The enhancement of immunosuppressive effects of cyclosporine A on human T-cells using fusogenic liposomes

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Abstract: The aim of this study was to prepare and characterize neutral, positively charged, negatively charged and fusogenic liposomes of different sizes that contain cyclosporine A (CyA) and to evaluate their immunosuppressive activity on human T-cells. Neutral liposomes containing CyA were prepared from dipalmitoylphosphatidylcholine (DPPC) and cholesterol using the solvent evaporation method. To prepare positively charged, negatively charged and fusogenic liposomes containing CyA; stearylamine (SA), dicetylphosphate (DCP) and dioleoylphosphatidylethanolamine (DOPE) were added to the neutral liposome formulation, respectively. To reduce the size of liposomes containing CyA, extrusion through polycarbonate filters (١٠٠٠, ٤٠٠ and ١٠٠ nm) was used. The liposomes were characterized by their size, zeta potential and encapsulation efficiency. The in vitro immunosuppressive effects of an aqueous solution of CyA and different liposomes containing CyA were determined on human T-cells by the MTT [٣-(٤,٥-dimethylthiazol-٢-yl)-٢,٥-diphenyl tetrazolium bromide] assay. The mean diameter of the various multilamellar vesicle (MLV) liposomes containing CyA was between ١,٧٦ and ٢,٤٩ mu m. The encapsulation efficiency for the different MLV and extruded liposomes containing CyA ranged from ٧٣٪ to ٩٠٪. In vitro immunosuppressive evaluation by T-cell culture showed that fusogenic liposomes have the best inhibitory effects on T-cell proliferation compared to the other liposomes. Reducing the size of the liposomes did not so for the aqueous solution of CyA and the affect the in vitro immunosuppressive activity. The average IQ neutral, positively charged, negatively charged and fusogenic liposomes containing CyA was ٤,٩٨ x ١٠(-٢), ٧,٣٨, ١,٤٣, ٣,٨٤ x ١٠(-٣) and ٧,٩٣ x ١٠(-٥) mM, respectively. The results of this study indicate that fusogenic liposomes have the strongest immunosuppressive activity and Could be considered as a suitable delivery system for CyA. (C) ٢٠٠٨ Elsevier B.V. All rights reserved.

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