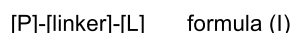


SUMMARY

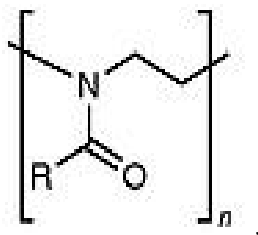
In one example, the present disclosure relates to novel polymer conjugated lipids which are useful for the delivery of nucleic acids into living cells.

- 5 In a specific example, the polymer conjugated lipids are compounds according to formula (I):



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

[P] is a homopolymer moiety comprising at least one polyoxazoline (POZ) monomer unit



10

wherein R is C1-9 alkyl or C2-9 alkenyl, preferably C1 or C2 alkyl, and n has a mean value ranging from about 45 to about 55, preferably n is about 50 or wherein n is selected such that the [P] moiety has an average molecular weight of about 4.2 kDa to about 4.4 kDa, or most preferably about 4.3 kDa

- 15 [linker] is an optional linker group, and

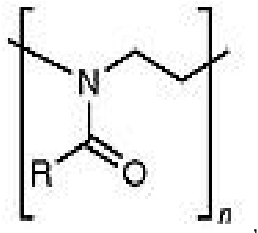
[L] is a lipid moiety.

In an aspect, there is provided a polymer conjugated lipid according to formula (I):

- 20 [P]-[linker]-[L] formula (I)

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

[P] is a heteropolymer moiety or homopolymer moiety, preferably a homopolymer moiety, comprising at least one polyoxazoline (POZ) monomer unit



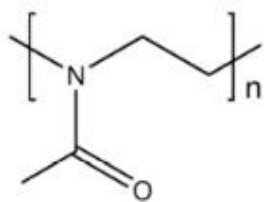
25

wherein R is C1-9 alkyl or C2-9 alkenyl, preferably C1 or C2 alkyl, and n has a mean value ranging from 45 to 55, preferably n is 50 or wherein n is selected such that the [P] moiety has an average molecular weight of 4.4 kDa, or most preferably 4.3 kDa

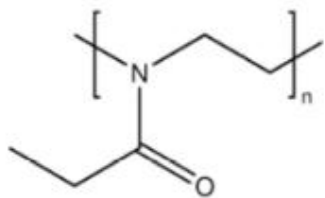
[linker] is an optional linker group, and

- 30 [L] is a lipid moiety.

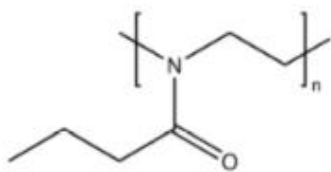
In another example, the polymer conjugated lipid comprises as [P] a heteropolymer moiety or homopolymer moiety comprising multiple monomer units selected from the group consisting of poly(2-methyl-2-oxazoline) (PMOZ)



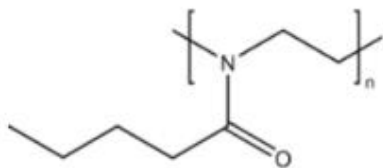
5 poly(2-ethyl-2-oxazoline) (PEOZ)



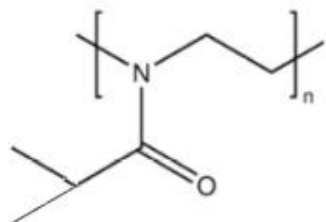
poly(2-propyl-2-oxazoline) (PPOZ)



poly(2-butyl-2-oxazoline) (PBOZ)



poly(2-isopropyl-2-oxazoline) (PIPOZ)



5

poly(2-methoxymethyl-2-oxazoline) (PMeOMeOx), and

poly(2-dimethylamino-2-oxazoline) (PDMAOx),

preferably wherein [P] is a homopolymer moiety comprising multiple PMOZ or PEOZ monomer units, more preferably wherein [P] comprises or preferably consists of multiple PMOZ monomer units,

10 wherein

(i) n has a mean value ranging from about 45 to about 55, preferably n is about 50 or wherein

(ii) n is selected such that the [P] moiety has an average molecular weight of about 4.2 kDa to about 4.4 kDa, or most preferably about 4.3 kDa.

