



US005264618A

**United States Patent** [19][11] **Patent Number:** **5,264,618****Felgner et al.**[45] **Date of Patent:** **Nov. 23, 1993**[54] **CATIONIC LIPIDS FOR INTRACELLULAR DELIVERY OF BIOLOGICALLY ACTIVE MOLECULES**[75] **Inventors:** Philip L. Felgner, Rancho Santa Fe; Raj Kumar; Channa Basava, both of San Diego; Richard C. Border, Poway; Jiin-Yu Hwang-Felgner, Rancho Santa Fe, all of Calif.[73] **Assignee:** Vical, Inc., San Diego, Calif.[21] **Appl. No.:** 686,746[22] **Filed:** Apr. 16, 1991**Related U.S. Application Data**

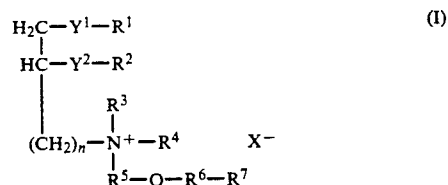
[63] Continuation of Ser. No. 563,444, Aug. 7, 1990, abandoned, which is a continuation of Ser. No. 511,219, Apr. 19, 1990, abandoned.

[51] **Int. Cl.<sup>5</sup>** ..... C07C 69/52[52] **U.S. Cl.** ..... 560/224; 560/155; 560/252; 530/323; 554/227; 554/224; 554/223; 564/292; 574/549; 574/552[58] **Field of Search** ..... 560/224; 554/227, 226, 554/223; 530/323; 574/292, 549, 552[56] **References Cited****U.S. PATENT DOCUMENTS**3,931,397 7/1976 Harnden ..... 424/85  
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(List continued on next page.)

*Primary Examiner*—Paul J. Killos  
*Attorney, Agent, or Firm*—Knobbe, Martens, Olson & Bear[57] **ABSTRACT**

Disclosed are cationic lipids capable of facilitating transport of biologically active agents into cells, including the transfection of cells by therapeutic polynucleotides, the delivery of antiviral drugs, and the introduction of immunogenic peptides. The cationic lipids, comprising an ammonium group, have the general structure



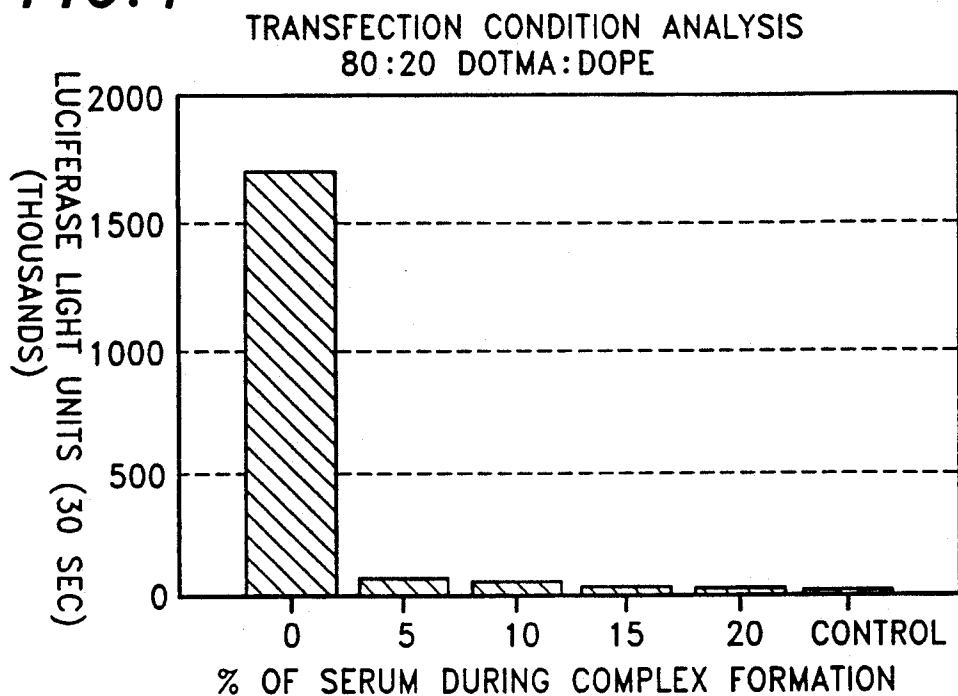
Also disclosed are adducts of these compounds comprising additional cationic sites that enhance the transfective or transport activity. Structure-activity correlations provide for the selection of preferred compounds to be synthesized for this purpose. Compositions disclosed for use of these cationic lipid include formulations for in vitro transfection and pharmaceutical formulations for parenteral and topical administration of therapeutic agents.

