

DRUG DELIVERY TO THE MIDDLE AND THE INNER EAR

Currently systemic drug therapy of ear diseases overexceeds local therapy due to hurdles such as low blood flow in the cochlea, the blood - perilymph barrier, rapid drainage of solutions through the Eustachian tube, sometimes poor accessibility of the desired site of action and formation of bacterial biofilms upon infection of the middle ear. Systemic administration, however, is associated with low efficacy requiring high dosage and long-term treatment altogether provoking side effects.

To alleviate parts of the problem, bioadhesive drug delivery systems for intratympanic administration are developed to prolong the residence time of the drug in the tympanic cavity or to improve drug transport across the round window membrane into the inner ear. In terms of non-specific bioadhesion, solutions that solidify at body temperature within 20 seconds provoked therapeutically relevant drug levels in the perilymph of guinea pigs even for more than 10 days.

As a first step towards specific bioadhesive drug delivery, the glycosylation pattern of the middle ear mucosa has been screened. Wheat germ agglutinin specifically bound to sialic acid and N-acetyl-glucosamine moieties at the tips of the cilia. Thus, lectin-mediated drug delivery by grafted micro- and nanospheres is proposed as a new concept for therapy of ear diseases or traumata after cochlea implantation.

Tools:

- Preparation and characterization of hydrogels: rheology (amplitude -, frequency-, temperature sweep, ORO)
- Preparation and characterization of micells and nanoparticles as drug delivery systems: size and zeta potential by dynamic light scattering and nanoparticle tracking analysis; PLGA content by HPLC-analysis; incorporation of hydrophobic dyes as a label for fluorescence detection in the microscope (deconvolution) or quantification (fluorescence reader)
- Cells and tissues: isolation of middle ear mucosa, cochlea and Corti-organ from guinea pigs
- Detection: staining and co-localisation studies with lectins for microscopy (deconvolution) and semi-quantitative evaluation by image analysis
- In-vitro release model of the round window membrane
- Perilymph, plasma and liquor levels of glucocorticoids in-vitro and in-vivo: HPLC/MS in collaboration
- Toxicity: counting of viable/dead hair cells

References:

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