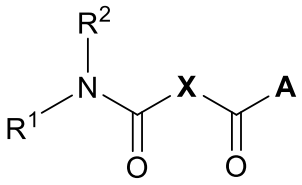
CLAIMS

1. A compound comprising a structure represented by general formula (1) or ionized forms thereof for preparing lipid nanoparticles encapsulating a cationic therapeutic and/or cationic prophylactic agent:



(1)

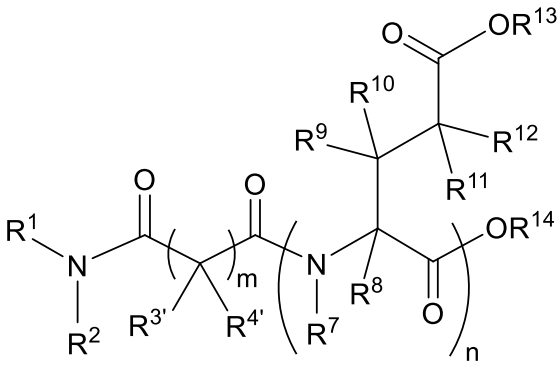
wherein

R^1 and R^2 are each independently a hydrophobic group;

X comprises an optionally substituted linear aliphatic, optionally substituted branched aliphatic and/or optionally substituted cyclic hydrocarbons; and

A comprises a peptide sequence of 1-5 anionic amino acids.

2. The compound of claim 1, wherein the structure is represented by general formula (1A):



(1A)

and wherein

$R^{3'}$, $R^{4'}$, R^7 to R^{14} are each independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, and combinations thereof;
m is 1, 2, 3, 4 or 5; and
n is 1, 2, 3, 4 or 5.

3. The compound of any one of the preceding claims, wherein the hydrophobic group at R^1 and R^2 each independently comprises optionally substituted alkyl.

4. The compound of any one of the preceding claims, wherein the compound is an ionized form of general formula (1).

5. The compound of any one of claims 2 to 4, wherein the compound is an ionized form of general formula (1A), where $–C(=O)OR^{13}$ and/or $–C(=O)OR^{14}$ has been ionized to become a negatively charged group.

6. The compound of any one of the preceding claims, wherein the cationic therapeutic and/or cationic prophylactic agent comprises an antimicrobial agent, optionally wherein the cationic therapeutic and/or cationic prophylactic agent comprises polymyxin.

7. A method of preparing a compound represented by general formula (1) according to any one of the preceding claims, the method comprising:

(a-i) reacting a resin with a fully protected (i.e., N- and C-protected) amino acid to attach the fully protected amino acid to the resin;

(a-ii) removing N-protecting group from the fully protected amino acid to obtain a partially protected (i.e., C-protected) amino acid;

(a-iii) reacting the partially protected (i.e., C-protected) amino acid with another fully protected amino acid to attach the fully protected

amino acid to the partially protected amino acid *via* the N-terminus to obtain a resin-supported fully protected peptide represented by general formula (2):



(2)

wherein

● represents resin; and
A^{FP} represents fully protected peptide (e.g., oligopeptide);

(a-iv) removing N-protecting group from the resin-supported fully protected peptide represented by general formula (2) to obtain a resin-supported partially protected (i.e. C-protected) peptide represented by general formula (3):

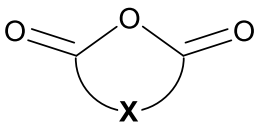


(3)

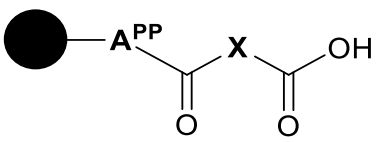
wherein

● represents resin; and
A^{PP} represents partially protected peptide (e.g., oligopeptide);

(a-v) reacting the resin-supported partially protected (i.e., C-protected) peptide represented by general formula (3) with an acid anhydride represented by general formula (4) to obtain a first intermediate compound represented by general formula (5);

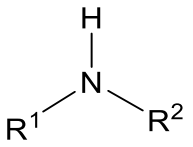


(4)

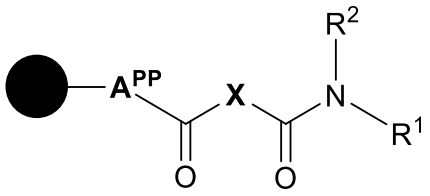


(5)

(a-vi) reacting the first intermediate compound represented by general formula (5) with an amine compound represented by general formula (6) to obtain a second intermediate represented by general formula (7); and

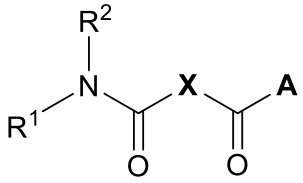


(6)



(7)

(a-vii) removing the resin from the second intermediate represented by general formula (7) to obtain a compound represented by general formula (1); and



(1)

(a-viii) optionally ionizing **A** to become a negatively charged group.

