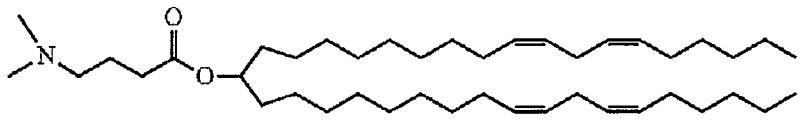
CLAIMS

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. A method of delivering an siRNA therapeutic agent to a cell comprising administering to a subject the lipid formulation of claim **8**.

15. The method of claim **14**, wherein the siRNA therapeutic agent is a dsRNA.

16. A method of modulating the expression of a target gene in a cell, the method comprising providing to a cell the lipid formulation of claim **8**.

17. 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.

18. 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.

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

20. The lipid formulation of claim **6**, wherein the neutral lipid is DSPC, the sterol is cholesterol, the PEG-modified lipid is PEG-DMG.

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

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

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

24. The method of claim **14**, wherein the neutral lipid is DSPC, the sterol is cholesterol, the PEG-modified lipid is PEG-DMG.

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

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

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

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

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

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

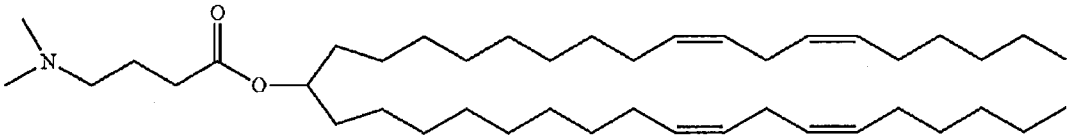
31. The lipid formulation of claim **7**, wherein the formulation is prepared by a method comprising (i) extruding a liposome formed from components (a)-(d), and (ii) addition of a nucleic acid therapeutic agent to the liposome.

32. 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.

33. 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.

34. The nucleic acid-lipid particle of claim **33**, wherein the nucleic acid-lipid particle has a size ranging from about 70 to about 200 nm.

35. The nucleic acid-lipid particle of claim **34**, wherein the nucleic acid-lipid particle has a size ranging from about 90 to about 130 nm.