**12 Claims, 18 Drawing Sheets**

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**FIG. 1**



**FIG. 2**

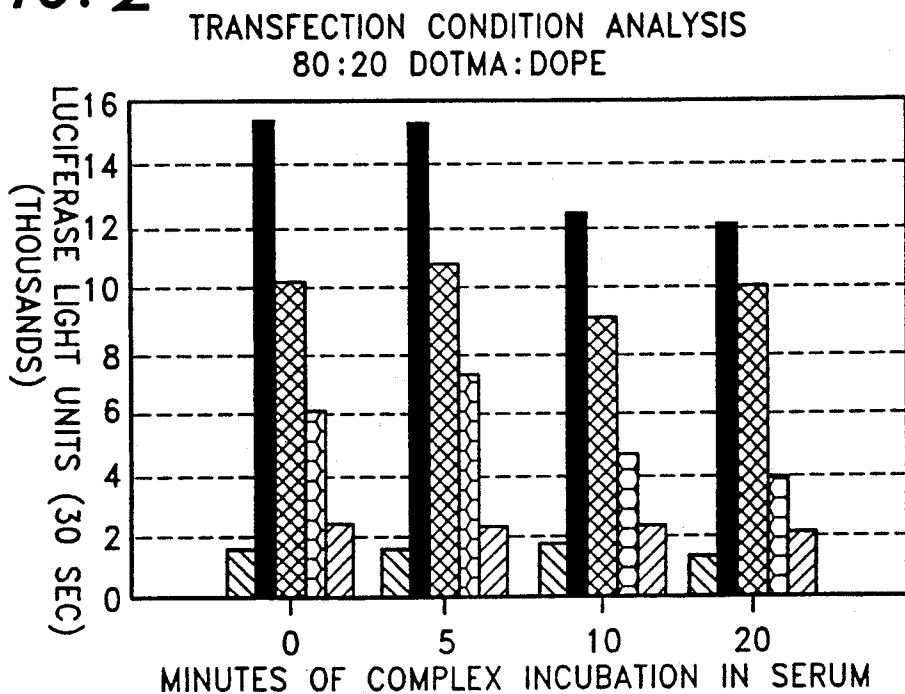
