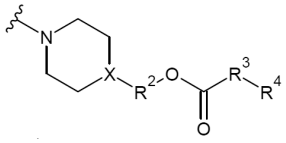
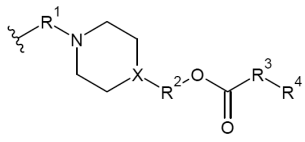
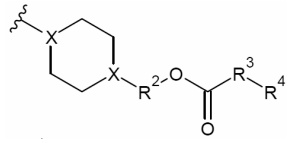
SUMMARY ~~OF THE INVENTION~~

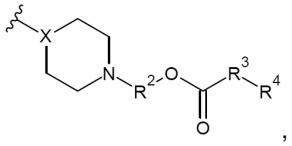
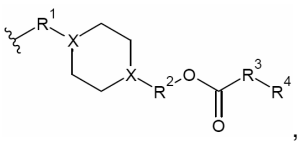
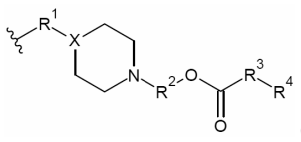
~~In one aspect, the~~The present ~~invention~~ disclosure describes ~~relates to~~ novel cationic lipids which are useful for the delivery of nucleic acids into living cells. The cationic lipids are compounds according to formula (I):

R^a–A–R^b formula (I)

wherein

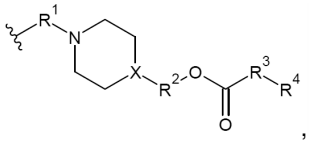
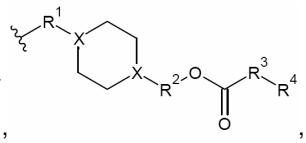
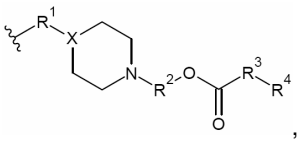
R^a is selected from:

 ,  ,  ,

 ,  ,  or

–R^1–N(H)–C(O)–R^3–R^4;

R^b is selected from:

 ,  ,  ,

–R^1–N(H)–C(O)–R^3–R^4, or

–R^1–N(CH_3)$_2$;

A is –S–, –S–S–, –S–C(O)– –NH–C(O)–, –NH–C(O)O–, –NH–C(O)–NH–, –S–C(O)–N(H)–, –C(O)O–, or –O–P(O)(OH)–O–;

R^1 is an optionally substituted ethanediyl, propanediyl, butanediyl, or linear or unbranched alkanediyl having 2 to 8 carbon atoms;

R^2 is an alkanediyl having 2 to 8 carbon atoms;

R^3 is optional, and if present, is –R^5–C(O)–O–, or –R^5–O–C(O)–, –R^5–C(O)–NH–, –R^5–OC(O)–NH–, or R^5–NH–C(O)O–;

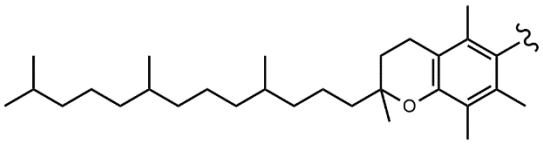
R^4 is a lipophilic substituent with 12 to 36 carbon atoms;

R^5 is an alkanediyl having 1 to 6 carbon atoms;

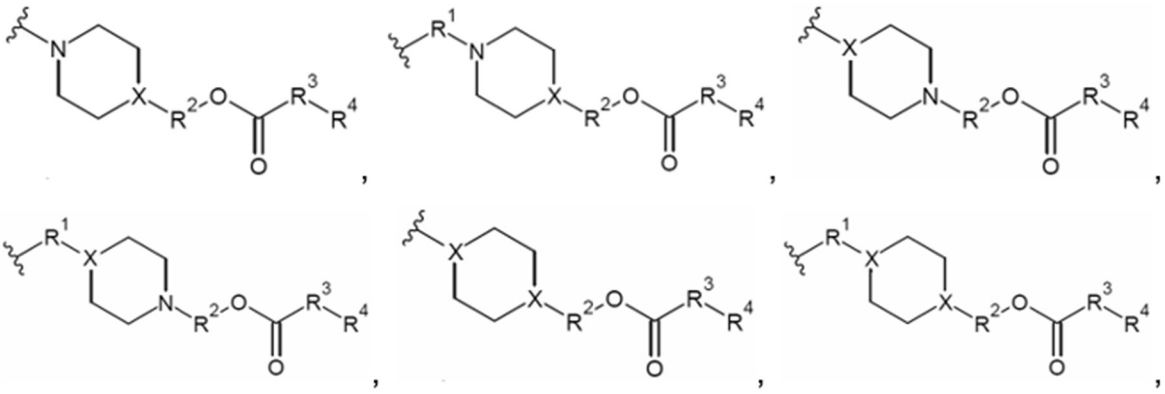
X is a carbon or nitrogen atom;

wherein all selections are independent of one another,

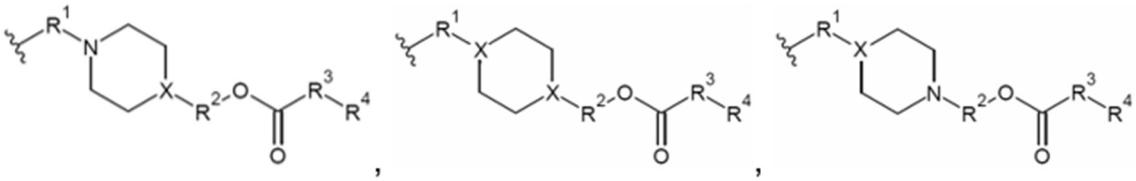
optionally provided that if R^1, R^2 and R^5 are all ethanediyl, A is –S–S–, and R^a and R^b are identical, then R^4 is not

 .

In one aspect, the present disclosure refers to a cationic lipid according to formula (I), $R^a–A–R^b$, or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof, wherein R^a is selected from:



Or $–R^1–N(H)–C(O)–R^3–R^4$; R^b is selected from:



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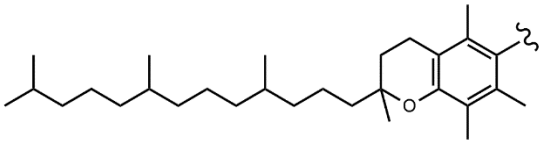
$–R^1–N(H)–C(O)–R^3–R^4$, or $–R^1–N(CH_3)_2$; A is –S–, –S–S–, –NH–C(O)–, –NH–C(O)O–, –NH–C(O)–NH–, –S–C(O)–N(H)–, –C(O)O–, or –O–P(O)(OH)–O–; R^1 is an ethanediyl, propanediyl, butanediyl, or linear or unbranched alkanediyl having 2 to 8 carbon atoms, wherein each substitutable carbon atom is unsubstituted or substituted with one or more C_1-C_4 alkyl, C_1-C_4 alkenylene, C_3-C_8 cycloalkylene, or C_3-C_8 cycloalkenylene; R^2 is an alkanediyl having 2 to 8 carbon atoms; R^3 is optional, and if present, is $–R^5–C(O)–O–$, $–R^5–O–C(O)–$, $–R^5–C(O)–NH–$, $–R^5–OC(O)–NH–$, or $R^5–NH–C(O)O–$; R^4 is a lipophilic substituent with 12 to 36 carbon atoms, wherein the lipophilic substituent with 12 to 36 carbon atoms is either (i) a linear or branched alkyl or alkenyl having 12 to 25 carbon atoms or (ii) derived from tocopherol or tocotreinol; R^5 is an alkanediyl having 1 to 6 carbon atoms; X is a carbon atom bonded to a hydrogen atom (CH) or a nitrogen atom; wherein all selections are independent of one another.

In this regard, an alkanediyl is a term for a ($–C_nH_{2n}–$) group; f.e. an “alkanediyl having 2 to 8 carbon atoms” accordingly equals an alkanediyl group having the formula $–C_2H_4–$, $–C_3H_6–$, $–C_4H_8–$, $–C_5H_{10}–$, $–C_6H_{12}–$, $–C_7H_{14}–$, or respectively $–C_8H_{16}–$. In other words, an alkanediyl is a series of divalent radicals of the general formula C_nH_{2n} derived from aliphatic hydrocarbons. Unless specified otherwise, such alkanediyls include substituted alkanediyls.

In another ~~embodiment~~example, in case R^1, R^2 and R^5 are all ethanediyl, A is –S–S–, and R^a and R^b are identical, then R^4 is not



, or respectively in one ~~embodiment~~example, a lipid according to formula (I) is not lipid C23 as disclosed in **Table 1** herein or respectively lipid SS-EC as described herein below (for the avoidance of doubt i.e. in some selected ~~embodiments~~examples, cationic lipid COATSOME® SS-EC is disclaimed from ~~embodiments~~ examples which are related to cationic lipids according to formula (I)).

In another ~~aspect~~example, the ~~invention provides~~disclosure describes novel compositions incorporating cationic lipids such as the novel cationic lipids defined above. In one aspect, the present disclosure refers to a composition comprising (i) the cationic lipid as disclosed herein; (ii) the cationic lipid C15 as listed in **Table 1**; (iii) the cationic lipid C2 as listed in **Table 1**; or (iv) the cationic lipid C26 as listed in **Table 1;** preferably further comprising one or more of the following excipients: (i) a steroid, preferably cholesterol; (ii) a neutral lipid; wherein said neutral lipid preferably is 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (DPhyPE), optionally in combination with the neutral lipid 1,2-diheptanoyl-sn-glycero-3-phosphocholine (DHPC); or wherein said neutral lipid is a zwitterionic compound, optionally a zwitterionic compound having two fatty acid moieties selected from myristoyl, palmitoyl, stearoyl and oleyol, in combination with a zwitterionic compound having two fatty acid moieties selected from pentanoyl, hexanoyl, heptanoyl, octanoyl, nonaoyl and decanoyl; and/or (iii) a polymer conjugated lipid; wherein said polymer conjugated lipid is a compound according to formula (II): P-A-L; wherein P is a hydrophilic polymer moiety, A is an optional linker, and L is a lipid moiety; preferably wherein the polymer conjugated lipid is a pegylated lipid. In another aspect, the present disclosure describes a composition comprising one or more of the following excipients: (i) a cationic lipid as disclosed herein or a cationic lipid comprising a tertiary or quaternary nitrogen / amino group or a cationic lipid carrying a net positive charge at physiological pH; (ii) a steroid, preferably cholesterol; (iii) a neutral lipid as described in subitem (ii) as disclosed herein; and/or (iv) a polymer conjugated lipid, wherein said polymer conjugated lipid is a compound according to formula (II): P-A-L; wherein P is a hydrophilic polymer moiety, A is an optional linker, and L is a lipid moiety; preferably wherein the polymer conjugated lipid is a pegylated lipid; more preferably, wherein the lipid moiety L comprises at least one fatty acid ("tail") comprising 8, 10 or 12 carbon atoms, preferably 8 or 10 carbon atoms; even more preferably, wherein the pegylated lipid is selected from the group consisting of 1,2-dicapryl-rac-glycero-3-methylpolyoxyethylene glycol 2000 (C_{10}-PEG 2000); and N-octanoyl-sphingosine-1-{succinyl[methoxy(polyethylene glycol)2000]} (Cer8-PEG 2000). In a further aspect, the present disclosure refers to a composition comprising one or more of the following excipients: (i) a cationic lipid as described in subitem (i) as disclosed herein; (ii) a steroid, preferably cholesterol; (iii) a neutral lipid as described in subitem (ii) as disclosed herein, or preferably a combination of two neutral lipids wherein the combination comprises a neutral lipid or phospholipid having at least two alkyl chains, whereby each alkyl chain independently has a length of preferably C_6, C_7, C_8, C_9, or C_{10}, more preferably with a length of C_6, C_7, C_8, most preferably with a length of C_7, further most preferably a phospholipid selected from the group consisting of DHPC (1,2-diheptanoyl-sn-glycero-3-phosphocholine), 05:0 PC (1,2-dipentanoyl-sn-glycero-3-phosphocholine), 04:0 PC (1,2-dibutyryl-sn-glycero-3-phosphocholine), 06:0 PC (DHPC, 1,2-dihexanoyl-sn-glycero-3-phosphocholine), 08:0 PC (1,2-dioctanoyl-sn-glycero-3-phosphocholine), and 09:0 PC (1,2-dinonanoyl-sn-glycero-3-phosphocholine); and/or (iv) a polymer conjugated lipid, wherein said polymer conjugated lipid is a compound according to formula (II): P-A-L; wherein P is a hydrophilic polymer moiety, A is an optional linker, and L is a lipid moiety; preferably wherein the polymer conjugated lipid is a pegylated lipid; more preferably wherein the pegylated lipid is 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol 2000 (DMG-PEG 2000). In another aspect, the present disclosure refers to a use of

the composition as disclosed herein in the manufacture of a medicament (i) in the treatment or prophylaxis of infectious diseases; cancer or tumour diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease; disorder or condition; and/or (ii) for enzyme replacement therapy in treating metabolic or endocrine disorders; the composition preferably comprising at least one coding RNA, wherein said at least one coding RNA comprises at least one coding sequence encoding at least one peptide or protein for use in treatment or prevention of a disease, disorder or condition, wherein said composition is to be administered via intramuscular or intradermal injection a subject in need thereof.

The cationic lipids and the compositions have been found to be particularly effective in introducing nucleic acids into living cells. For example, they enable improved RNA (e.g. mRNA) vaccines i.e. mRNA-based vaccines against certain infectious diseases or tumours.

In further ~~aspects~~examples, the ~~invention provides~~disclosure describes the use of the compositions incorporating a cationic lipid and a nucleic acid compound as medicines, and in particular as vaccines, as well as vaccination methods based on these vaccines. In one aspect, the present disclosure refers to use of the composition as described herein in the manufacture of a medicament (i) in the treatment or prophylaxis of infectious diseases; cancer or tumour diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease; disorder or condition; and/or (ii) for enzyme replacement therapy in treating metabolic or endocrine disorders; the composition preferably comprising at least one coding RNA, wherein said at least one coding RNA comprises at least one coding sequence encoding at least one peptide or protein for use in treatment or prevention of a disease, disorder or condition, wherein said composition is to be administered via intramuscular or intradermal injection a subject in need thereof.

In another aspect of the present ~~invention~~disclosure, the present ~~invention~~ disclosure also describes~~provides~~ a kit, in particular a kit of parts, comprising the mRNA compound comprising mRNA sequence as defined herein and at least one lipid according to formula (I) or formula (II) as defined herein. In yet another aspect, the present disclosure refers to a kit or kit of parts, comprising any one of the compositions as disclosed herein, optionally comprising a liquid vehicle for solubilizing, and, optionally, technical instructions providing information on administration and dosage of the components. In a further aspect, the present disclosure describes a use of the composition or a kit or kit of parts as described herein in the manufacture of a vaccine for prevention, prophylaxis, treatment and/or amelioration of a disease selected from infectious diseases including viral, bacterial or protozoological infectious diseases, cancer or tumour diseases. In another aspect, the present disclosure refers to a pharmaceutical composition comprising a composition or a kit or kit of parts as described herein for use as a medicament in vaccination of a subject comprising an effective dose of mRNA encoding a virus antigen.

DEFINITIONS

For the sake of clarity and readability, the following scientific background information and definitions are provided. Any technical features mentioned herein or disclosed thereby can be part of or may be read on each and every embodiment of the invention. Additional definitions and explanations can be provided in the context of this disclosure.

Unless defined otherwise, or unless the specific context requires otherwise, all technical terms used herein have the same meaning as is commonly understood by a person skilled in the relevant technical field.

Unless the context indicates or requires otherwise, the words “comprise”, “comprises” and “comprising” and similar expressions are to be construed in an open and inclusive sense, as “including, but not limited to” in this description and in the claims.

