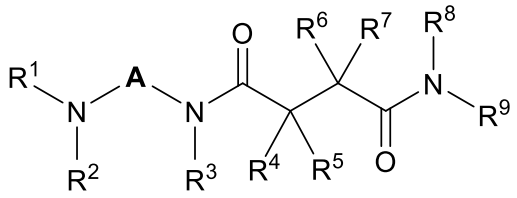
CLAIMS

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



(1)

wherein

NR^1R^2 is a group that is ionizable at a pH range of from 3 to physiological pH;

A comprises a linear aliphatic, branched aliphatic and/or cyclic hydrocarbons optionally comprising one or more groups selected from –OH, –NR–, –O–, $–O–C_xH_{2x}–O–$, where $x \geq 1$; and where R is H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^3, R^4, R^5, R^6 and R^7 are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl; and

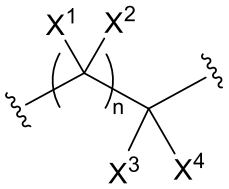
R^8 and R^9 are each independently hydrophobic group.

2. The compound of claim 1, wherein R^1 and R^2 are each independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, and combinations thereof.

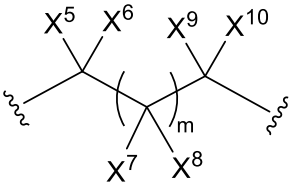
3. The compound of any one of the preceding claims, wherein R^1 and R^2 are both H and $–NR^1R^2$ is a primary amine group.

4. The compound of any one of the preceding claims, wherein the hydrophobic group at R^8 and R^9 each independently comprises optionally substituted alkyl.

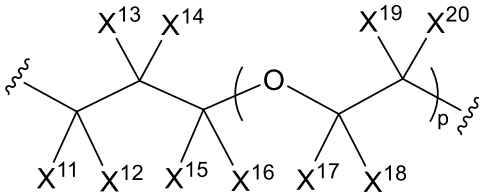
5. The compound of any one of the preceding claims, wherein **A** is selected from the following general formula (2), (3), (4) and/or (5):



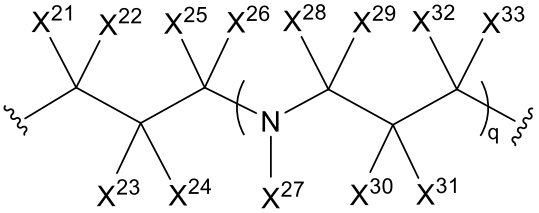
(2)



(3)



(4)



(5)

wherein

X^1 to X^{31} are each independently selected from –H, –OH, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

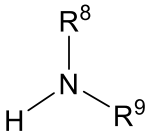
$n \geq 1$; $m \geq 1$; $p \geq 1$; and $q \geq 1$.

6. The compound of any one of the preceding claims, wherein the compound is selected from the group consisting of DnO-EDEA, DD-EDEA, DTD-EDEA, HO-DnO-NH_2, HO-DD-NH_2, HO-DTD-NH_2, DnO-NH_2, DD-NH_2, DTD-NH_2, DMAPAPA-DTD and combinations thereof.

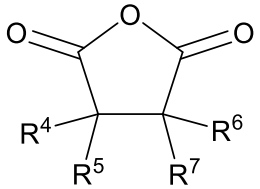
7. The compound of any one of the preceding claims, wherein the compound is an ionized form of general formula (1), where $–NR^1R^2$ has been ionized to become a positively charged group.

8. A method of preparing a compound as claimed in any one of the preceding claims, the method comprising:

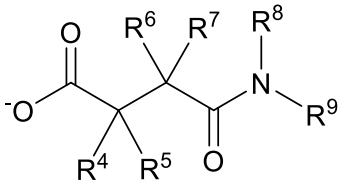
(a-i) reacting an amine compound represented by general formula (6) with a cyclic anhydride represented by general formula (7) to obtain a first intermediate compound comprising carboxylate group represented by general formula (8):



(6)



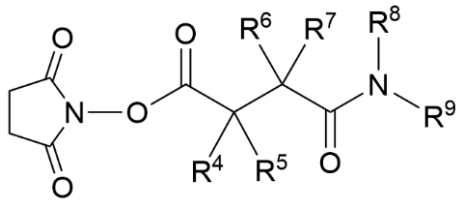
(7)



(8)

(a-ii) reacting the first intermediate compound represented by general formula (8) with a N-hydroxysuccinimide (NHS) in the presence of

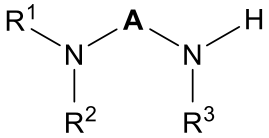
a coupling agent to obtain a second intermediate compound comprising amide group represented by general formula (9):



(9)

optionally wherein the coupling agent comprises carbodiimide selected from the group consisting of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC), N,N'-dicyclohexylcarbodiimide (DCC), N,N'-Diisopropylcarbodiimide (DIC), and combinations thereof;

(a-iii) reacting the second intermediate compound represented by general formula (9) with an amine compound represented by general formula (10) to obtain a compound represented by general formula (1):



(10)

wherein

A comprises a linear aliphatic, branched aliphatic and/or cyclic hydrocarbons optionally comprising one or more groups selected from –OH, –NR–, –O–, –O–C_xH_{2x}–O–, where x ≥ 1; and where R is H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^1, R^2, R^3, R^4, R^5, R^6 and R^7 are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl; and

R^8 and R^9 are each independently hydrophobic group; and

(a-iv) optionally ionizing $–NR^1R^2$ to become a positively charged group.

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

a compound as claimed in any one of claims 1 to 7; and

a therapeutic, prophylactic and/or biological agent that is encapsulated in said compound as claimed in any one of the preceding claims 1 to 7.

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

(a) helper lipid;

(b) sterol; and

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

11. The nanoparticle composition of claim 10, wherein the compound represented by general formula (1), helper lipid, sterol, and PEG-modified lipid are mixed at a weight ratio of 10 – 50 : 2 – 20 : 4 – 30 : 1 – 15;

and/or the helper lipid is present in an amount of from 1 mol% to 20 mol%, the sterol is present in an amount of from 10 mol% to 50 mol%, and PEG-modified lipid is present in an amount of from 0.5 mol% to 10 mol%;

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, PEG-modified/PEGylated lipid, 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.

12. The nanoparticle composition of any one of claims 9 to 11, wherein the nanoparticle composition comprises nanoparticles having a N/P ratio from 2:1 to 40:1;

and/or 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 -15 mV to +20 mV in phosphate-buffered saline (PBS).

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

14. The nanoparticle composition as claimed in any one of claims 9 to 12 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 a coronavirus, and

optionally wherein the coronavirus is a SARS-CoV-2 coronavirus.

15. Use of a nanoparticle composition as claimed in any one of claims 9 to 12 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 a coronavirus, and

optionally wherein the coronavirus is a SARS-CoV-2 coronavirus.