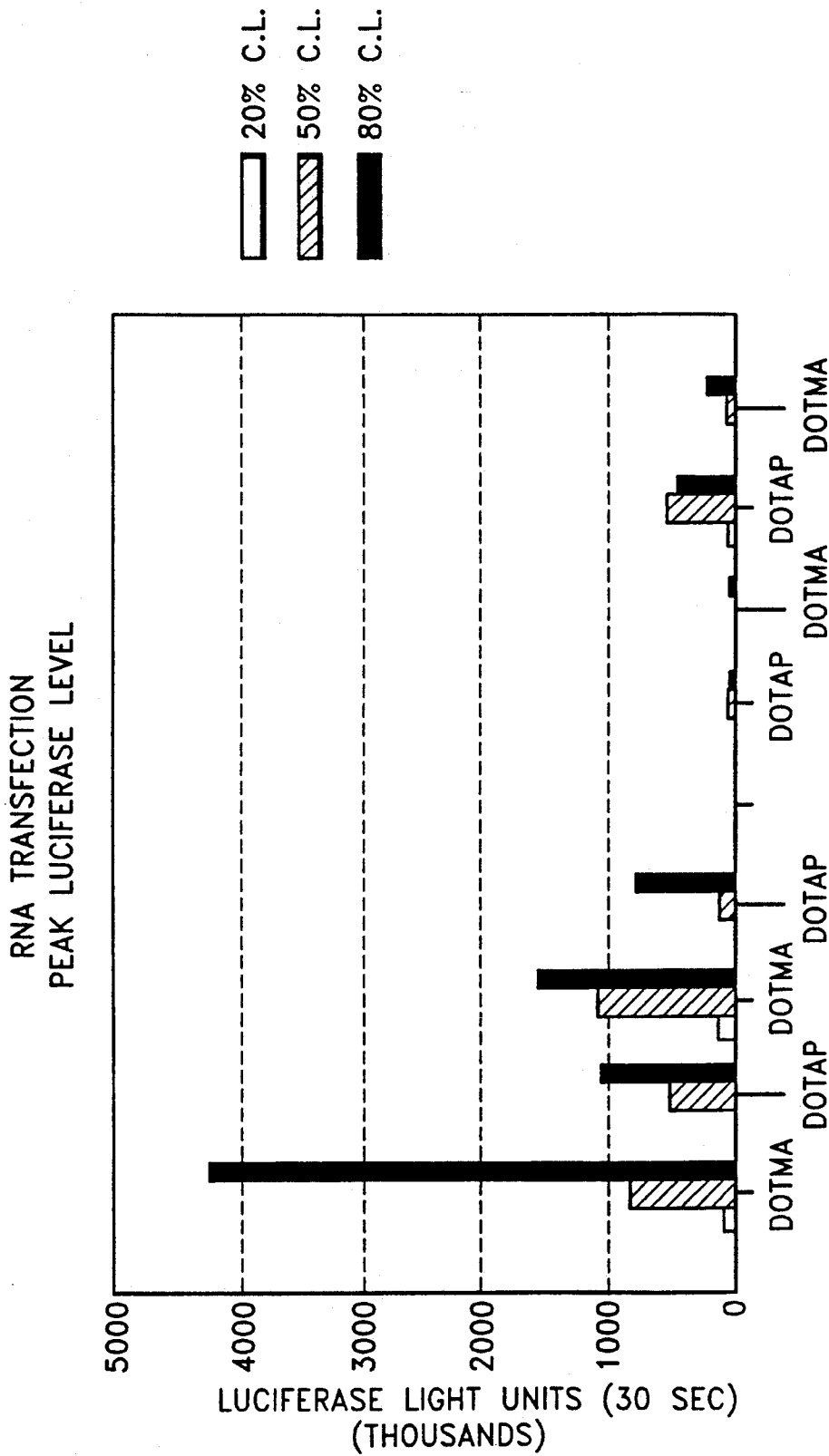
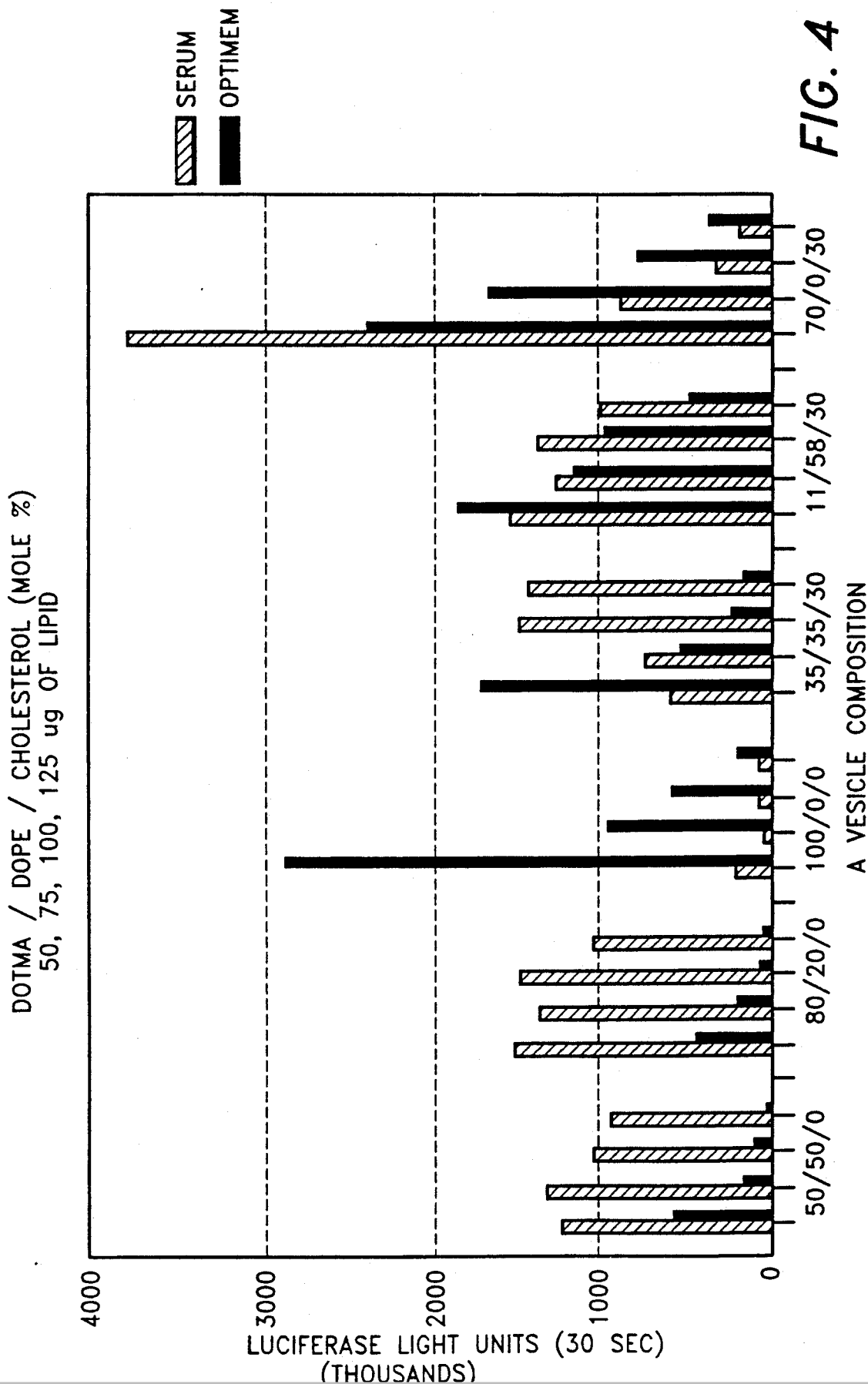


FIG. 3





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