5 The expressions, “one embodiment”, “an embodiment”, “a specific embodiment” and the like mean that a particular feature, property or characteristic, or a particular group or combination of features, properties or characteristics, as referred to in combination with the respective expression, is present in at least one of the embodiments of the invention. The occurrence of these expressions in various places throughout this description do not necessarily

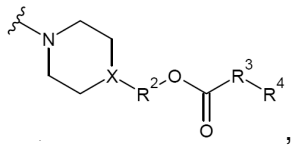
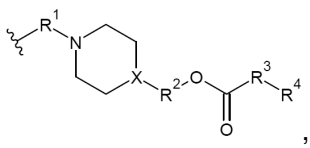
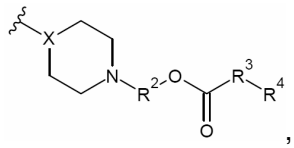
CLAIMS

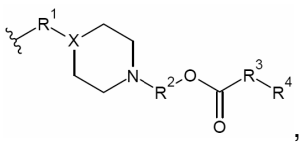
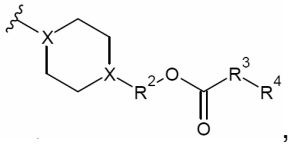
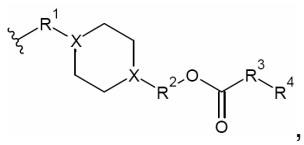
1. A cationic lipid according to formula (I):

R^a–A–R^b formula (I)

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof, wherein

R^a is selected from:

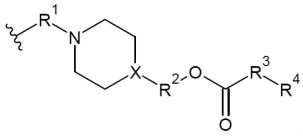
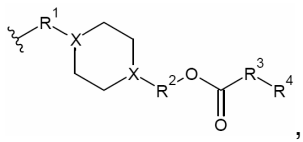
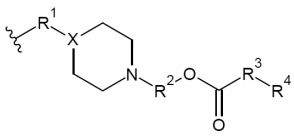
 ,  ,  ,

 ,  ,  ,

or

–R^1–N(H)–C(O)–R^3–R^4;

R^b is selected from:

 ,  , 

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–R^1–N(H)–C(O)–R^3–R^4, or

–R^1–N(CH_3)$_2$;

A is –S–, –S–S–, –NH–C(O)–, –NH–C(O)O–, –NH–C(O)–NH–, –S–C(O)–N(H)–, –C(O)O–, or –O–P(O)(OH)–O–;

R^1 is an ethanediyl, propanediyl, butanediyl, or linear or unbranched alkanediyl having 2 to 8 carbon atoms, wherein each substitutable carbon atom is unsubstituted or substituted with one or more C_1-C_4 alkyl, C_1-C_4 alkenylene, C_3-C_8 cycloalkylene, or C_3-C_8 cycloalkenylene;

R^2 is an alkanediyl having 2 to 8 carbon atoms;

R^3 is optional, and if present, is –R^5–C(O)–O–, –R^5–O–C(O)–, –R^5–C(O)–NH–, –R^5–OC(O)–NH–, or R^5–NH–C(O)O–;

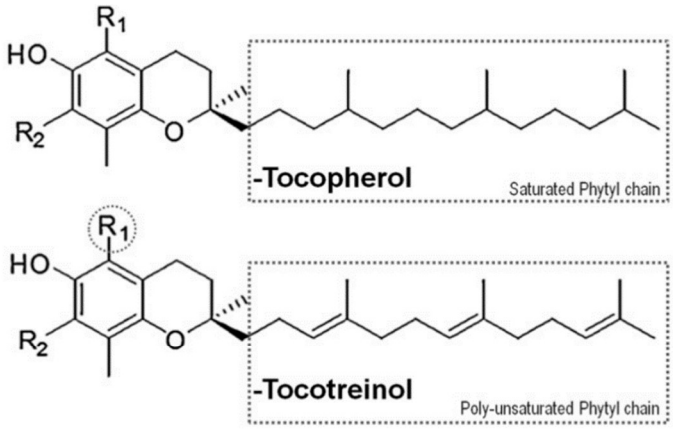
R^4 is a lipophilic substituent with 12 to 36 carbon atoms, wherein the lipophilic substituent with 12 to 36 carbon atoms is either (i) a linear or branched alkyl or alkenyl having 12 to 25 carbon atoms or (ii) derived from tocopherol or tocotreinol;

R^5 is an alkanediyl having 1 to 6 carbon atoms;

X is a carbon atom bonded to a hydrogen atom (CH) or a nitrogen atom;

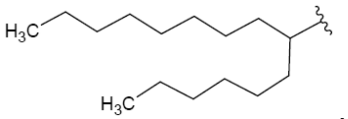
wherein all selections are independent of one another.

2. The cationic lipid according to **claim 1**, wherein R^4 is either (i) a linear or branched alkyl or alkenyl having 12 to 25 carbon atoms or (ii) selected from the group of derivatives of tocopherol and tocotreinol shown in **Scheme 1:**



Isoform	R_1	R_2
Alpha (α)	CH3	CH3
Beta (β)	CH3	H
Gamma (γ)	H	CH3
Delta (δ)	H	H

3. The cationic lipid according to **claim 1 or claim 2**, wherein R^4 is independently selected at each occurrence from the group consisting of



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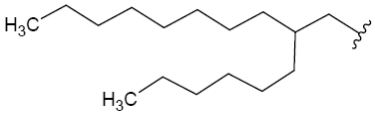

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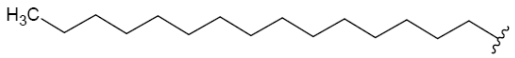

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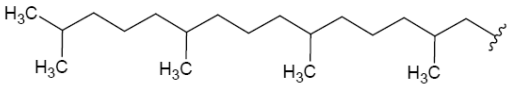

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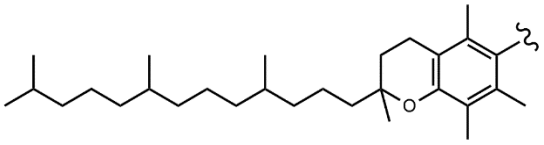

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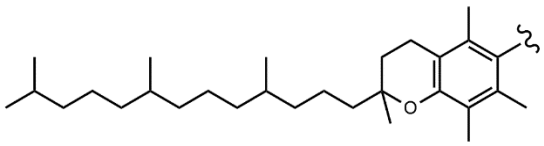
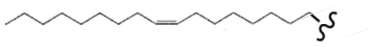
4. The cationic lipid according to any one of **claims 1 to 3**, with the proviso that if (i) R^3 is present as $–R^5–C(O)–O–$, (ii) R^1 and R^2 are linear unsubstituted ethanediyl, (iii) R^5 is either linear unsubstituted ethanediyl, linear unsubstituted propanediyl or linear unsubstituted butanediyl, (iv) A is –S–S–, and (v) R^a and R^b are identical, then R^4 is not



and with the further proviso that if (i) R^3 is absent, (ii) R^1 and R^2 are linear unsubstituted ethanediyl, (iii) A is –S–S–, and (iv) R^a and R^b are identical, then R^4 is not  and not 

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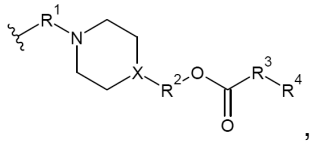
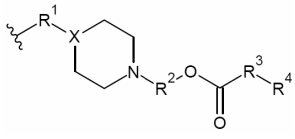
5. The cationic lipid according to any one of **claims 1 to 3**, wherein A is –S–.

6. The cationic lipid according to **claim 1 or claim 2**, wherein R^3 is present and selected from the group consisting of $–R^5–C(O)–O–$, $–R^5–O–C(O)–$, $–R^5–C(O)–NH–$, $–R^5–OC(O)–NH–$, and $R^5–NH–C(O)O–$; and R^4 is a linear or branched alkyl or alkenyl having 12 to 25 carbon atoms.

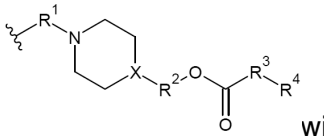
7. The cationic lipid according to **any one of claims 1 to 6**, wherein R^a and R^b are independently selected from



,


, with X being CH or $–R^1–N(H)–C(O)–R^3–R^4$.

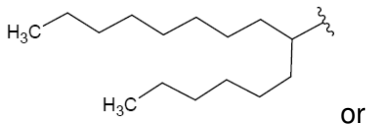
8. The cationic lipid according to **any one of claims 1 to 7**, wherein each of R^a and R^b is:



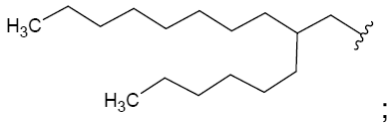
with X being CH; and

R^3 is present and R^5 is an alkanediyl having 2 to 6 carbon atoms, selected independently at each occurrence.

9. The cationic lipid according to **any one of claims 1 to 8**, wherein
R^3 is present and is $–R^5–C(O)–O–$ or $–R^5–O–C(O)–$, preferably $–R^5–C(O)–O–$;
R^4 is:



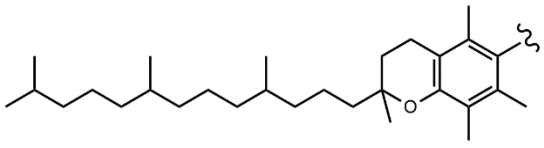
or



;

and wherein R^a and R^b are identical.

10. The cationic lipid according to **any one of claims 1 to 8**, wherein
R^3 is present and is $–R^5–C(O)–O–$ or $–R^5–O–C(O)–$, preferably $–R^5–C(O)–O–$;
R^4 is:



;

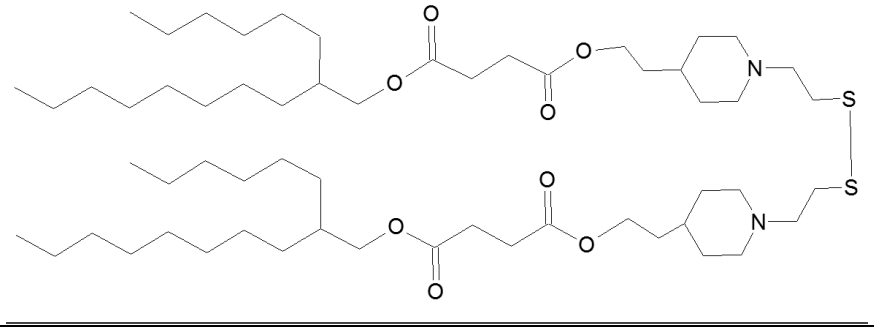
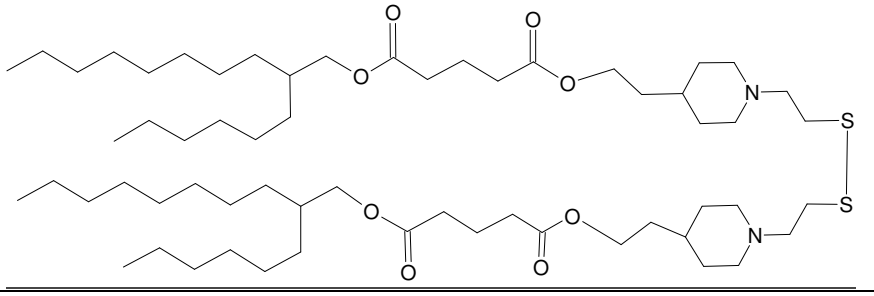
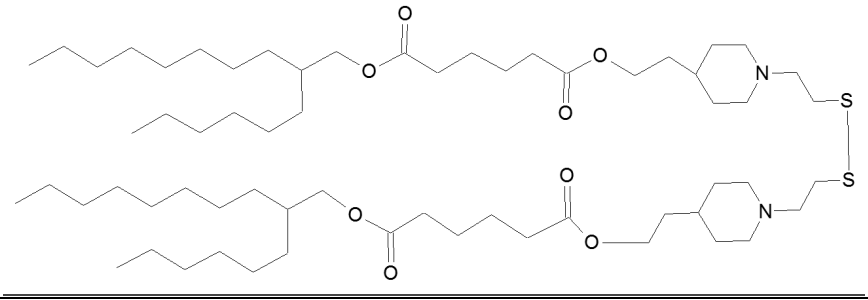
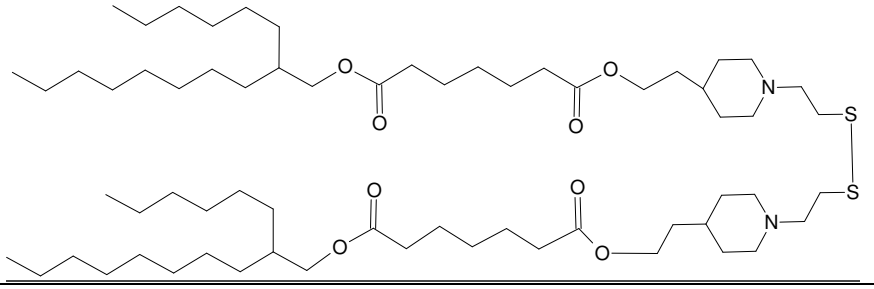
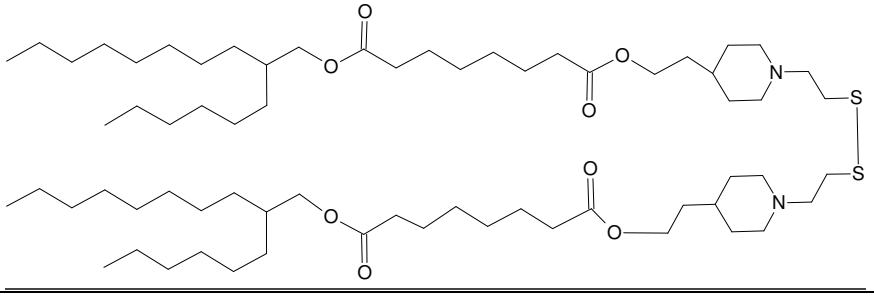
and wherein R^a and R^b are identical; ~~.~~

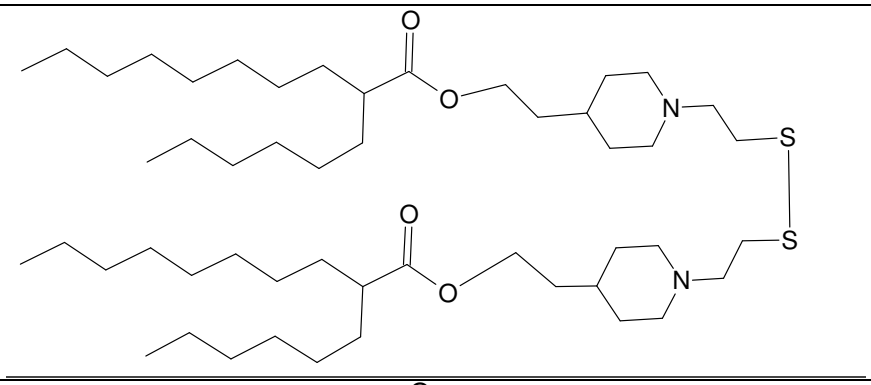
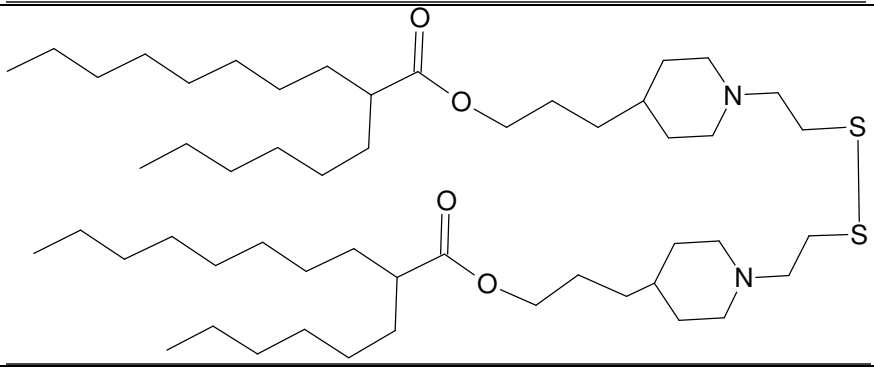
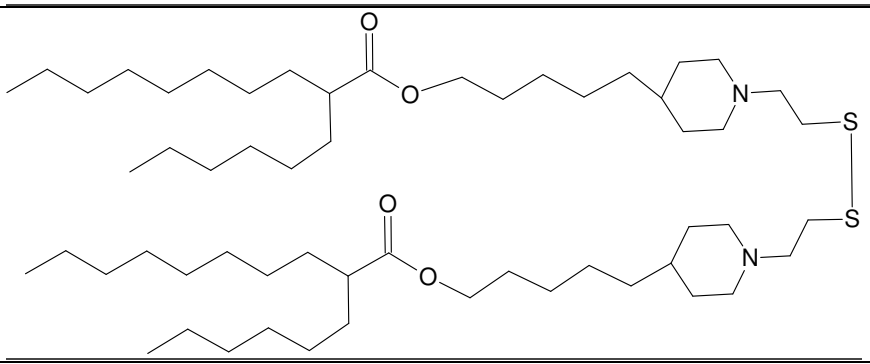
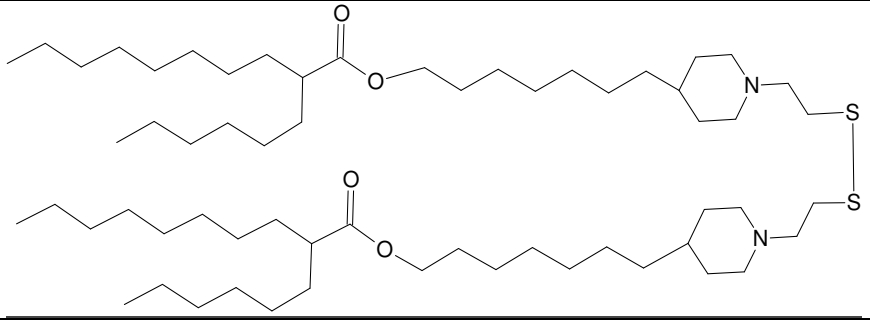
~~11. The cationic lipid according to **claim 9 or claim 10**, wherein R^3 is $–R^5–C(O)–O–$.~~

