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Hyaluronic acid liposomal gel sustains delivery of a corticoid to the inner ear

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Abstract

The inner ear is one of the most challenging organs for drug delivery, mainly because of the blood-perilymph barrier. Therefore, local rather than systemic drug delivery methods are being developed for inner ear therapy. In this work, we have evaluated the benefit of a hyaluronic acid liposomal gel for sustained delivery of a corticoid to the inner ear after local injection into the middle ear in a guinea pig model. The liposomal gel was easily injectable as a result of the shear-thinning behavior of hyaluronic acid. A prolonged residence time at the site of injection as well as in the round window was achieved without any negative effect on the hearing thresholds of the animals. The presence of liposomes in the formulation resulted in sustained release of the drug in the perilymph for 30 days and promoted the conversion of the prodrug loaded within the liposomes (dexamethasone phosphate) into its active form (dexamethasone). In this way, therapeutic doses were attained in the perilymph. A small amount of intact liposomes was visualized in the perilymph, whereas the main proportion of liposomes seemed to be trapped in the round window resulting in a reservoir effect. Thus, the administration of hyaluronic acid liposomal gel to the middle ear is an efficient strategy for delivering corticoids to the inner ear in a sustained manner.

Keywords. Dexamethasone phosphate, local drug delivery, liposomes, local injection, perilymph, round window.

Abbreviations. Chol: cholesterol, DSPE-PEG2000: 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy-poly-(ethyleneglycol)-2000], Dex: dexamethasone, DexP: dexamethasone phosphate, DLS: dynamic light scattering, EPC: Egg phosphatidylcholine, Flu: flumethasone, HA: hyaluronic acid, Lip: liposomes, LC-MS: liquid chromatography coupled to mass spectroscopy, PE: phosphatidylethanolamine, Rh: rhodamine, RW: round window.

Chemical compounds. Cholesterol (PubChem CID: 5997); Dexamethasone (PubChem CID: 5743); Dexamethasone sodium phosphate (PubChem CID: 16961); 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy-poly-(ethyleneglycol)-2000] (PubChem CID: 406952) ; Phosphatidylcholine (PubChem CID: 52922911) ; Sodium hyaluronate (PubChem CID: 3084049).

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