

NON-GLYCEROL BASED LIPOFECTINS FOR GENE DELIVERY

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Agents that safely and efficiently deliver nucleic acids into the cells are critical to successful gene therapy. Cationic and amphiphilic nature of the lipofectin molecules allow stable formation of complexes with DNA and also efficient delivery DNA into cells. To a large extent the cationic lipids that are in vogue are synthesized using glycerol as the backbone. These have led to very useful transfection formulations and are routinely used in transient cell transfections and in few clinical gene therapy protocols. We have synthesized a number of non-glycerol based cationic lipids, more than 50, with variations incorporated in polar and non-polar portions of the molecule. The head group variations included monocationic group with lactic acid, simple sugars and cyclic head groups and also dicationic moieties. A variation in non-polar portion included both ether and ester linkages of acyl groups and also changes in chain lengths from C₁₀ to C₁₈ [1,2]. When tested in several cell lines along with commercial formulations, dihydroxy- containing lipids show excellent transfection properties. Interestingly these formulations prefer cholesterol as colipid instead of unsaturated phosphatidylethanolamine. Biophysical characterization, DNA uptake studies and transfection studies indicated that C₁₄ and C₁₆ containing lipids are preferred. The cell biological basis for observed variations in transfections with various formulations is being pursued presently.

REFERENCES

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