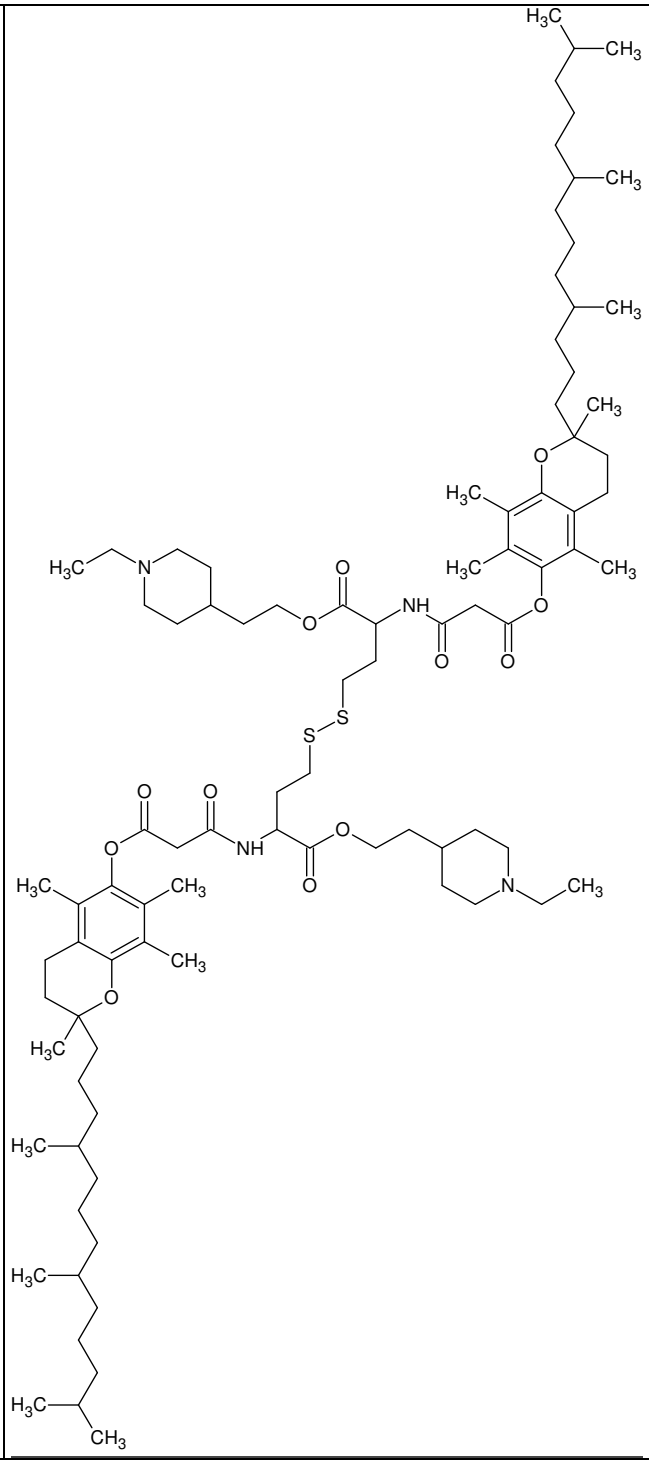
~~12.~~11. The cationic lipid according to **claim 7 or 8**, wherein R^1 is ethanediyl.

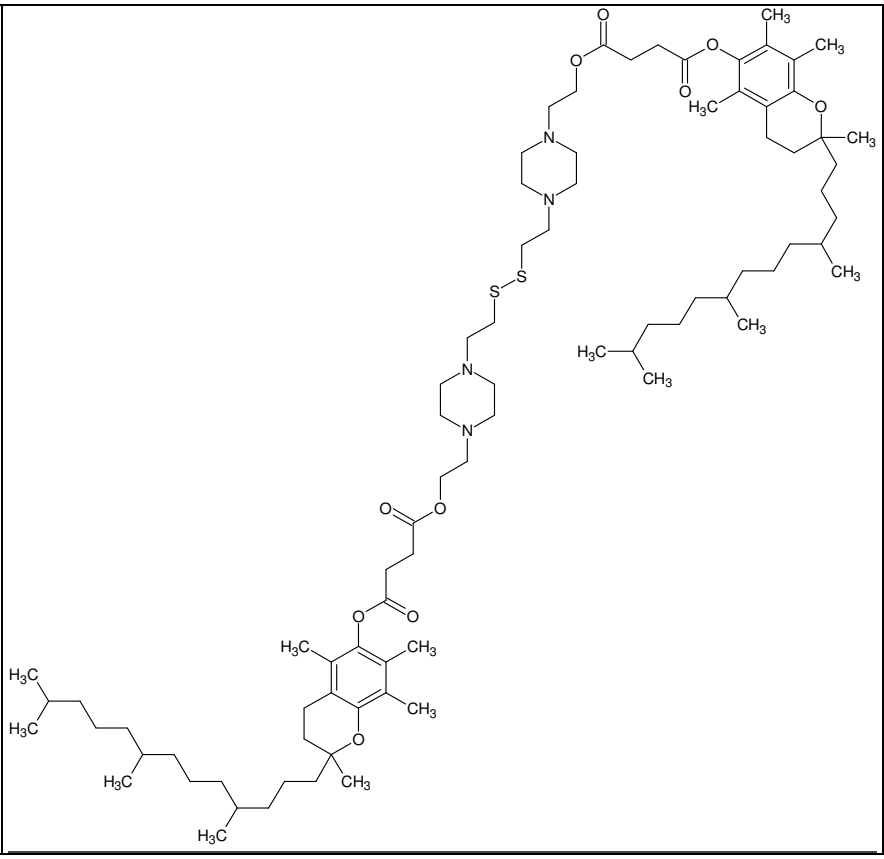
~~13.~~12. The cationic lipid of any of the **preceding claims**, further exhibiting one or more of the following features, independently selected at each occurrence:
(i) R^1 is an unsubstituted ethanediyl, propanediyl, or butanediyl;
(ii) R^2 is an linear, unbranched alkanediyl having 2 to 8 carbon atoms;
(iii) R^3 is$–R^5–C(O)–O–$ or $–R^5–O–C(O)–$;
(iv) R^5 is an alkanediyl having 2 to 6 carbon atoms; and/or
(vi) X is CH.

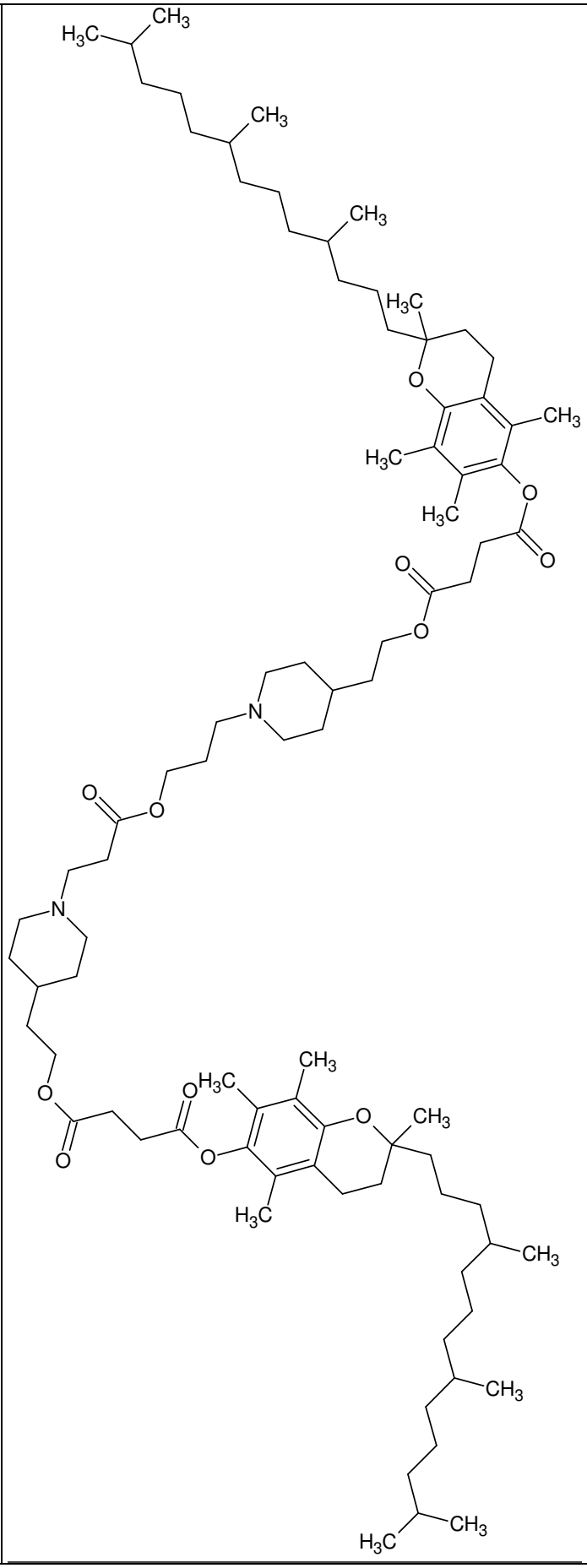
~~14.~~13. The cationic lipid of **claim 1**, being selected from one of the compounds as listed in **Table 1**:

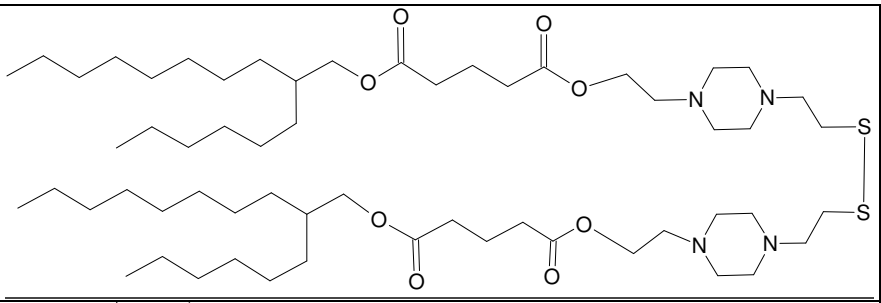
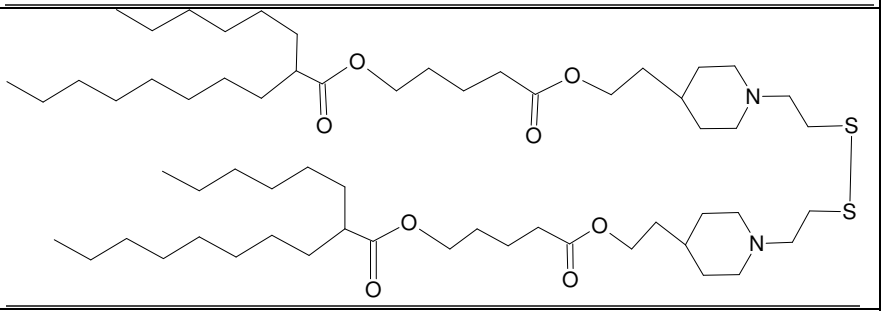
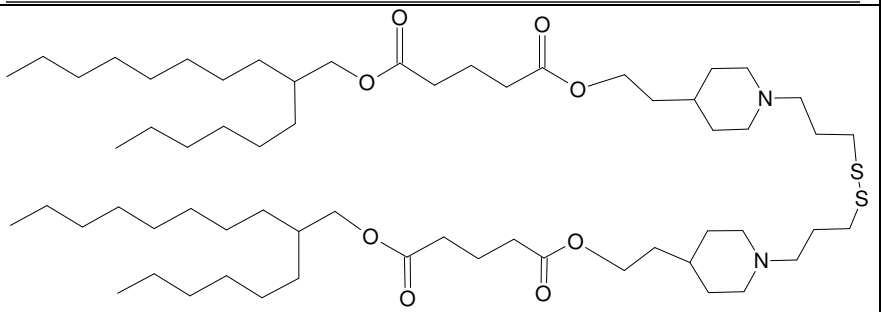
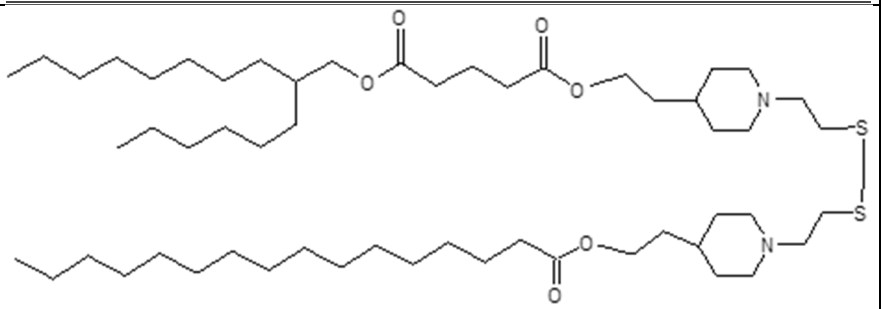
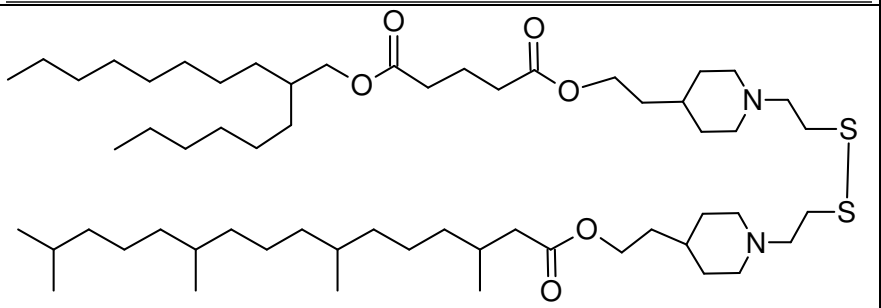
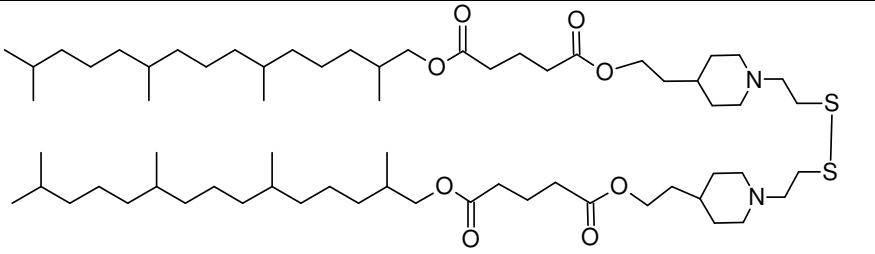
Cationic Lipid Compound No.	Structure	Ref. in Figures / Name
C1		Fig. 1A / HEXA-C4DE-PipSS
C2		Fig. 1B / HEXA-C5DE-PipSS (GN02-lipid)
C3		Fig. 1C / HEXA-C6DE-PipSS
C4		Fig. 1D / HEXA-C7DE-PipSS
C5		Fig. 1E / HEXA-C8DE-PipSS

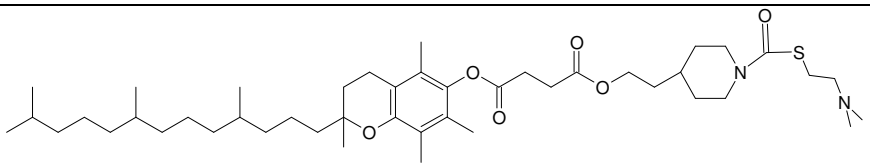
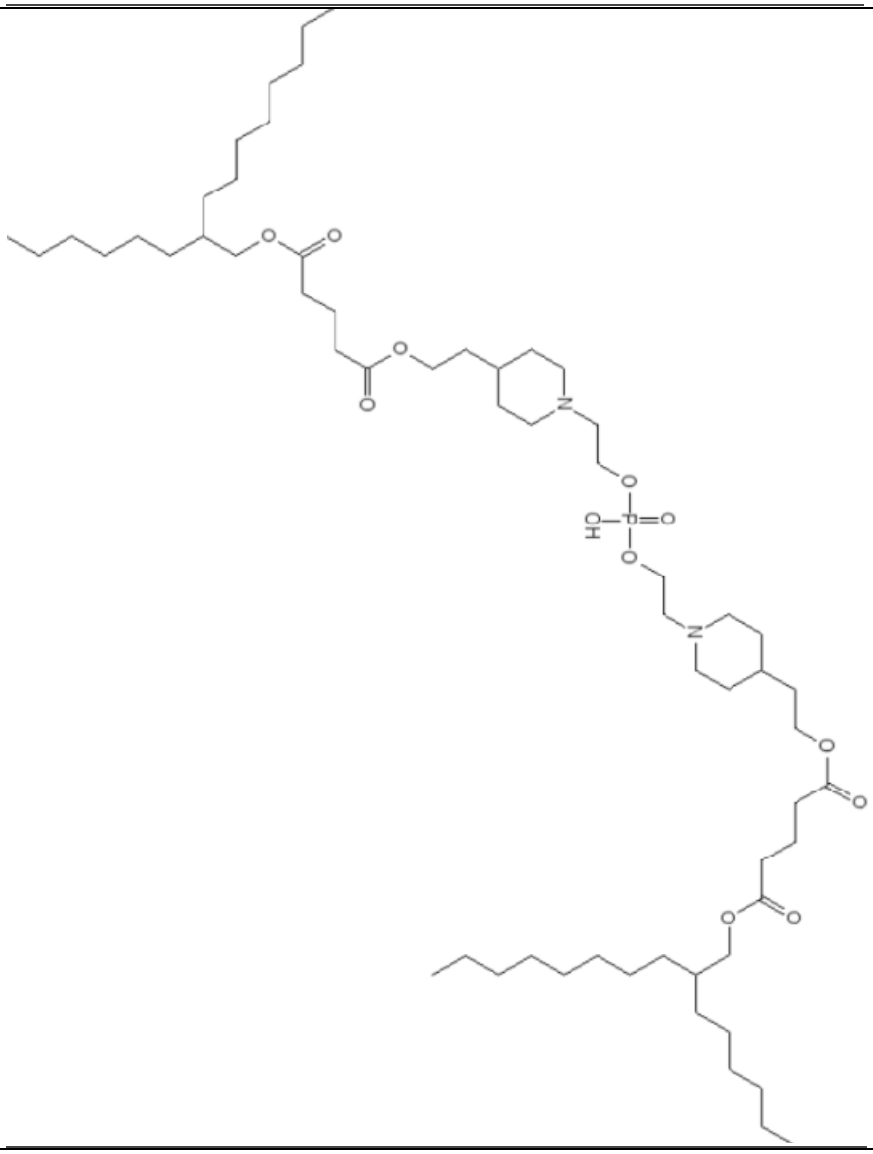
C6		Fig. 1F / HEXACA - C3ME-PipSS
C7		Fig. 1G / HEXACA- C4ME-PipSS
C8		Fig. 1H / HEXACA- C6ME-PipSS
C9		Fig. 1I / HEXACA- C8ME-PipSS