15 In very preferred examples, the homopolymer moieties [P] are selected from the group consisting of PMeOz50 (polymethyloxazoline or poly(2-methyl-2-oxazoline) with 50 repeats), PEtOz50 (polyethyloxazoline with 50 repeats), PMeOz25 (polymethyloxazoline with 25 repeats) and PEtOz25 (polyethyloxazoline with 25 repeats), preferably PMeOz50 (polymethyloxazoline or poly(2-methyl-2-oxazoline) with 50 repeats).

20 In another example, the polymer conjugated lipid is selected from the group consisting of a POZ-monoacylglycerol conjugate, POZ-diacylglycerol conjugate, a POZ-dialkyloxypropyl conjugate, a POZ-steroid or POZ-sterol conjugate, a POZ-phospholipid conjugate, a POZ-ceramide conjugate, and a mixture thereof. In a further example, the lipid moiety [L] comprises at least one straight or branched, saturated or unsaturated alkyl chain containing from 6 to 30 carbon atoms, preferably wherein the lipid moiety [L] comprises at least one straight or branched saturated

25 alkyl chain, wherein the alkyl chain is optionally interrupted by one or more biodegradable group(s) and/or optionally comprises one terminal biodegradable group, wherein the biodegradable group is selected from the group consisting of but not limited to a pH-sensitive moiety, an alkyl or alkenyl moiety (C₁₋₉ alkyl or C₂₋₉ alkenyl), a zwitterionic linker, non-ester containing linker moieties and ester-containing linker moieties (—C(O)O— or —OC(O)—), amido (—C(O)NH—), disulfide (—S—S—), carbonyl (—C(O)—), ether (—O—), thioether (—S—), oxime

30 (e.g., —C(H)=N—O— or —O—N=C(H)—), carbamate (—NHC(O)O—), urea (—NHC(O)NH—),

succinyl ($-(O)CCH_2CH_2C(O)-$), succinamidyl ($-(NHC(O)CH_2CH_2C(O)NH)-$), ($-(NHC(O)CH_2CH_2C(O)-$), $-C(R^5)=N-$, $-N=C(R^5)-$, $-C(R^5)=N-O-$, $-O-N=C(R^5)-$, $-O-C(O)O-$, $-C(O)N(R^5)-$, $-N(R^5)C(O)-$, $-C(S)(NR^5)-$, $(NR^5)C(S)-$, $-N(R^5)C(O)N(R^5)-$, $-C(O)S-$, $-SC(O)-$, $-C(S)O-$, $-OC(S)-$, $-OSi(R^5)_2O-$, $-C(O)(CR^3R^4)C(O)O-$, or $-OC(O)(CR^3R^4)C(O)-$, carbonate ($-OC(O)O-$), nitrogen (N), succinoyl, succinate, phosphate esters ($-O-(O)POH-O-$), cyclic compound, heterocyclic compound, piperidine, pyrazine, pyridine, piperazine, and sulfonate esters, as well as combinations thereof, wherein R^3 , R^4 and R^5 are, independently H or alkyl (e.g. C₁-C₄ alkyl).

