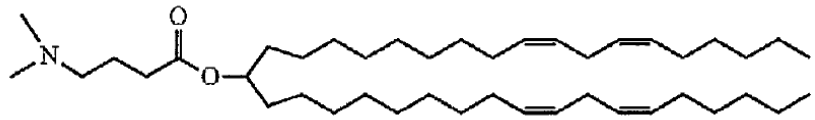
CLAIMS

1. A lipid formulation comprising: (a) a compound having the formula



or a salt thereof; (b) a neutral lipid; (c) a sterol; and (d) a PEG-modified lipid.

2. The lipid formulation of claim 1, comprising: (a) 40-65% of the compound, (b) 5-10% of the neutral lipid, (c) 25-40% of the sterol, and (d) 0.5-10% of the PEG-modified lipid.

3. The lipid formulation of claim 1, wherein the neutral lipid is selected from DSPC, DPPC, DMPC, POPC, DOPE and SM.

4. The lipid formulation of claim 1, wherein the sterol is cholesterol.

5. The lipid formulation of claim 1, wherein the PEG lipid is PEG-C_{14} to PEG-C_{22}, PEG-Cer$_{14}$ to PEG-C_{20}, or PEG-DSPE.

6. The lipid formulation of claim 1, comprising: (a) about 57.5% of the compound, (b) about 7.5% of the neutral lipid, (c) about 31.5% of the sterol, and (d) about 3.5% of the PEG-modified lipid.

7. The lipid formulation of claim 1, further comprising a therapeutic agent, which comprises a nucleic acid.

8. The lipid formulation of claim 7, wherein the nucleic acid is an siRNA.

9. The lipid formulation of claim 8, wherein the molar ratio of lipid : nucleic acid is about 3 to about 15.

10. The lipid formulation of claim 9, wherein the molar ratio of lipid : nucleic acid about 5 to about 13.

11. The lipid formulation of claim 1, comprising: (a) about 50% of the compound, (b) about 10% of the neutral lipid, (c) about 38.5% of the sterol, and (d) about 1.5% of the PEG-modified lipid.

12. The lipid formulation of claim 1, comprising: (a) about 50% of the compound, (b) about 10% of the neutral lipid, (c) about 35% of the sterol, and (d) about 5% of the PEG-modified lipid.

13. The lipid formulation of claim 1, comprising: (a) about 57.2% of the compound, (b) about 7.1% of the neutral lipid, (c) about 34.3% of the sterol, and (d) about 1.4% of the PEG-modified lipid.

14. The lipid formulation of claim 1, comprising: (a) 20-60% of the compound cationic lipid of formula I, (b) 5-25% of the neutral lipid, (c) 25-55% of the sterol, and (d) 0.5-15% of the PEG-modified lipid.

15. The lipid formulation of claim 1, comprising: (a) 20-75% of the compound lipid of formula I, (b) 5-15% of the neutral lipid, (c) 5-50% of the sterol, and (d) 0.5-20% of the PEG-modified lipid.

16. The lipid formulation of claim 1, wherein the neutral lipid is DSPC, the sterol is cholesterol, the PEG-modified lipid is PEG-DMG.

17. The lipid formulation of claim 6, wherein the neutral lipid is DSPC, the sterol is cholesterol, the

PEG-modified lipid is PEG-DMG.

18. The lipid formulation of claim 11, wherein the neutral lipid is DSPC, the sterol is cholesterol, the PEG-modified lipid is PEG-DMG.

19. The lipid formulation of claim 12, wherein the neutral lipid is DSPC, the sterol is cholesterol, the PEG-modified lipid is PEG-DMG.

20. The lipid formulation of claim 13, wherein the neutral lipid is DSPC, the sterol is cholesterol, the PEG-modified lipid is PEG-DMG.

21. The lipid formulation of claim 16, wherein the PEG moiety of the PEG-DMG has an average molecular weight of 2,000 Da.

22. The lipid formulation of claim 17, wherein the PEG moiety of the PEG-DMG has an average molecular weight of 2,000 Da.

23. The lipid formulation of claim 18, wherein the PEG moiety of the PEG-DMG has an average molecular weight of 2,000 Da.

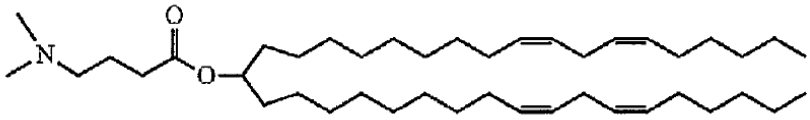
24. The lipid formulation of claim 19, wherein the PEG moiety of the PEG-DMG has an average molecular weight of 2,000 Da.

25. The lipid formulation of claim 20, wherein the PEG moiety of the PEG-DMG has an average molecular weight of 2,000 Da.

26. The lipid formulation of claim 7, wherein the formulation is prepared by a method comprising (i) extruding a liposome formed from components (a)-(d), and (ii) addition of a nucleic acid therapeutic agent to the liposome.

27. The lipid formulation of claim 7, wherein the formulation is prepared by a method comprising mixing components (a)-(d) and a nucleic acid therapeutic agent in parallel into a mixing chamber.

28. A nucleic acid-lipid particle comprising: (a) a lipid particle comprising: (i) a compound having the



formula

or a salt thereof, (ii) a neutral lipid, (iii) a sterol, (iv) a PEG-modified lipid; and (b) a therapeutic siRNA encapsulated in the lipid particle.

29. The nucleic acid-lipid particle of claim 28, wherein the nucleic acid-lipid particle has a size ranging from about 70 to about 200 nm.

30. The nucleic acid-lipid particle of claim 29, wherein the nucleic acid-lipid particle has a size ranging from about 90 to about 130 nm.