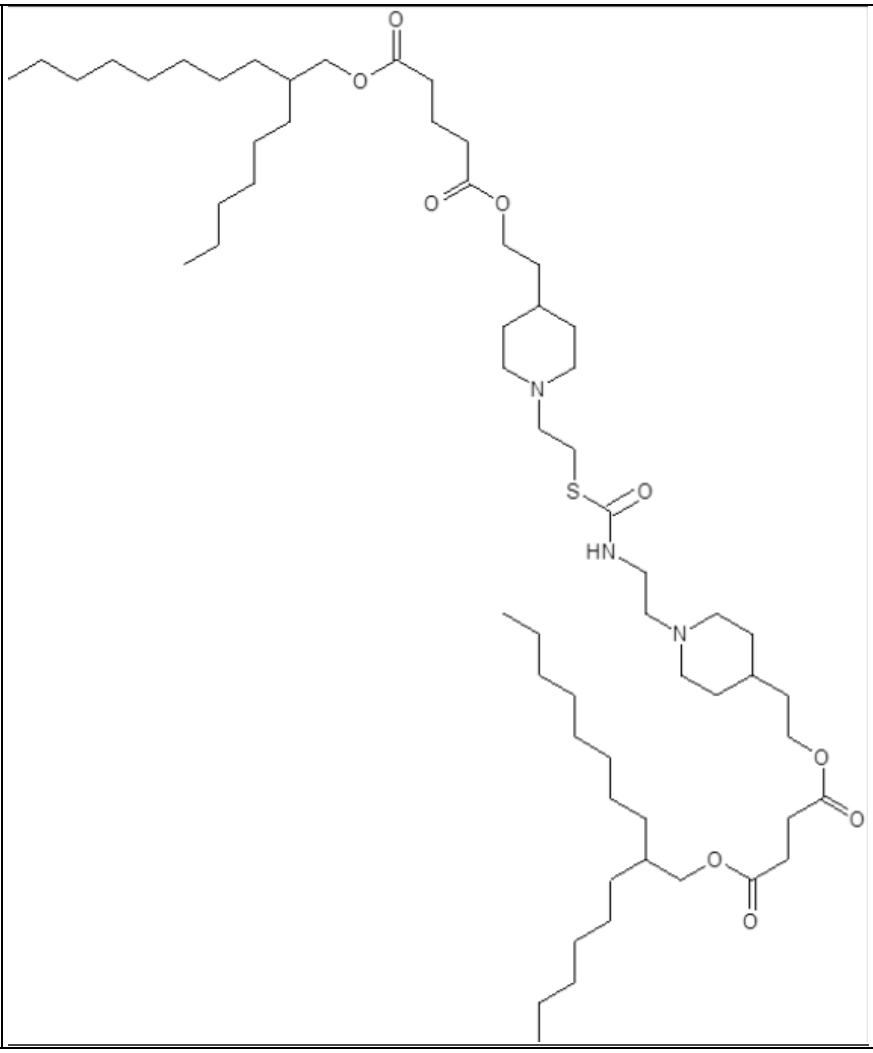
C10		Fig. 3A

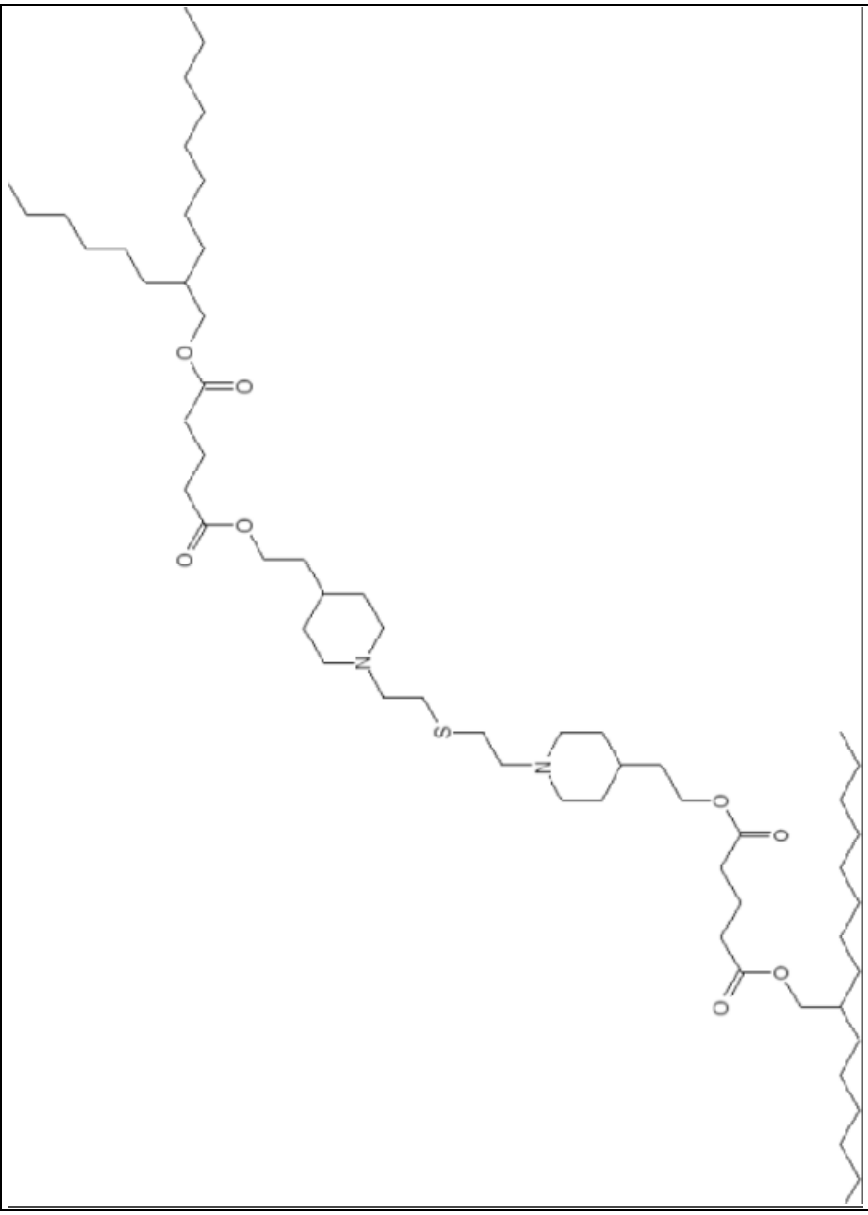
C11		Fig. 3B

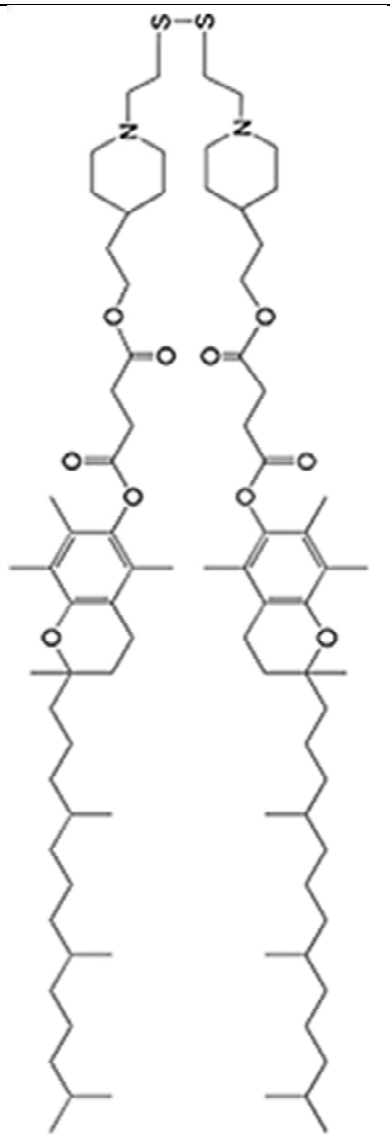
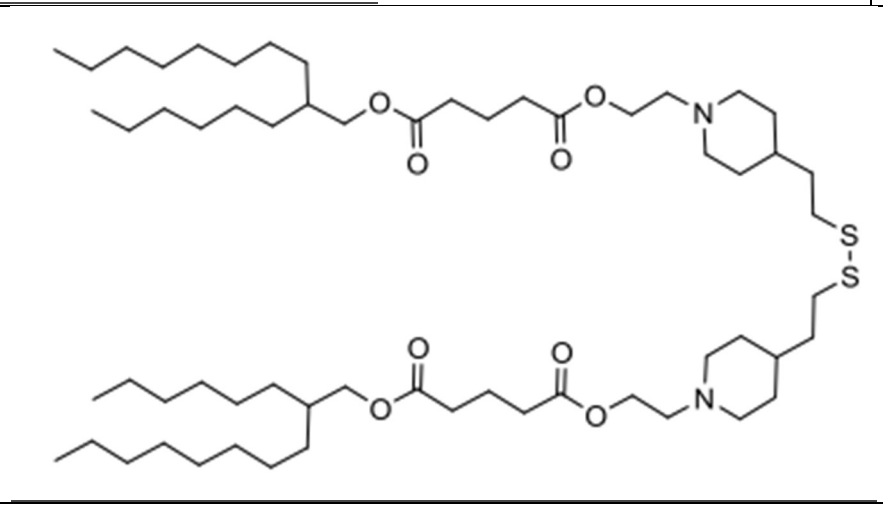
C12		Fig. 3C

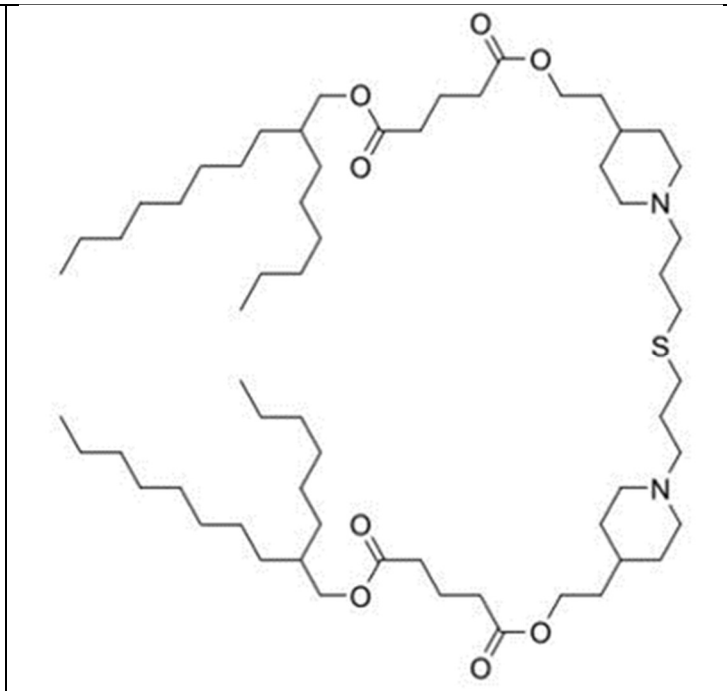
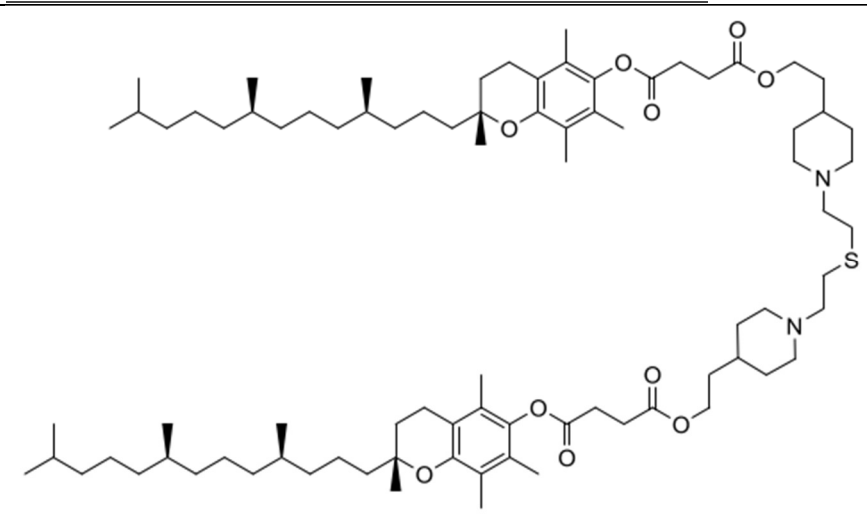
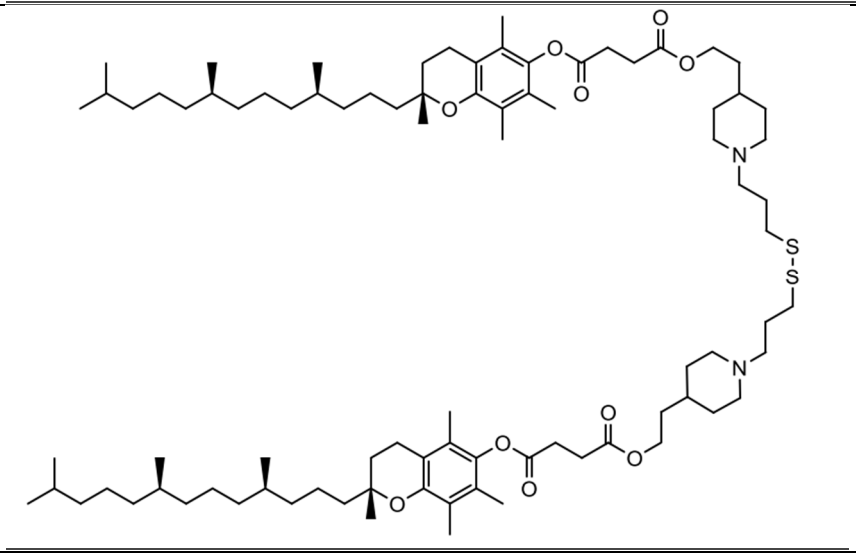
C13		HEXA-C5DE-PipAZSS
C14		HEXACA-C5DE-PipSS
C15		HEXA-C5DE-PipC3SS
C16		C16-HEXA-C5DE-PipSS
C17		DPhy-HEXA-C5DE-PipSS
C18		2DPhy-C5DE-PipSS

C19		Vit E-C5DE-Pip-TEN
C20		HEXA-C5DE-Pip-Phosphate

	C21		HEXA-C5DE-Pip-Thiocarbamate

	C22		HEXA-C5DE-Pip-Thioether

C23		COATSOME® SS-EC
C24		HEXA-C5DE-inverted-PipSS

C25		HEXA-C5DE-Pip-C3 thioether or HEXA-C5DE-piperidine-C3 thioether
C26		THIOETHER or VitE-C4DE-Piperidine-Thioether
C27		C3SS or VitE-C4DE-Piperidine-C3SS