In a further example, the lipid moiety [L] comprises two straight unsaturated alkyl chain containing from 6 to 30 carbon atoms, preferably wherein the lipid moiety [L] comprises at least one straight or branched saturated alkyl chain, wherein the alkyl chain is optionally interrupted by one or more biodegradable group(s) and/or optionally comprises one terminal biodegradable group, wherein the biodegradable group is selected from the group consisting of but not limited to a pH-sensitive moiety, an alkyl or alkenyl moiety (C₁₋₉ alkyl or C₂₋₉ alkenyl), a zwitterionic linker, non-ester containing linker moieties and ester-containing linker moieties ($-C(O)O-$ or $-OC(O)-$), amido ($-C(O)NH-$), disulfide ($-S-S-$), carbonyl ($-C(O)-$), ether ($-O-$), thioether ($-S-$), oxime (e.g., $-C(H)=N-O-$ or $-O-N=C(H)-$), carbamate ($-NHC(O)O-$), urea ($-NHC(O)NH-$), succinyl ($-(O)CCH_2CH_2C(O)-$), succinamidyl ($-(NHC(O)CH_2CH_2C(O)NH)-$), ($-(NHC(O)CH_2CH_2C(O)-$), $-C(R^5)=N-$, $-N=C(R^5)-$, $-C(R^5)=N-O-$, $-O-N=C(R^5)-$, $-O-C(O)O-$, $-C(O)N(R^5)-$, $-N(R^5)C(O)-$, $-C(S)(NR^5)-$, $(NR^5)C(S)-$, $-N(R^5)C(O)N(R^5)-$, $-C(O)S-$, $-SC(O)-$, $-C(S)O-$, $-OC(S)-$, $-OSi(R^5)_2O-$, $-C(O)(CR^3R^4)C(O)O-$, or $-OC(O)(CR^3R^4)C(O)-$, carbonate ($-OC(O)O-$), nitrogen (N), succinoyl, succinate, phosphate esters ($-O-(O)POH-O-$), cyclic compound, heterocyclic compound, piperidine, pyrazine, pyridine, piperazine, and sulfonate esters, as well as combinations thereof, wherein R^3 , R^4 and R^5 are, independently H or alkyl (e.g. C₁-C₄ alkyl).

In a further example, the lipid moiety [L] comprises two straight unsaturated alkyl chain each containing 14 carbon atoms.

In a further most preferred example, the polymer conjugated lipid comprises a lipid moiety [L] comprising ditetradecylamin and a linker group [linker], preferably wherein the linker group [linker] is ($-NHC(O)CH_2CH_2C(O)-$). In a further preferred example, the lipid moiety [L] comprises ditetradecylamin, wherein the linker moiety [linker], preferably ($-NHC(O)CH_2CH_2C(O)-$), is forming an amide connection by connection to the N-atom of ditetradecylamin. In most preferred examples, the polymer conjugated lipid comprises a linker ($-NHC(O)CH_2CH_2C(O)-$), wherein the linker is orientated in such way, that an carboxamide connection is formed through connection to the N-atom of ditetradecylamin.

In a further most preferred example, the polymer conjugated lipid comprises a lipid moiety [L] comprising ditetradecylamin and a linker group [linker], preferably wherein the linker group [linker] is ($C(O)CH_2CH_2C(O)NH$). In a further preferred example, the lipid moiety [L] comprises ditetradecylamin, wherein the linker moiety [linker], preferably ($-NHC(O)CH_2CH_2C(O)-$), is forming an amide connection by connection to the N-atom of ditetradecylamin.

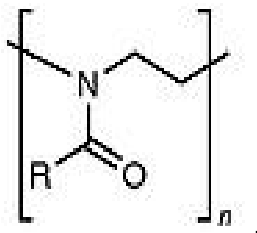
In a further preferred example, the lipid moiety [L] is the lipid moiety as used in "PMOZ 2".

In a further preferred example, the linker moiety [linker] is the linker moiety as used in "PMOZ 2".

In further most preferred example, the disclosure relates to a polymer conjugated lipid having a lipid moiety [L], being the lipid moiety as used in "PMOZ 4". In another most preferred example, the disclosure relates to a polymer conjugated lipid having a linker moiety [linker], being the linker as used in "PMOZ 4".

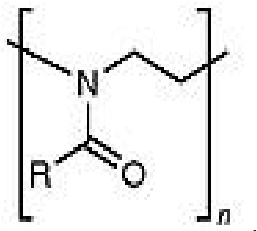
- 5 comprises ditetradecylamin, preferably wherein the linker group [linker] is ($\text{—NHC(O)CH}_2\text{CH}_2\text{C(O)—}$). In a preferred example, the lipid moiety [L] comprises ditetradecylamin, wherein the linker moiety [linker] is connected to the N-atom of ditetradecylamin.

