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Perspective of novel liposomal formulation for immunosuppressants after organ transplantation

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Statement of the Problem: Immune-suppressive agents such as methylprednisolone and cyclosporine exert tremendous side effects, because of high dosage and long-term application required for immune suppression after organ transplantation. Major side effects of methylprednisolone include bleeding of the GI tract, hypertension, and osteoporosis, whereas cyclosporine is nephrotoxic. Liposomes are phospholipid particles that allow delivery of drugs preferentially to the reticuloendothelial system (RES). Liposomes as vehicles for drug delivery can be applied both systematically and topically.

Methodology & Theoretical Background: Liposomes can be prepared from phospholipids, such as lecithin from soybean or egg yolk, other specific or modified lipids or from membrane-spanning tetraether lipid (TEL), which can be extracted and purified from archaeal cell membranes. One advantage in the use of liposomal application is reduced toxicity of many drugs. Here we report on various liposomal preparations of methylprednisolone (L-MPL) and its palmitate derivative (L-MPLP).

Findings: It has been documented that liposomal cyclosporine A (L-CsA), 1.75 mg/kg/day for seven days has a potential for use as an immune-suppressive agent in rats with increased efficacy and decreased nephrotoxicity compared to the commercially available form of intravenous CsA. Liposomal methylprednisolone (L-MPL) 2 mg/kg, intravenously, twice a week has significantly prolonged cardiac allograft survival in rats and shows tissue-selective sequestration of the drug in comparison with the same dosage regimen of methylprednisolone in solution, administered daily. We report on organ distribution of L-MPLP in rats after intraperitoneal (IP) administration.

Conclusion & Significance: Liposomal preparations of immunosuppressants have significantly higher immune-suppressive potential and lower toxicity than common preparations. Bipolar tetraether lipids can be extracted, fractionated and purified from Indonesian volcanoes to form stable liposomes which are extremely resistant, even to gastric fluid. Hence, tetraether lipid liposomes allow (besides IV and IP) for oral administration of immunosuppressants after organ transplantation with similar pharmacological and toxicological advantages as common liposomal phospholipid bilayer preparations.

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