~~15.~~14. A composition comprising

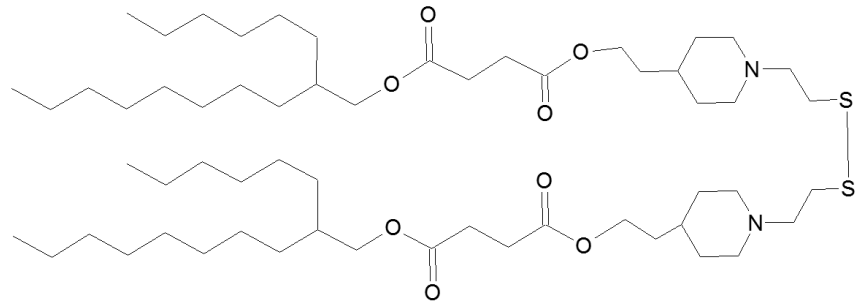
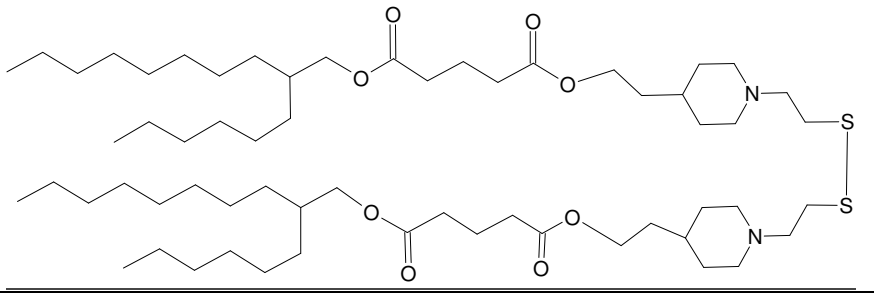
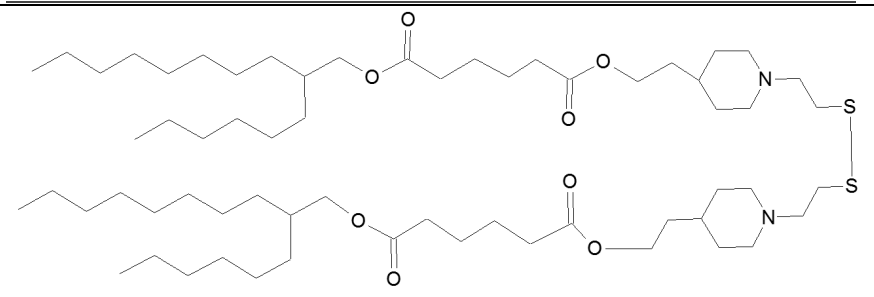
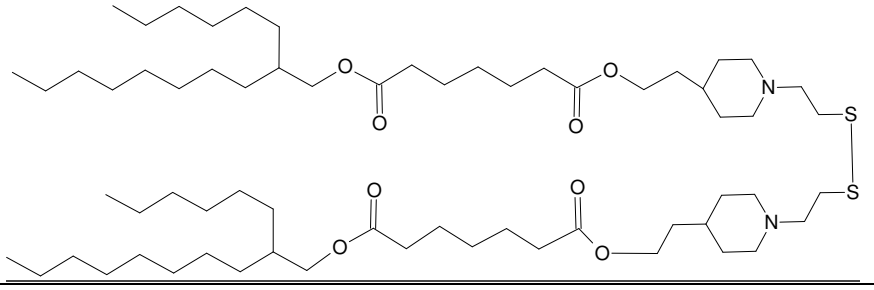
(i) the cationic lipid of any one of **claims 1 to 13~~14~~**;

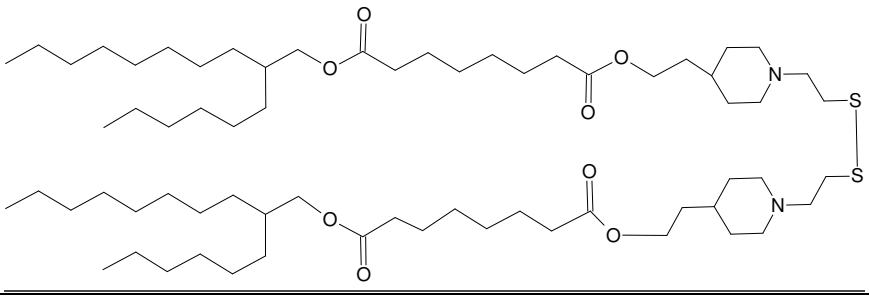
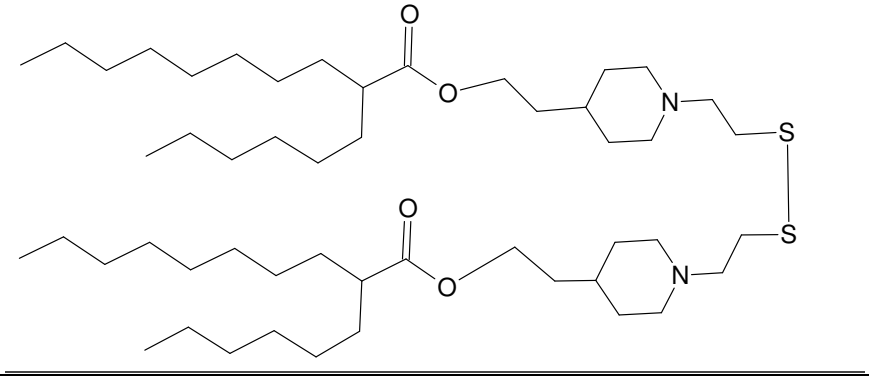
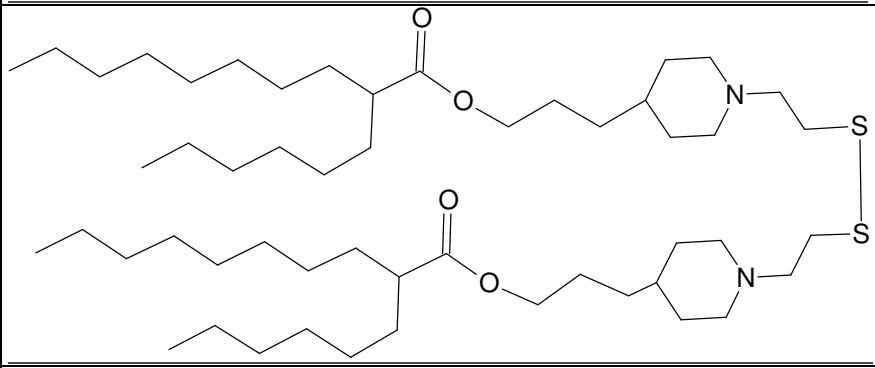
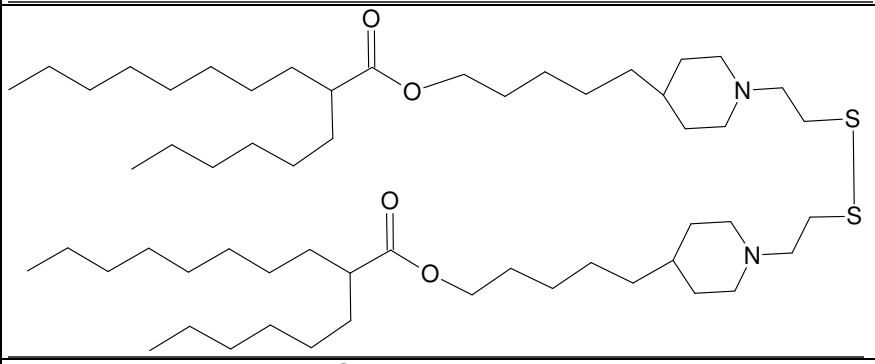
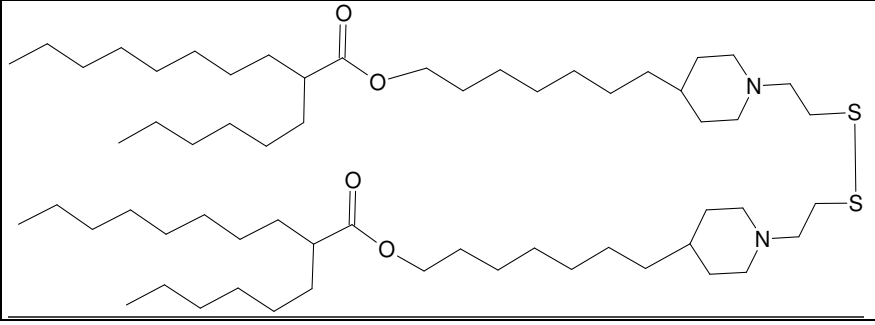
(ii) the cationic lipid C15 as listed in **Table 1**;

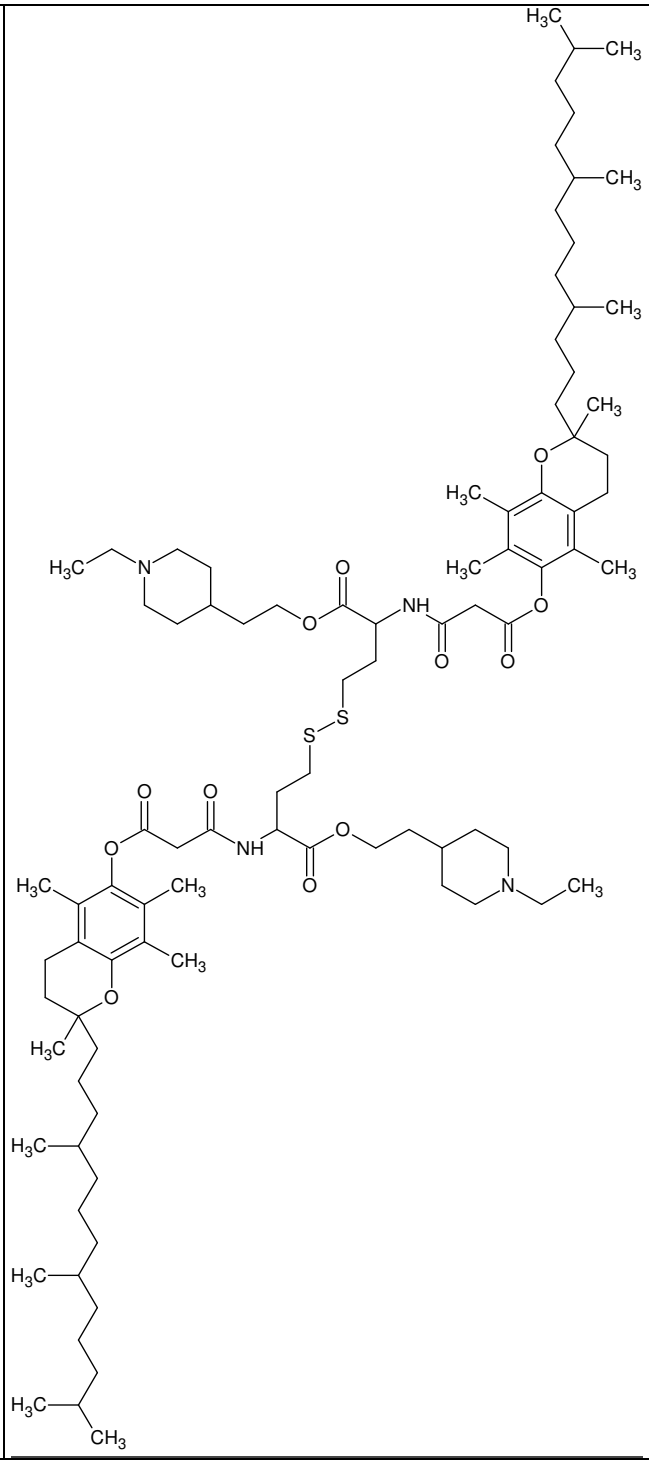
(iii) the cationic lipid C2 as listed in **Table 1**; or

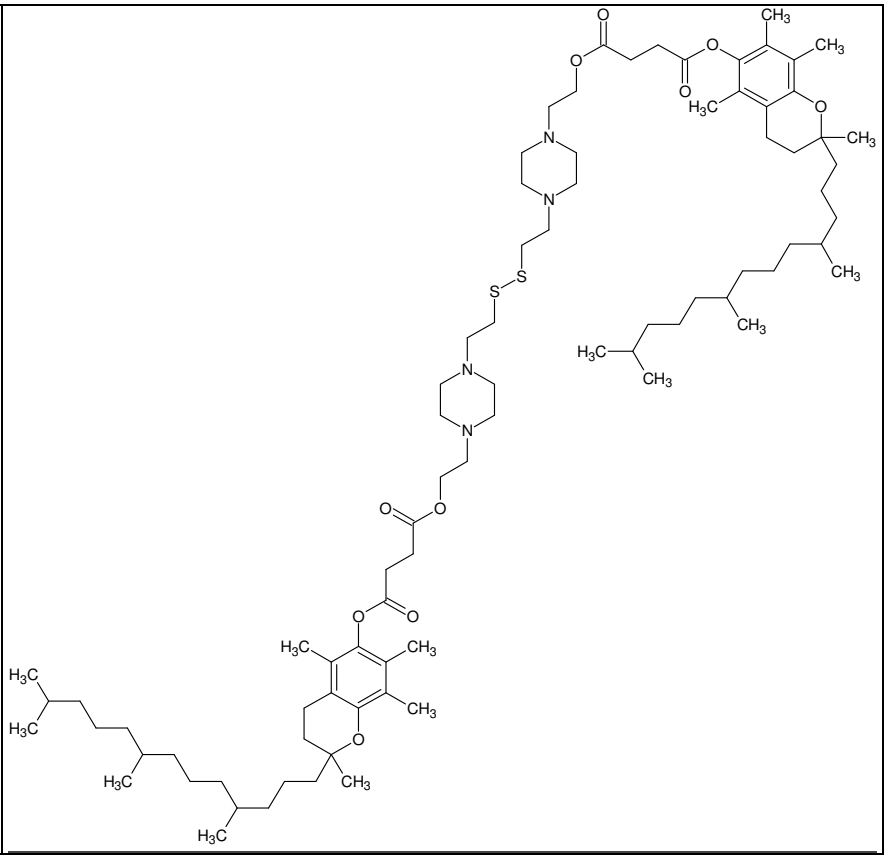
(iv) the cationic lipid C26 as listed in **Table 1**

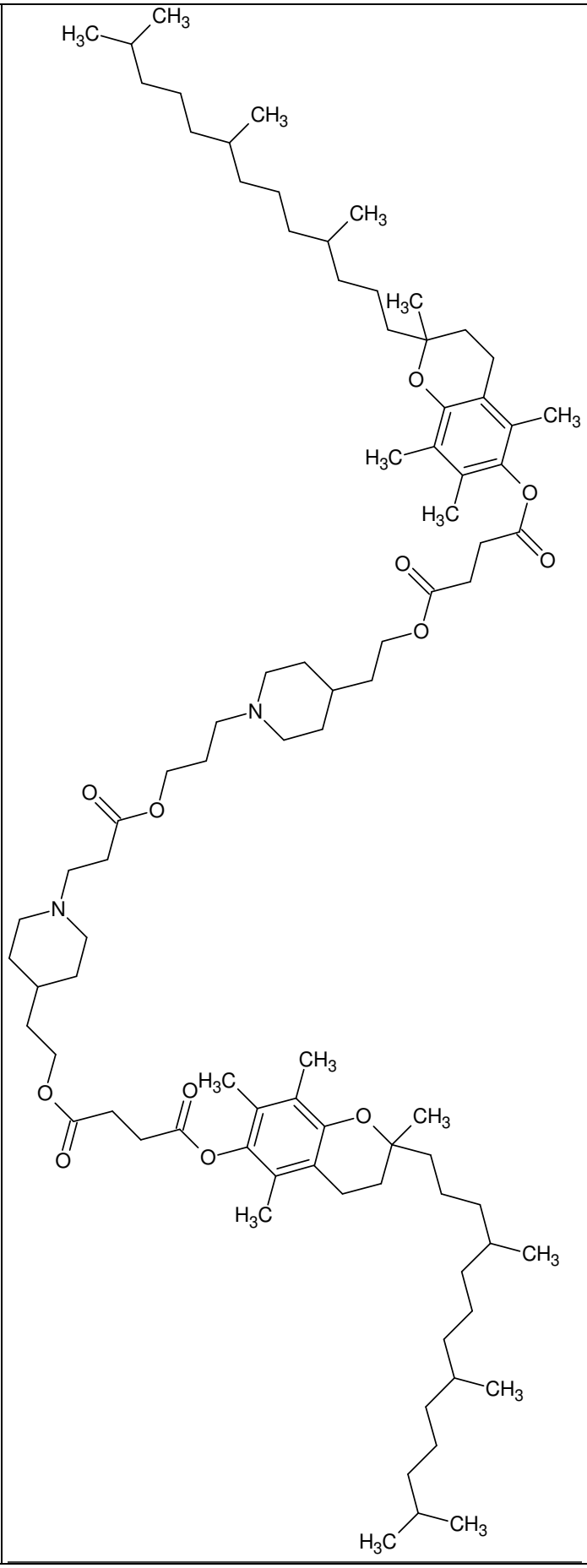
Table 1:

