Benzothiazolyl-decorated liposomes effectively inhibit $A\beta_{1-42}$ aggregation in vitro

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ABSTRACT

In order to evaluate the potential use of liposomes as potential theranostic systems for Alzheimer's disease (AD), we prepared pegylated nanoliposomes decorated with benzothiazolyl-groups which are known to effectively reduce amyloid beta pathology in-vitro and in-vivo [1-2]. Two types of benzothiazolyl-groups were selected: (a) un-substituted 2-benzothiazoles [1] and (b) 2-(4-aminophenyl)benzothiazoles [2].

For this reason we synthesized a lipid-2-benzothiazole (Lipid-BTH) and a lipid-2-(4-aminophenyl)benzothiazole (Lipid-AP-BTH) conjugate, and these were incorporated in pegylated DSPC/Chol liposomes to the corresponding BTH and AP-BTH decorated liposomes (5%, 10% and 20% benzothiazole/lipid molar ratio).

The benzothiazolyl-decorated nanoliposomes were physicochemically characterized for their size, polydispersity index and ζ-potential and were further examined for their interaction with the Aβ species, for a 15-day time period, by using circular dichroism spectroscopy (CD). The ability of the benzothiazolyl-decorated nanoliposomes to inhibit Aβ aggregation was examined by Thioflavin-T (ThT) assay of the aged samples (after the 15-days interaction).

The most effective types of liposomes were further characterized for their size distribution, surface charge and physical stability during storage at 4°C for a 30-day time period, and were further subjected to membrane integrity experiments during incubation at 37°C in presence of buffer and plasma proteins. Finally, FITC-dextran-containing nanoliposomes with 5% and 10% actives were subjected to cell uptake studies by hCMEC/D3 cells (a cellular model of human blood-brain barrier (BBB)).

Experimental results (interaction between liposomes:Aβ species with CD, inhibition of Aβ aggregation by ThT measurements and transport across BBB model) were very promising, showing that specific types of benzothiazolyl-decorated nanoliposomes deserve further exploitation as for novel targeted theragnostic systems against AD.

REFERENCES

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