaction was confirmed by FTIR analysis. The cytotoxicity and internalization of loaded MNPs were analyzed *in vitro* in HEK293 cell cultures. Finally, the ability of MNPs@FA.Dfc to cross the RWM was studied in dissected murine cochleae. To that end, MNPs were deposited in the RWM niche and then exposed to an EMF. We found by inductively coupled plasma-optical emission spectrometry a significant increase in the total Fe in the treated tissue. This result is consistent with the entry of MNPs. Statistical analysis was conducted using ANOVA test. These studies are of fundamental importance for future *in vivo* trials employing the developed nanosystem.