Feasibility of Superparamagnetic Nanoparticles for Drug Delivery to the Inner Ear

ABSTRACT

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OBJECTIVE: An obstacle of inner ear medicine is effective, atraumatic, nontoxic delivery of therapeutic molecules, including genes, proteins, oligonucleotides to the fluid compartments of the inner ear. We sought to determine the feasibility of using superparamagnetic nanoparticles for targeted drug delivery.

METHODS: Silica-coated superparamagnetic nanoparticles (NP) were assayed for hermeticity and free radical generation using a hydroxyl radical spin trap agent and measuring ESR spectra. Similar particles were added to organotypic cultures of Corti's organ to assess in vitro toxicity. NP were tested for movement through epithelial cells in culture in response to an external magnetic field. NP also were placed on the round window membrane (RWM) in anesthetized guinea pigs and rats. A 0.3 Tesla magnetic field was then applied on the opposite side of the RWM (20 min.) to draw the particles through RWM into perilymphatic fluid, which was collected and examined by electron microscopy for the presence of NP. A similar experiment was performed on a fresh human cadaver temporal bone.

RESULTS: The NPs remained resistant to oxidation and no free radicals were formed. Exposure of mouse-pup organotypic Corti's organ culture to NP at a concentration of 100 ug/ml for 24 hours demonstrated no hair cell loss after 3 days. NP were detected in guinea pig perilymphatic fluid and confirmed using transmission electron microscopy (TEM) with electron energy loss spectroscopy (EELS) and scanning electron microscopy with windowless, energy dispersive X-ray spectroscopy. NP were also detected in the perilymphatic fluid of human temporal bones as confirmed by TEM with EELS.

CONCLUSIONS: Silica-coated superparamagnetic NP were shown to be non toxic and susceptible to an external magnetic field. They could be rapidly and atraumatically pulled into inner ear perilymph. On-going experiments are aimed at payload attachment, polymer coatings, and in vivo studies of toxicity and therapeutic efficacy.

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