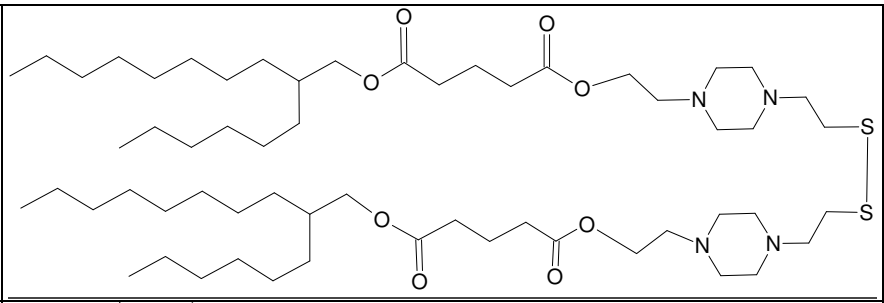
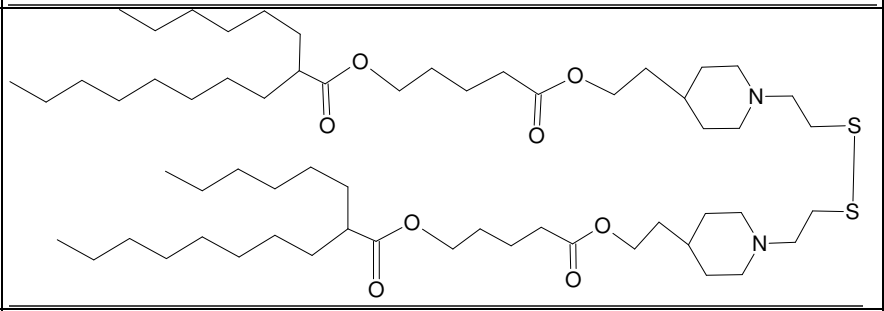
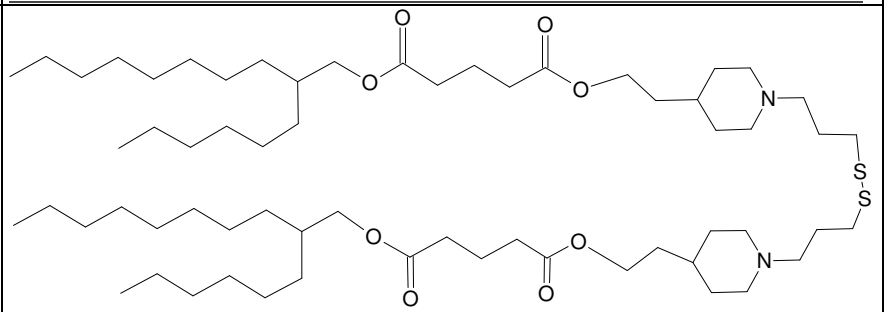
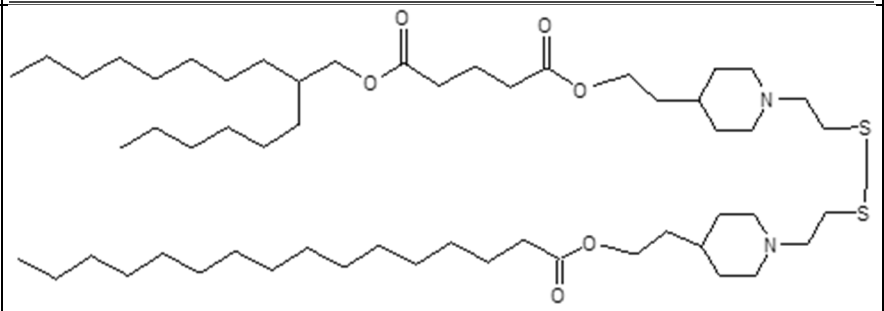
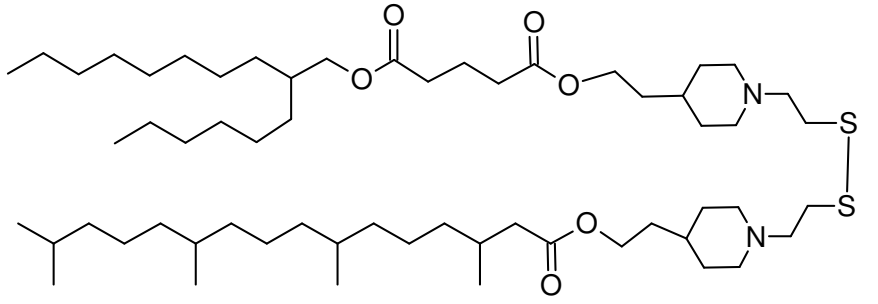
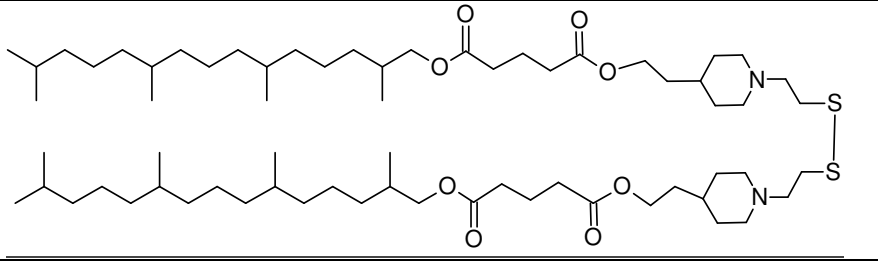
Cationic Lipid Compound No.	Structure	Ref. in Figures / Name
C1		Fig. 1A / HEXA-C4DE-PipSS
C2		Fig. 1B / HEXA-C5DE-PipSS (GN02-lipid)
C3		Fig. 1C / HEXA-C6DE-PipSS
C4		Fig. 1D / HEXA-C7DE-PipSS

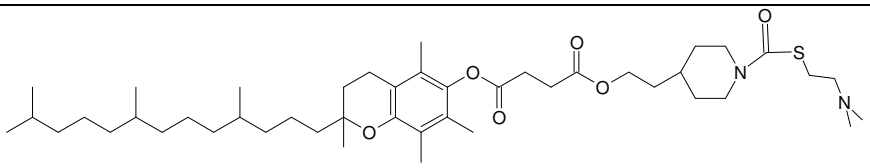
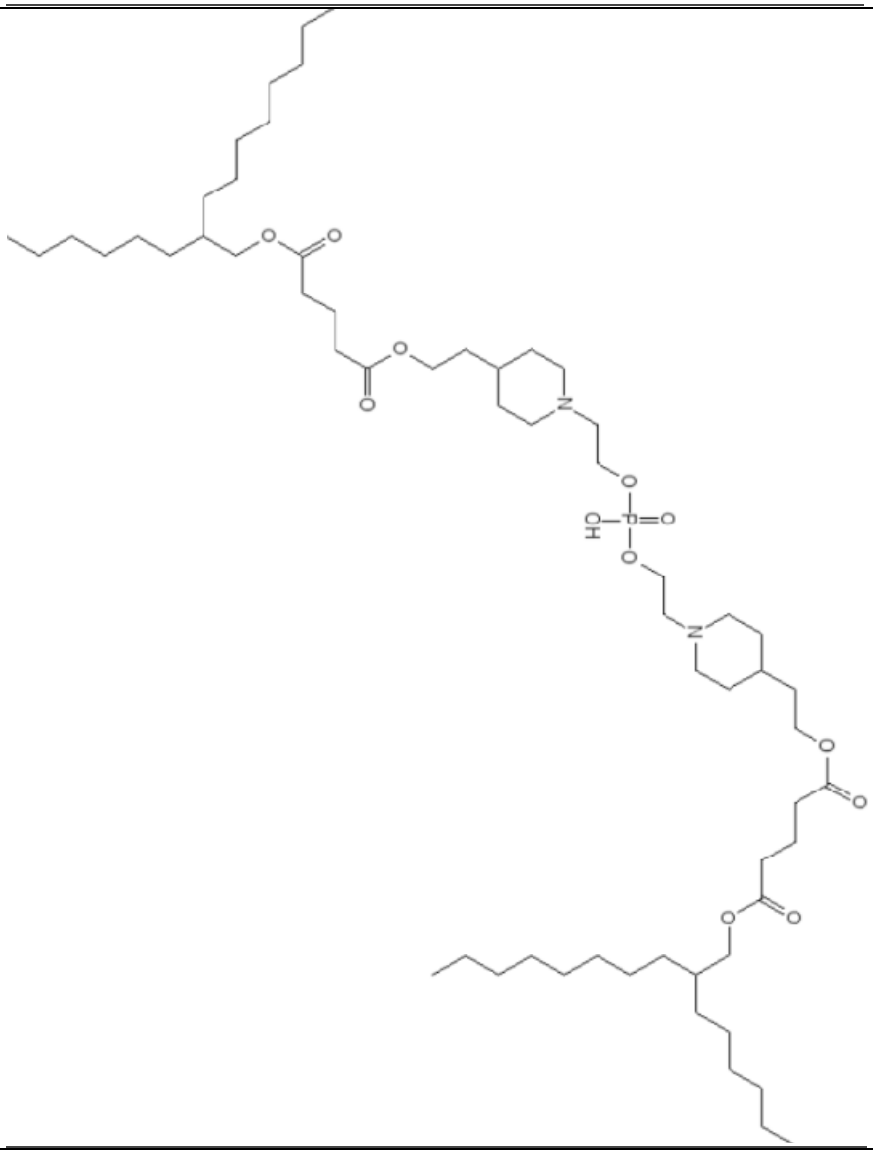
C5		Fig. 1E / HEXA-C8DE-PipSS
C6		Fig. 1F / HEXACA - C3ME-PipSS
C7		Fig. 1G / HEXACA-C4ME-PipSS
C8		Fig. 1H / HEXACA-C6ME-PipSS
C9		Fig. 1I / HEXACA-C8ME-PipSS

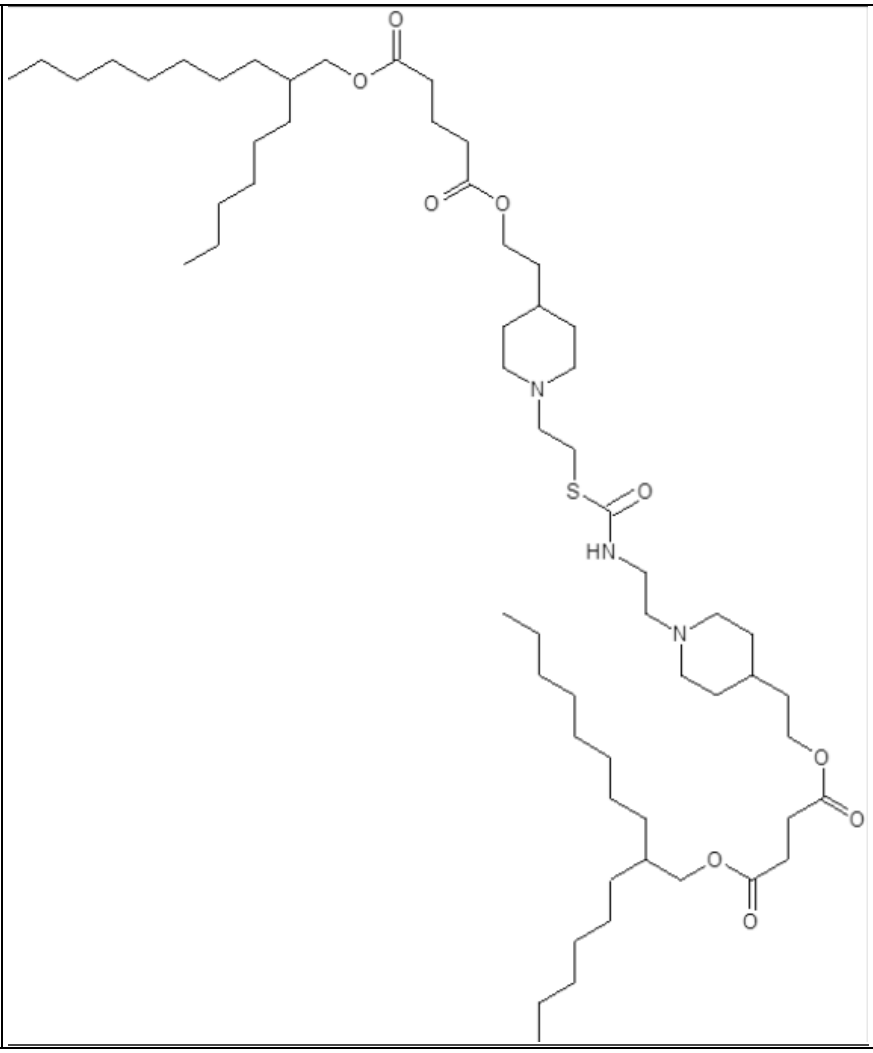
C10		Fig. 3A

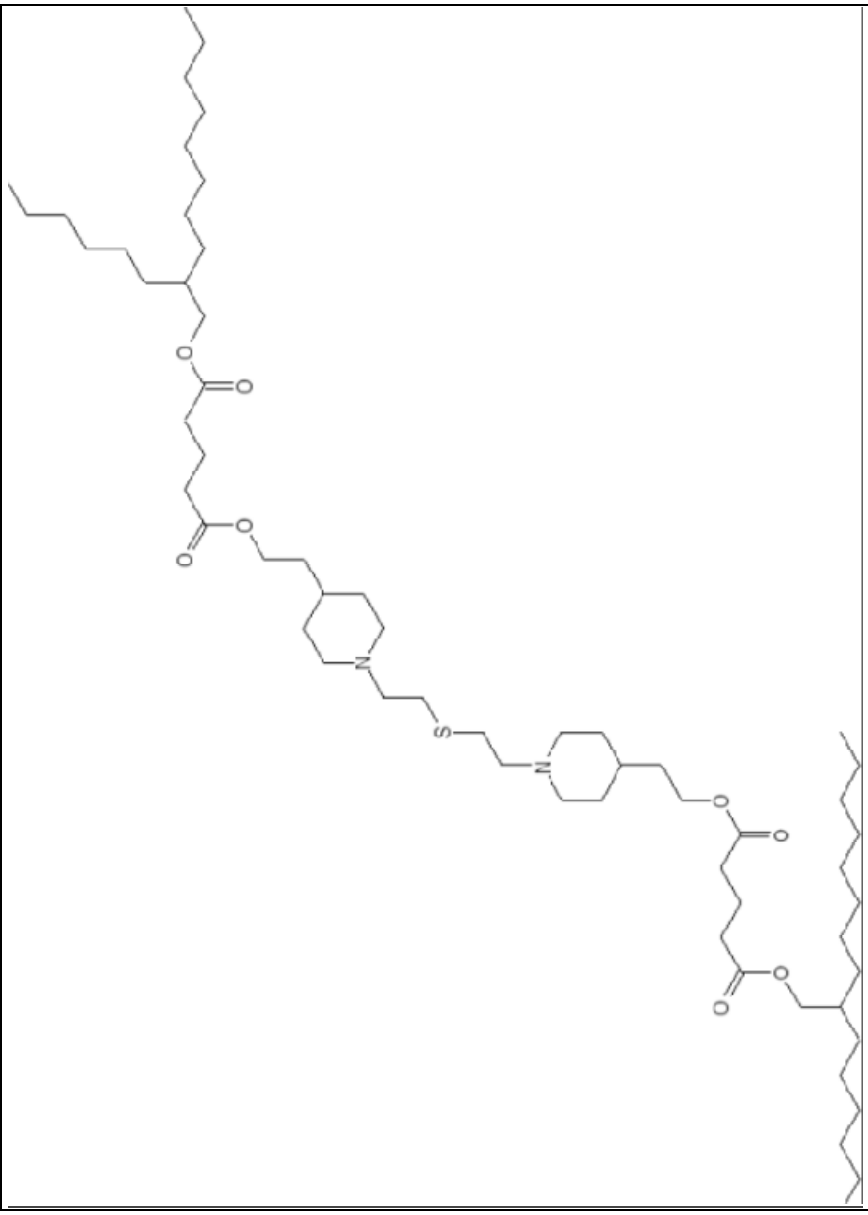
C11		Fig. 3B

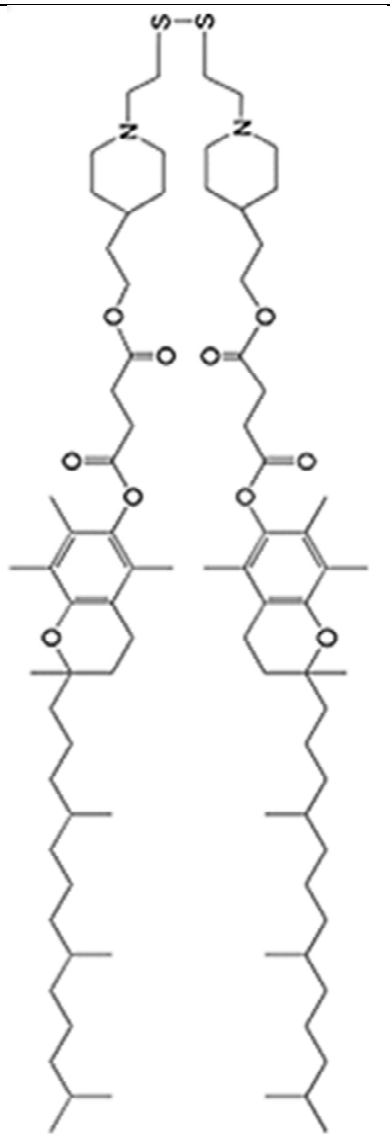
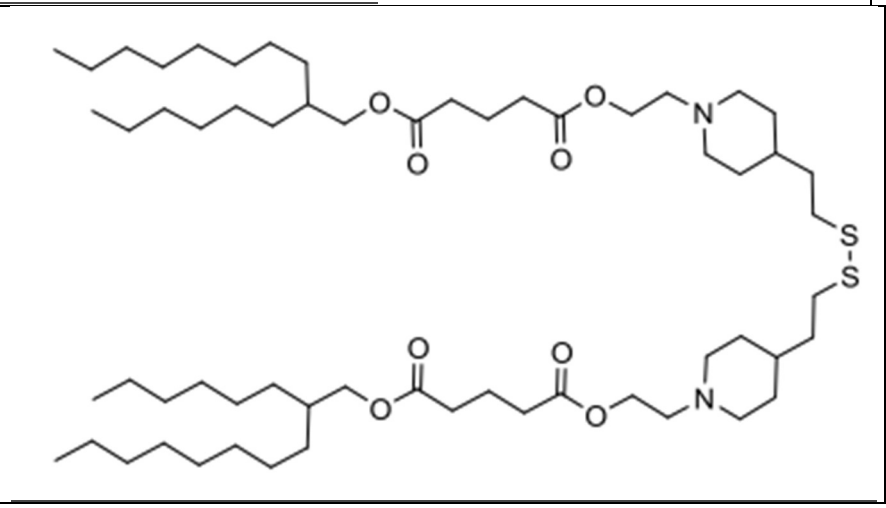
C12		Fig. 3C