8. The method according to claim 7, wherein the method further comprises repeating step (a-ii) and/or step (a-iii) until an oligopeptide of a desired length is obtained.

9. A nanoparticle composition for delivery of a cationic therapeutic and/or cationic prophylactic agent, the nanoparticle composition comprising:

a compound as claimed in any one of claims 1 to 6; and

a cationic therapeutic and/or cationic prophylactic agent that is encapsulated in said compound as claimed in any one of claims 1 to 6,

optionally wherein the charge ratio of the cationic therapeutic and/or cationic prophylactic agent that is encapsulated in the compound as claimed in any one of claims 1 to 6 to said compound is from 1:1 to 10:1.

10. The nanoparticle composition of claim 9, wherein the composition further comprises:

(a) helper lipid;

(b) sterol; and

(c) polyethylene glycol (PEG)-modified lipid,

optionally wherein the cationic therapeutic and/or cationic prophylactic agent, helper lipid, sterol, compound represented by general formula (1), and PEG-modified lipid are mixed at a molar ratio of 10 – 120 : 3 – 30 : 10 – 130 : 2 – 30 : 0.5 – 10;

optionally wherein the helper lipid is selected from the group consisting of 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), 1,2-dilinoleoyl-sn-glycero-3-phosphocholine (DLPC), 1,2-dimyristoyl-sn-glycero-phosphocholine (DMPC), 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC), 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), 1,2-diundecanoyl-sn-glycero-phosphocholine (DUPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), 1,2-di-O-octadecenyl-sn-glycero-3-phosphocholine (18:0 Diether PC), 1-oleoyl-2-cholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (OChemsPC), 1-hexadecyl-sn-glycero-3-phosphocholine (C16 Lyso PC), 1,2-dilinolenoyl-sn-glycero-3-phosphocholine, 1,2-diarachidonoyl-sn-glycero-3-phosphocholine, 1,2-didocosahexaenoyl-sn-glycero-3-phosphocholine, 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (ME 16.0 PE), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinoleoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinolenoyl-sn-glycero-3-phosphoethanolamine, 1,2-diarachidonoyl-sn-glycero-3-phosphoethanolamine, 1,2-didocosahexaenoyl-sn-glycero-3-phosphoethanolamine, 1,2-dioleoyl-sn-glycero-3-phospho-rac-(1-glycerol) sodium salt (DOPG), sphingomyelin and combinations thereof;

optionally wherein the sterol is selected from cholesterol, fecosterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, avenasterol and combinations thereof; and

optionally wherein the PEG-modified lipid is selected from PEG-modified phosphatidylethanolamines, PEG-modified phosphatidic acids, PEG-modified ceramides, PEG-modified dialkylamines, PEG-modified diacylglycerols, PEG-modified dialkylglycerols, 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159), R-3-[(ω-methoxy-poly(ethylene glycol)2000)carbamoyl]-1,2-dimyristyloxlpropyl-3-amine (PEG-c-DOMG), 3-N-[(ω-methoxypoly (ethyleneglycol)2000)carbamoyl]-1,2-dimyristyloxy-propylamine (PEG-S-DMG), PEG-DMPE (1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine-N-[(polyethylene glycol)-methoxy] (sodium salt)), PEG-DPPC, PEG-DSPE lipid and combinations thereof.

11. The nanoparticle composition of any one of claims 9 to 10, wherein the nanoparticle composition comprises nanoparticles having an average particle size of from 20 nm to 200 nm;

and/or the nanoparticle composition comprises nanoparticles having a zeta potential of from -20 mV to +20 mV;

and/or the nanoparticle composition comprises nanoparticles having a minimum bactericidal concentration (MBC) to minimum inhibitory concentration (MIC) ratio that is no more than 6.

12. The nanoparticle composition as claimed in any one of claims 9 to 11 for use in medicine.

13. The nanoparticle composition as claimed in any one of claims 9 to 11 for use in the treatment or prophylaxis of a disease, disorder or condition in a subject in need thereof, wherein the disease, disorder or condition is mediated by Gram-negative bacteria.

14. Use of a nanoparticle composition as claimed in any one of claims 9 to 11 in the manufacture of a medicament for treatment or prophylaxis of a

disease, disorder or condition in a subject in need thereof, wherein the disease, disorder or condition is mediated by Gram-negative bacteria.

15. The nanoparticle composition of claim 13, or the use of claim 14, wherein the Gram-negative bacteria is selected from the group consisting of *escherichia coli*, *pseudomonas aeruginosa*, and combinations thereof.