Photoactive liposomal formulation of PVP-conjugated chlorin e6 for photodynamic reduction of atherosclerotic plaque.

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Rok wydania

2019

Czasopismo

International Journal of Molecular Sciences

Numer woluminu

20

Strony

3852/1-3852/15

DOI

10.3390/ijms20163852

Streszczenie

Background: Liposomes serve as delivery systems for biologically active compounds. Existing technologies inefficiently encapsulate large hydrophilic macromolecules, such as PVP-conjugated chlorin e6 (Photolon). This photoactive drug has been widely tested for therapeutic applications, including photodynamic reduction of atherosclerotic plaque. Methods: A novel formulation of Photolon was produced using “gel hydration technology”. Its pharmacokinetics was tested in Sus scrofa f. domestica. Its cellular uptake, cytotoxicity, and ability to induce a phototoxic reaction were demonstrated in J774A.1, RAW264.7 macrophages, and vascular smooth muscle (T/G HA-VSMC) as well as in vascular endothelial (HUVEC) cells. Results: Developed liposomes had an average diameter of 124.7 ± 0.6 nm (polydispersity index (PDI) = 0.055) and contained >80% of Photolon). The half-life of formulation in S. scrofa was 20 min with area under the curve (AUC) equal to 14.7. The formulation was noncytotoxic in vitro and was rapidly (10 min) and efficiently accumulated by macrophages, but not T/G HA-VSMC or HUVEC. The accumulated quantity of photosensitizer was sufficient for induction of phototoxicity in J774A.1, but not in T/G HA-VSMC. Conclusions: Due to the excellent physical and pharmacokinetic properties and selectivity for macrophages, the novel liposomal formulation of Photolon is a promising therapeutic candidate for use in arteriosclerosis treatment when targeting macrophages but not accompanying vascular tissue is critical for effective and safe therapy.

Słowa kluczowe

liposomes, Photolon, photodynamic therapy, arteriosclerosis, macrophages, pharmacokinetics, vascular smooth muscle cells, vascular endothelial cells