Optimization of the click reaction on nanoliposome surface for preparation of various types of vesicles decorated with a curcumin-derivative

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Amyloid β (Aβ) aggregates are considered as possible targets for therapy and/or diagnosis of Alzheimer disease (AD). It has been shown that nanoliposomes which are decorated with a novel curcumin derivative (TREG) demonstrate high affinity for amyloid-β1-42-peptide, suggesting a potential role in prevention or treatment of AD (Biomaterials, 2011, 32, 1635-1645). For formation of these novel nanoliposome preparations, a click chemistry method is utilized in which pre-formed nanoliposomes bearing azide groups on their surface react with a planar curcumin-alkyne derivative, in order to generate nanoliposomes decorated with curcumin moieties which maintain the planar structure required for interaction with Aβ.

Herein, we report our efforts to overcome the difficulties encountered for scale up of click chemistry reaction on DPPC/DPPG/Chol+20% lipid-peg-N₃ liposomes. In general the points investigated were: (i) the adjustment of the osmolarity of the reaction mixture; (ii) strategies for avoiding liposome aggregation and (iii) purification strategies, which may require special consideration when lipid and reactant concentrations are increased during scaling-up. As an alternative/comparative method for the preparation of TREG decorated nanoliposomes, we incorporated the corresponding lipid-TREG derivative in DPPC/DPPG/Chol liposomes. These liposomes were subjected to stability tests (regarding membrane integrity and size increment or aggregation).

Furthermore, we report here our first observations during the preparation of TREG-decorated nanoliposomes which encapsulate Iron Oxide (IO) nanoparticles (USPIOs, provided by Guerbet, Paris, FR), or TREG-decorated nanoliposomes which also have OX-26 MAb on their surface for BBB targeting. We also describe a very simple click method for the decoration of nanoliposomes avoiding the use of copper and other reactants, which may be very helpful for the synthesis of TREG and OX-26 MAb double decorated nanoliposomes.
The results obtained from the above experiments improve our efforts for the preparation of (a) TREG decorated nanoliposomes; (b) IO encapsulating TREG-nanoliposomes and (c) nanoliposomes which are dually decorated with TREG and OX-26 MAb.

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