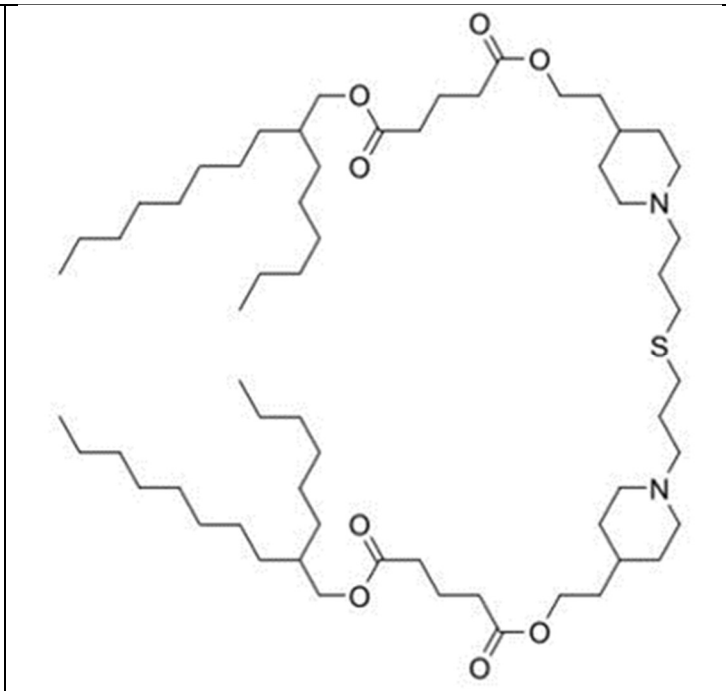
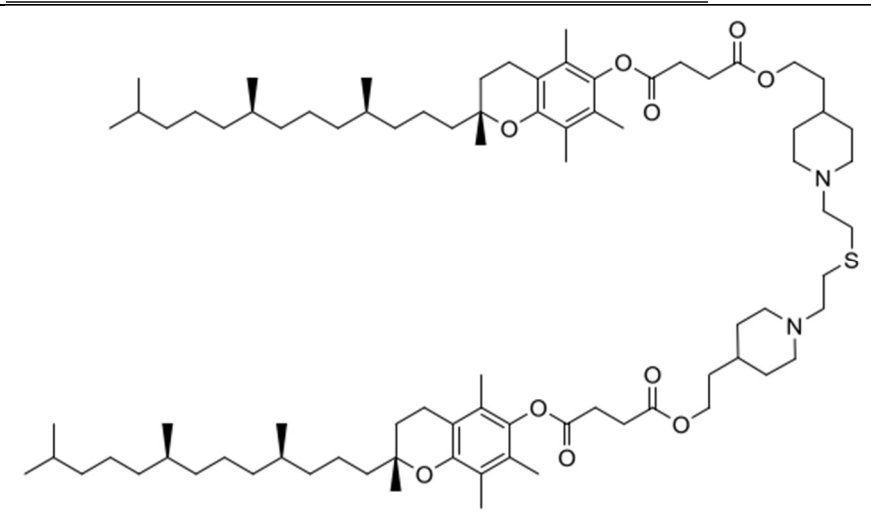
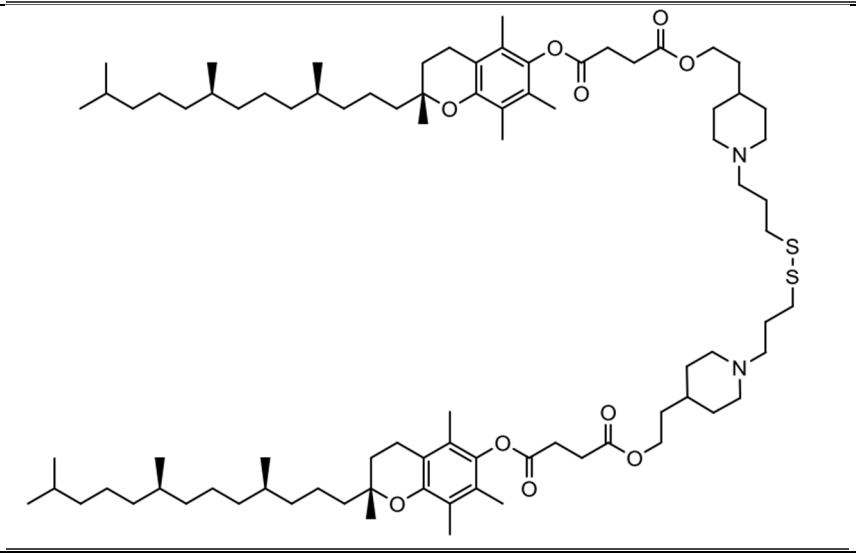
C13		HEXA-C5DE-PipAZSS
C14		HEXACA-C5DE-PipSS
C15		HEXA-C5DE-PipC3SS
C16		C16-HEXA-C5DE-PipSS
C17		DPhy-HEXA-C5DE-PipSS
C18		2DPhy-C5DE-PipSS

C19		Vit E-C5DE-Pip-TEN
C20		HEXA-C5DE-Pip-Phosphate

C21		HEXA-C5DE-Pip-Thiocarbamate

	C22		HEXA-C5DE-Pip-Thioether

C23		COATSOME® SS-EC
C24		HEXA-C5DE-inverted-PipSS

C25		HEXA-C5DE-Pip-C3 thioether or HEXA-C5DE-piperidine-C3 thioether
C26		THIOETHER or VitE-C4DE-Piperidine-Thioether
C27		C3SS or VitE-C4DE-Piperidine-C3SS

~~16. The composition of **claim 15,**~~ preferably further comprising one or more of the following excipients:

(i) a steroid, preferably cholesterol;

(ii) a neutral lipid;

wherein said neutral lipid preferably is 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (DPhyPE), optionally in combination with the neutral lipid 1,2-diheptanoyl-sn-glycero-3-phosphocholine (DHPC); or wherein said neutral lipid is a zwitterionic compound, optionally a zwitterionic compound having two fatty acid moieties selected from myristoyl, palmitoyl, stearoyl and oleyol, in combination with a zwitterionic compound having two fatty acid moieties selected from pentanoyl, hexanoyl, heptanoyl, octanoyl, nonaoyl and decanoyl;

and/or

(iii) a polymer conjugated lipid;

wherein said polymer conjugated lipid is a compound according to formula (II):

P-A-L formula (II);

wherein P is a hydrophilic polymer moiety, A is an optional linker, and L is a lipid moiety; preferably wherein the polymer conjugated lipid is a pegylated lipid.

~~17.~~15. A composition comprising one or more of the following excipients:

(i) a cationic lipid of any one of **claims 1 to 13~~14~~** or a cationic lipid comprising a tertiary or quaternary nitrogen / amino group or a cationic lipid carrying a net positive charge at physiological pH;

(ii) a steroid, preferably cholesterol;

(iii) a neutral lipid as described in subitem (ii) of **claim 14~~16~~**; and/or

(iv) a polymer conjugated lipid, wherein said polymer conjugated lipid is a compound according to formula (II):

P-A-L formula (II);

wherein P is a hydrophilic polymer moiety, A is an optional linker, and L is a lipid moiety;

preferably wherein the polymer conjugated lipid is a pegylated lipid;

more preferably, wherein the lipid moiety L comprises at least one fatty acid (“tail”) comprising 8, 10 or 12 carbon atoms, preferably 8 or 10 carbon atoms;

even more preferably, wherein the pegylated lipid is selected from the group consisting of 1,2-dicapryl-rac-glycero-3-methylpolyoxyethylene glycol 2000 (C_{10}-PEG 2000); and N-octanoyl-sphingosine-1-{succinyl[methoxy(polyethylene glycol)2000]} (Cer8-PEG 2000).

~~18.~~16. A composition comprising one or more of the following excipients:

(i) a cationic lipid as described in subitem (i) of **claim** 15~~17~~;

(ii) a steroid, preferably cholesterol;

(iii) a neutral lipid as described in subitem (ii) of **claim** 14~~16~~, or preferably a combination of two neutral lipids wherein the combination comprises a neutral lipid or phospholipid having at least two alkyl chains, whereby each alkyl chain independently has a length of preferably C_6, C_7, C_8, C_9, or C_{10}, more preferably with a length of C_6, C_7, C_8, most preferably with a length of C_7, further most preferably a phospholipid selected from the group consisting of DHPC (1,2-diheptanoyl-sn-glycero-3-phosphocholine), 05:0 PC (1,2-dipentanoyl-sn-glycero-3-phosphocholine), 04:0 PC (1,2-dibutyryl-sn-glycero-3-phosphocholine), 06:0 PC (DHPC, 1,2-dihexanoyl-sn-glycero-3-phosphocholine), 08:0 PC (1,2-dioctanoyl-sn-glycero-3-phosphocholine), and 09:0 PC (1,2-dinonanoyl-sn-glycero-3-phosphocholine); and/or

(iv) a polymer conjugated lipid, wherein said polymer conjugated lipid is a compound according to formula (II):

P-A-L formula (II);

wherein P is a hydrophilic polymer moiety, A is an optional linker, and L is a lipid moiety;

preferably wherein the polymer conjugated lipid is a pegylated lipid;

more preferably wherein the pegylated lipid is 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol 2000 (DMG-PEG 2000).

~~19.~~17. The composition of any one of **claims** 14~~15~~ **to** 16~~18~~ wherein ~~preferably~~ the composition comprises excipients in a ratio selected from the group consisting of

(a-i) the cationic lipid at an amount of 30-70 mol%; the steroid at an amount of 20-50 mol%; the neutral lipid at an amount of 5-25 mol%; and the polymer conjugated lipid at an amount of 0.5-5 mol%;

(a-ii) the cationic lipid at an amount of 40-70 mol%; the steroid at an amount of 20-50 mol%; the neutral lipid at an amount of 5-15 mol%; and the polymer conjugated lipid at an amount of 0.5-5 mol%;

(a-iii) the cationic lipid at an amount of 20-60 mol%; the steroid at an amount of 25-55 mol%; the phospholipid at an amount of 5-25 mol%; and the polymer conjugated lipid at an amount of 0.5-15 mol%;

(a-iv) the cationic lipid at an amount of 45-65 mol%; the steroid at an amount of 25-45 mol%; the phospholipid at an amount of 8-12 mol%; and the polymer conjugated lipid at an amount of 1-3 mol%;

(a-v) the cationic lipid at an amount of 45-65 mol%; cholesterol at an amount of 25-45 mol%; the neutral lipid at an amount of 8-12 mol%; and the polymer conjugated lipid at an amount of 1-3 mol%;

(a-vi) the cationic lipid at an amount of 45-65 mol%; cholesterol at an amount of 25-45 mol%; DPhyPE at an amount of 8-12 mol% and optionally DHPC at an amount of 1 to 10 mol%; and the polymer conjugated lipid at an amount of 1-3 mol%; and

(a-vi) the cationic lipid at an amount of 45-65 mol%; cholesterol at an amount of 25-45 mol%; DPhyPE at an amount of 8-12 mol% and optionally DHPC at an amount of 1 to 10 mol%; and PEG-DMG 2000 at an amount of 1-3 mol%; or

more preferably the composition comprises excipients in a ratio selected from the group consisting of

(b-i) the cationic lipid at an amount of 59 mol%; the steroid at an amount of 29.3 mol%; the neutral lipid at an amount of 10 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-ii) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 29.3 mol%; the neutral lipid at an amount of 10 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-iii) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 29.3 mol%; DPhyPE at an amount of 10 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-iv) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 29.3 mol%; DPhyPE at an amount of 10 mol%; and C_{10}-PEG 2000 at an amount of 1.7%;

(b-v) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 29.3 mol%; DPhyPE at an amount of 10 mol%; and Cer8-PEG 2000 at an amount of 1.7%;

(b-vi) the cationic lipid at an amount of 59 mol%; the steroid at an amount of 28.3 mol%; the neutral lipid at an amount of 11 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-vii) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 28.3 mol%; the neutral lipid at an amount of 11 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-viii) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 28.3 mol%; DPhyPE at an amount of 10 mol% and DHPC at an amount of 1 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-ix) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 28.3 mol%; DPhyPE at an amount of 10 mol% and DHPC at an amount of 1 mol%; and C_{10}-PEG 2000 at an amount of 1.7%; and

(b-x) the cationic lipid at an amount of 59 mol%; cholesterol at an amount of 28.3 mol%; DPhyPE at an amount of 10 mol% and DHPC at an amount of 1 mol%; and Cer8-PEG 2000 at an amount of 1.7%;

(b-xi) the cationic lipid at an amount of 49 mol%; the steroid at an amount of 29.3 mol%; the neutral lipid at an amount of 20 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-xii) the cationic lipid at an amount of 49 mol%; cholesterol at an amount of 29.3 mol%; the neutral lipid at an amount of 20 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-xiii) the cationic lipid at an amount of 49 mol%; cholesterol at an amount of 29.3 mol%; DPhyPE at an amount of 10 mol% and DHPC at an amount of 10 mol%; and the polymer conjugated lipid at an amount of 1.7 mol%;

(b-xiv) the cationic lipid at an amount of 49 mol%; cholesterol at an amount of 29.3 mol%; DPhyPE at an amount of 10 mol% and DHPC at an amount of 10 mol%; and C_{10}-PEG 2000 at an amount of 1.7%; and

(b-xv) the cationic lipid at an amount of 49 mol%; cholesterol at an amount of 29.3 mol%; DPhyPE at an amount of 10 mol% and DHPC at an amount of 10 mol%; and Cer8-PEG 2000 at an amount of 1.7%;

each amount being relative to the total molar amount of all lipidic excipients of the lipid nanoparticles;

more preferably the composition comprises excipients in a ratio selected from the group consisting of

(c-i) a lipid excipient combination selected from the group consisting of **E1 to E108** as disclosed in **Table E** at mol-percentages selected from the group consisting of **F1 to F62** as disclosed in **Table F**; -

~~20. The composition of any one of **claims 15 to 19**~~ wherein preferably the composition comprises excipients in a ratio of

(i) 59 mol% cationic lipid C23 (COATSOME® SS-EC) as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DPhyPE and 1.7 mol% DMG-PEG 2000;

(ii) 59 mol% cationic lipid C2 as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DPhyPE and 1.7 mol% DMG-PEG 2000;

(iii) 59 mol% cationic lipid C15 as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DPhyPE and 1.7 mol% DMG-PEG 2000;

(iv) 59 mol% cationic lipid C26 as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DPhyPE and 1.7 mol% DMG-PEG 2000;
(v) 59 mol% cationic lipid C23 (COATSOME® SS-EC) as disclosed in Table 1, 28.3 mol% cholesterol, 10 mol% DPhyPE, 1 mol% DHPC and 1.7 mol% DMG-PEG 2000;
(vi) 59 mol% cationic lipid C2 as disclosed in Table 1, 28.3 mol% cholesterol, 10 mol% DPhyPE, 1 mol% DHPC and 1.7 mol% DMG-PEG 2000;
(vii) 59 mol% cationic lipid C15 as disclosed in Table 1, 28.3 mol% cholesterol, 10 mol% DPhyPE, 1 mol% DHPC and 1.7 mol% DMG-PEG 2000;
(viii) 59 mol% cationic lipid C26 as disclosed in Table 1, 28.3 mol% cholesterol, 10 mol% DPhyPE, 1 mol% DHPC and 1.7 mol% DMG-PEG 2000;
(ix) 49 mol% cationic lipid C23 (COATSOME® SS-EC) as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DphyPE, 10 mol% DHPC and 1.7 mol% DMG-PEG 2000;
(x) 49 mol% cationic lipid C2 as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DPhyPE, 10 mol% DHPC and 1.7 mol% DMG-PEG 2000;
(xi) 49 mol% cationic lipid C15 as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DPhyPE, 10 mol% DHPC and 1.7 mol% DMG-PEG 2000; or
(xii) 49 mol% cationic lipid C26 as disclosed in Table 1, 29.3 mol% cholesterol, 10 mol% DPhyPE, 10 mol% DHPC and 1.7 mol% DMG-PEG 2000.

