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Design of lipoprotein-adsorbed liposomes retaining Mn-porphyrins for SOD mimic delivery to brains

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ABSTRACT

Drug delivery to brains is becoming more and more important but is severely restricted by the blood–brain barrier (BBB). In this study, we have prepared an antioxidant for brain targeting by apolipoprotein E (ApoE), which was suggested to mediate this drug transport across the BBB. Superoxide dismutase (SOD) catalyzing the reduction from superoxide radical anion ($O_2^{\bullet -}$) to hydrogen peroxide (H_2O_2) is the key enzyme for the protection from oxidative stress. The oxidative stress is considered to be implicated in the pathogenesis of a number of diseases, such as Alzheimer's disease. The SOD mimic manganese porphyrins (Mn-porphyrins) have been retained by a liposome composed of 1,2-dimyristoyl-sn-glycero-3-phosphatidylcholine, sodium oleate, and Tween-80. The Tween-80 is reported to lead to the adsorption of ApoE. The resulting liposomes were incubated with serum proteins containing ApoE. After the incubation, the protein determination proved that the amount of adsorbed proteins on the liposome surface increased almost in proportion to the amount of the Tween-80 of the liposome. Subsequently, sodium dodecylsulphate–polyacrylamide gel electrophoresis (SDS–PAGE) revealed that the adsorbed proteins contained ApoE. Furthermore, the cellular uptake of the liposome was examined using cells expressing low-density lipoprotein receptors which recognize ApoE. The intracellular Mn-porphyrin retained by the liposome increased in proportion to the amount of the Tween-80 of the liposome. Moreover, the brain uptake of the Mn-porphyrin was observed in our preliminary in vivo experiment, where i.v. injection of the resulting liposome was carried out. These results suggest that the Mn-porphyrin SOD mimic can be delivered across the BBB, probably after interaction with lipoprotein receptors on the brain capillary endothelial cell membranes. Our system is considered to be a promising approach for protection of the brain under oxidative stress.

Keywords: Mn-porphyrin; Liposome; SOD mimic; Brain targeting; Drug delivery system

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