~~21.~~18. The composition any one of **claims** 14~~15~~ **to** 17~~20~~, further comprising a biologically active ingredient~~.~~;

~~22. The composition of **claim 21**,~~ wherein the biologically active ingredient is preferably a nucleic acid compound selected from the group consisting of an artificial mRNA, chemically modified or unmodified messenger RNA (mRNA) comprising at least one coding sequence, self-replicating RNA, circular RNA, viral RNA, and replicon RNA; or any combination thereof, more preferably wherein the biologically active ingredient is an mRNA or an mRNA compound.

~~23.~~19. The composition of any one of **claims** 14~~15~~ **to** 18~~22~~, wherein the lipid nanoparticles comprise the mRNA
(i) at an amount such as to achieve an N/P ratio in the range of 10 to 20; or
(ii) at an amount such as to achieve a lipid~~-~~: mRNA weight ratio in the range of 20 to 60, preferably from ~~about~~ 3 to ~~about~~ 15, 5 to ~~about~~ 13, ~~about~~ 4 to ~~about~~ 8 or from ~~about~~ 7 to ~~about~~ 11; and/or~~.~~

~~24. The composition of any one of **claims 15 to 23**,~~ wherein the composition is a sterile solid composition for reconstitution with a sterile liquid carrier, and wherein the

composition further comprises one or more inactive ingredients selected from pH-modifying agents, bulking agents, stabilizers, non-ionic surfactants and antioxidants, and wherein the sterile liquid carrier is an aqueous carrier; and/or.

~~25. The composition of any one of **claims 15 to 24**,~~ wherein the composition is a sterile liquid composition, and wherein the lipid nanoparticles have a mean hydrodynamic diameter as determined by dynamic laser scattering from ~~about~~ 50 nm to ~~about~~ 300 nm, or from ~~about~~ 60 nm to ~~about~~ 250 nm, or from ~~about~~ 60 nm to ~~about~~ 200 nm, or from ~~about~~ 70 to 200 nm, or from ~~about~~ 75 nm to ~~about~~ 160, or from ~~about~~ 90 nm to ~~about~~ 140 nm, or from ~~about~~ 100 nm to ~~about~~ 140 nm;~~.~~ and/or

~~26. The composition of any one of **claims 15 to 25**,~~ wherein the lipid nanoparticles exhibit a zeta potential in the range of -50 mV to +50 mV.

~~27.~~20. The composition of any one of **claims** 18~~22~~ **to** 19~~26~~, wherein the mRNA compound is a mono-, bi-, or multicistronic mRNA; or.

~~28. The composition of any one **claims 22 to 26**,~~ wherein the mRNA compound comprises at least one chemical modification;~~.~~

~~29. The composition of **claim 28**,~~ wherein the chemical modification is preferably selected from the group consisting of base modifications, sugar modifications, backbone modifications and lipid modifications, more preferably wherein the chemical modification is a base modification, mostmore preferably wherein the base modification ~~preferably~~ is selected from the group consisting of pseudouracil (ψ), N1-methylpseudouracil (N1Mψ), 1-ethylpseudouracil, 2-thiouracil (s2U), 4-thiouracil, 5-methylcytosine, 5-methyluracil, 5-methoxyuracil, and any combination thereof.

~~30.~~21. The composition of any one of **claims** 18~~22~~ **to** 20~~29~~, wherein the mRNA compound comprises a coding region encoding a peptide or protein, wherein the coding region exhibits a sequence modification;~~.~~

~~31. The composition of **claim 30**,~~ wherein the sequence modification is preferably selected from a G/C content modification, a codon modification, a codon optimization or a C-optimization of the sequence; more preferably wherein

- the G/C content of the coding region is increased;
- the C content of the coding region is increased;

- the codon usage in the coding region is adapted to the human codon usage; and/or the codon adaptation index (CAI) is increased or maximised in the coding region compared with the coding region of the corresponding wild-type mRNA.

~~32.~~22. The composition of any one of **claims 18~~22~~ to 21~~31~~**, wherein the mRNA compound further comprises

a) a 5'-CAP structure;

b) at least one miRNA sequence, preferably wherein the microRNA binding site is for a microRNA selected from the group consisting of miR-126, miR-142, miR-144, miR-146, miR-150, miR-155, miR-16, miR-21, miR-223, miR-24, miR-27, miR-26a, or any combination thereof;

c) at least one 5'-UTR element;

d) at least one poly(A) sequence;

e) at least one poly(C) sequence;

f) at least one 3'-UTR element;

or any combinations of these; and/or~~.~~

~~33. The composition any one of **claims 22 to 32**,~~ wherein the least one coding RNA comprises a 5'-CAP structure, preferably m7G, CAP0, CAP1, CAP2, a modified CAP0 or a modified CAP1 structure; and/or~~.~~

~~34. The composition of any one of **claims 22 to 33**,~~ wherein the at least one coding RNA comprises at least one heterologous 5'-UTR and/or at least one heterologous 3'-UTR, preferably wherein the at least one heterologous 5'-UTR comprises a nucleic acid sequence derived from a 5'-UTR of a gene selected from HSD17B4, RPL32, ASAH1, ATP5A1, MP68, NDUFA4, NOSIP, RPL31, SLC7A3, TUBB4B and UBQLN2, or from a homolog, a fragment or variant of any one of these genes; and/or

preferably wherein the at least one heterologous 3'-UTR comprises a nucleic acid sequence derived from a 3'-UTR of a gene selected from PSMB3, ALB7, alpha-globin, CASP1, COX6B1, GNAS, NDUFA1 and RPS9, or from a homolog, a fragment or a variant of any one of these genes; and/or~~.~~

~~35. The composition of any one of **claims 22 to 34**,~~ wherein the at least one coding RNA comprises a (i) HSD17B4 5'-UTR and a PSMB3 3'-UTR or (ii) a RPL32 5'-UTR and an ALB7 3'-UTR; and/or~~.~~

~~36. The composition of any one of **claims 22 to 35**,~~ comprising the following elements in the 5' to 3' direction:

a) a 5’-CAP structure, preferably selected from the group consisting of m7G(5’), m7G(5')ppp(5')(2'OMeA) and m7G(5')ppp(5')(2'OMeG);

b) a 5'-UTR element comprising a nucleic acid sequence derived from the 5'-UTR of a TOP gene, said nucleic acid sequence preferably comprising an RNA sequence that corresponds to the nucleic acid sequence according to SEQ ID NO:22, 24, 26, or a homolog, a fragment or a variant thereof;

c) at least one coding sequence;

d) a 3'-UTR element comprising a nucleic acid sequence derived from an α-globin gene, said nucleic acid sequence preferably comprising an RNA sequence that corresponds to the nucleic acid sequence according to SEQ ID NO:6, 8, 10, 12, 14, 16, 18, 20, or a homolog, a fragment or a variant thereof; and/or a 3'-UTR element comprising a nucleic acid sequence derived from an albumin gene, said nucleic acid sequence preferably comprising an RNA sequence that corresponds to the nucleic acid sequence according to SEQ ID NO:18, or a homolog, a fragment or a variant thereof;

e) optionally, at least one poly(A) sequence, preferably consisting of 10 to 200, 10 to 100, 40 to 80, or 50 to 70 adenosine nucleotides;

f) optionally, at least one poly(C) sequence, preferably consisting of 10 to 200, 10 to 100, 20 to 70, 20 to 60 or 10 to 40 cytosine nucleotides; and

g) optionally, at least one histone stem-loop, preferably comprising the RNA sequence according to SEQ ID NO:4; and/or.

37. The composition of any one of **claims 21 to 36,** wherein the biologically active ingredient is

(a) an mRNA comprising at least one coding sequence encoding a peptide or protein, or a fragment or variant thereof, wherein the peptide or protein is an antigen, wherein the antigen preferably is derived from pathogenic antigens, tumour antigens, allergenic antigens or autoimmune self-antigens, or a fragment or variant thereof; or

(b) an mRNA comprising at least one coding sequence encoding a therapeutic protein, or a fragment or variant thereof, wherein the therapeutic protein is selected from the group consisting of

(i) therapeutic proteins for which are used in enzyme replacement therapy for the treatment of metabolic, endocrine or amino acid disorders or for use in replacing an absent, deficient or mutated protein;

(ii) therapeutic proteins for which are used in the treatment of blood disorders, diseases of the circulatory system, diseases of the respiratory system, infectious diseases or immune deficiencies;

(iii) therapeutic proteins for which are used in the treatment of cancer or tumour diseases;

(iv) therapeutic proteins for which are used in hormone replacement therapy;

(v) therapeutic proteins ~~for~~ which are used in reprogramming somatic cells into pluri- or omnipotent stem cells;

(vi) therapeutic proteins ~~for~~ which are used as adjuvant or immunostimulation;

(vii) therapeutic proteins being a therapeutic antibody;

(viii) therapeutic proteins being a gene editing agent; and

(ix) therapeutic proteins ~~for~~ which are used in treating or preventing a liver disease selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; ~~.~~

~~38. The composition of **claim 37 subitem (a),**~~ wherein the antigen of subitem (a) encodes a pathogenic antigen selected from the group consisting of a bacterial, viral, fungal and protozoal antigen; ~~.~~

~~39. The composition of **claim 38**,~~ wherein the pathogenic antigen is preferably derived from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV), Bunyavirales virus, Cytomegalovirus (CMV), Dengue viruses (DEN-1, DEN-2, DEN-3 and DEN-4), Ebola virus, Flavivirus, Hepatitis B virus (HBV), Herpes simplex virus (HSV), Human immunodeficiency virus (HIV), Human metapneumovirus (hMPV), Human Papilloma virus (HPV), Human parainfluenza viruses (HPIV), Influenza virus, extraintestinal pathogenic E. coli, Lassa mammarenavirus (LASV), MERS coronavirus, Mycobacterium tuberculosis, Nipah virus, Norovirus, Rabies virus, Respiratory Syncytial Virus (RSV), Rhinovirus, Rota virus, Vaccinia virus, Yellow Fever Virus, Zika virus, Chlamydia trachomatis (i.e. bacterium chlamydia causing chlamydia), or Malaria parasite (e.g. Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, or Plasmodium ovale).

~~40.~~23. Use of ~~T~~the composition of any one of **claims 14~~15~~ to 22~~39~~** in the manufacture of a medicament ~~for use~~

(i) in the treatment or prophylaxis of infectious diseases; cancer or tumour diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease; disorder or condition; and/or

(ii) for ~~use in~~ enzyme replacement therapy ~~for~~ in ~~the~~ treating~~ment of~~ metabolic or endocrine disorders ~~or for use in replacing an absent, deficient or mutated protein~~; ~~.~~

~~41. The composition of any one of **claims 15 to 39** for use in the treatment or prophylaxis of infectious diseases.~~

42. tThe composition for the use of **claims 40 or 41** preferably comprising at least one coding RNA, wherein said at least one coding RNA comprises at least one coding sequence encoding at least one peptide or protein for use in treatment or prevention of a disease, disorder or condition, wherein said composition is to be administered via intramuscular or intradermal injection a subject in need thereof.

43.24. A kit or kit of parts, comprising any one of the compositions of **claims 1821 to 2342**, optionally comprising a liquid vehicle for solubilizing, and, optionally, technical instructions providing information on administration and dosage of the components.

44.25. The composition of any one of **claims 1821 to 2342** or the kit or kit of parts of **claim 2443** for use as a medicament.

45. The composition for use as a medicament according to **claim 44**, wherein the medicament is for the prevention, prophylaxis, treatment and/or amelioration of a disease selected from infectious diseases including viral, bacterial or protozoological infectious diseases, cancer or tumour diseases, liver diseases, autoimmune diseases, allergies, monogenetic diseases including hereditary diseases, genetic diseases in general, diseases which have a genetic inherited background and which are typically caused by a defined gene defect and are inherited according to Mendel's laws; cardiovascular diseases, neuronal diseases, diseases of the respiratory system, diseases of the digestive system, diseases of the skin, musculoskeletal disorders, disorders of the connective tissue, neoplasms, immune deficiencies, endocrine, nutritional and metabolic diseases, eye diseases, ear diseases and diseases associated with a peptide or protein deficiency.

46. The composition for use as a medicament according to **claims 44 or 45**, wherein the medicament is a vaccine.

47.26. A vaccine comprising a composition Use of any one of **claims 1415 to 2342** or a kit or kit of parts of **claim 2443** in the manufacture of a vaccine for prevention, prophylaxis, treatment and/or amelioration of a disease selected from infectious diseases including viral, bacterial or protozoological infectious diseases, cancer or tumour diseases.

48. A method of treatment or prophylaxis of infectious diseases; cancer or tumour diseases, disorders or conditions; liver diseases selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer; allergies; or autoimmune disease; disorder or condition comprising the steps:

~~a) providing the mRNA as described in **any one of the above claims**, the composition as described in **any one of the above claims**, the vaccine of **claim 47**, the kit or kit of parts of **claim 43**; and~~

~~b) applying or administering the mRNA, the composition, the vaccine or the kit or kit of parts to a tissue or an organism.~~

~~49. The method according to **claim 48**, wherein the mRNA, the composition any one of **claims 15 to 42**, the vaccine of **claim 47** or the kit or kit of parts of **claim 43** is administered to the tissue or to the organism by intravenous, intramuscular, subcutaneous or intradermal injection.~~

~~50. A method of inducing an immune response in a subject, the method comprising administering to the subject the vaccine of **claim 47** in an amount effective to produce an antigen-specific immune response in the subject.~~

~~51.~~27. A pharmaceutical composition comprising a composition of any one of **claims 14~~15~~ to 23~~42~~** or a kit or kit of parts of **claim 24~~43~~** for use as a medicament in vaccination of a subject comprising an effective dose of mRNA encoding a virus antigen.

~~52. Use of a pharmaceutical composition comprising a composition of any one of **claims 15 to 42** or a kit or kit of parts of **claim 43** for (i) inducing an immune response, for (ii) inducing an antigen specific T-cell response or preferably for (iii) inducing CD8+ T cells responses.~~

~~53. Use of the pharmaceutical composition of **claim 52** for the prophylaxis of an infectious disease or in the manufacture of a medicament for the prophylaxis of an infectious disease, wherein said medicament preferably is a vaccine.~~

~~54. A method for preventing, ameliorating or treating a disease or condition in a subject in need comprising administering to the subject a composition of any one of **claims 15 to 42** or a kit or kit of parts of **claim 43**.~~

~~55. The method of any one of the **claims 48 to 50 and 54**, wherein administration of the composition results in expression of the antigen encoded by mRNA in the lymphocytes of the subject.~~

~~56. The method of any one of the **claims 48 to 50, 54 and 55**, wherein the administration of the composition results in an antigen specific antibody response,~~

~~preferably wherein the antigen specific antibody response is measured by the presence of antigen-specific antibodies in serum.~~

~~57. The composition of any one of **claims 15 to 39**, wherein the composition comprises a neutral lipid or phospholipid having at least one alkyl chain with a length of C5, C6, C7, C8, C9, C10, C11, C12, C13 or C14, preferably with a length of C6, C7, C8, C9, or C10, more preferably with a length of C6, C7, C8, most preferably with a length of C7, or further most preferably wherein the composition comprises a combination of two neutral lipids wherein the combination comprises a neutral lipid or phospholipid having at least two alkyl chains, whereby each alkyl chain independently has a length of preferably C6, C7, C8, C9, or C10, more preferably with a length of C6, C7, C8, most preferably with a length of C7, further most preferably a phospholipid selected from the group consisting of DHPC (1,2-diheptanoyl-sn-glycero-3-phosphocholine), 05:0 PC (1,2-dipentanoyl-sn-glycero-3-phosphocholine), 04:0 PC (1,2-dibutyryl-sn-glycero-3-phosphocholine), 06:0 PC (DHPC, 1,2-dihexanoyl-sn-glycero-3-phosphocholine), 08:0 PC (1,2-dioctanoyl-sn-glycero-3-phosphocholine), and 09:0 PC (1,2-dinonanoyl-sn-glycero-3-phosphocholine).~~

~~58. The composition of any one of **claims 15 to 39**, wherein the composition comprise a neutral lipid or phospholipid having at least two alkyl chains, whereby each alkyl chain independently has a length of C5, C6, C7, C8, C9, C10, C11, C12, C13 or C14, preferably with a length of C6, C7, C8, C9, or C10, more preferably with a length of C6, C7, C8, most preferably with a length of C7, or further most preferably wherein the composition comprises a combination of two neutral lipids wherein the combination comprises a neutral lipid or phospholipid having at least two alkyl chains, whereby each alkyl chain independently has a length of preferably C6, C7, C8, C9, or C10, more preferably with a length of C6, C7, C8, most preferably with a length of C7, further most preferably a phospholipid selected from the group consisting of DHPC (1,2-diheptanoyl-sn-glycero-3-phosphocholine), 05:0 PC (1,2-dipentanoyl-sn-glycero-3-phosphocholine), 04:0 PC (1,2-dibutyryl-sn-glycero-3-phosphocholine), 06:0 PC (DHPC, 1,2-dihexanoyl-sn-glycero-3-phosphocholine), 08:0 PC (1,2-dioctanoyl-sn-glycero-3-phosphocholine), and 09:0 PC (1,2-dinonanoyl-sn-glycero-3-phosphocholine).~~