- 10 In another example, the disclosure provides novel lipid nanoparticles comprising a homopolymer moiety comprising at least one polyoxazoline (POZ) monomer unit



- wherein R is C₁-9 alkyl or C₂-9 alkenyl, preferably C₁ or C₂ alkyl, and n has a mean value ranging from about 45 to about 55, preferably n is about 50 or wherein n is selected such that the [P] moiety has an average molecular weight of about 4.2 kDa to about 4.4 kDa, or most preferably about 4.3 kDa,
- 15 preferably, wherein the homopolymer moiety comprising multiple monomer units comprises poly(2-methyl-2-oxazoline) (PMOZ), poly(2-ethyl-2-oxazoline) (PEOZ), poly(2-propyl-2-oxazoline) (PPOZ), poly(2-butyl-2-oxazoline) (PBOZ), poly(2-isopropyl-2-oxazoline) (PIPOZ), poly(2-methoxymethyl-2-oxazoline) (PMeOMeOx), or poly(2-dimethylamino-2-oxazoline) (PDMAOx).

- 20 In another aspect, there is provided a lipid nanoparticle comprising a homopolymer moiety comprising at least one polyoxazoline (POZ) monomer unit



- wherein R is C₁-C₉ alkyl or C₂-C₉ alkenyl, preferably C₁ or C₂ alkyl, and n has a mean value ranging from 45 to 55, preferably n is 50 or wherein n is selected such that the [P] moiety has an average molecular weight of 4.2 kDa to 4.4 kDa, or most preferably 4.3 kDa,
- 25 preferably, wherein the homopolymer moiety comprising multiple monomer units comprises poly(2-methyl-2-oxazoline) (PMOZ), poly(2-ethyl-2-oxazoline) (PEOZ), poly(2-propyl-2-oxazoline) (PPOZ), poly(2-butyl-2-oxazoline) (PBOZ), poly(2-isopropyl-2-oxazoline) (PIPOZ), poly(2-methoxymethyl-2-oxazoline) (PMeOMeOx), or poly(2-dimethylamino-2-oxazoline) (PDMAOx),
- 30 more preferably the polymer conjugated lipid as defined above.

Most preferably, R is C₁ (i.e. CH₃ or methyl), yielding in polymethyloxazoline or poly(2-methyl-2-oxazoline) i.e. "PMOZ".

In further examples, the disclosure provides vaccine compositions comprising the lipid nanoparticle of the disclosure, or a kit or kit of parts comprising the inventive polymer conjugated lipids for use as a medicament, and/or for prevention, prophylaxis, treatment and/or amelioration of a disease selected from infectious diseases including viral, bacterial or protozoological infectious diseases, cancer or tumor diseases.

5

In a further example, the disclosure provides methods of treatment or prophylaxis of infectious diseases; cancer or tumor 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 a lipid nanoparticle, comprising a homopolymer moiety comprising at least one polyoxazoline (POZ) monomer, preferably the polymer conjugated lipid of the disclosure, the vaccine composition, or the kit or kit of parts of the disclosure; and
- b) applying or administering the mRNA, the lipid nanoparticle, the vaccine composition or the kit or kit of parts to a tissue or an organism.

10

15 In another aspect, there is provided the use of the lipid nanoparticle as defined above in the manufacture of a medicament

(i) in the treatment or prophylaxis of infectious diseases; cancer or tumor 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

20

(ii) for use in enzyme replacement therapy for the treatment of metabolic or endocrine disorders; 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 lipid nanoparticle is to be administered via local or locoregional injection,

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infusion or implantation, in particular intradermal, subcutaneous, intramuscular, intracameral, subconjunctival, suprachoroidal injection, subretinal, subtenon, retrobulbar, topical, posterior juxtasceral administration, or intrapulmonary inhalation, interstitial, locoregional, intravitreal, intratumoral, intralymphatic, intranodal, intra-articular, intrasynovial, periarticular, intraperitoneal, intra-abdominal, intracardial, intralesional, intrapericardial, intraventricular, intrapleural, perineural, intrathoracic, epidural, intradural, peridural, intrathecal, intramedullary, intracerebral, intracavernous, intracorporus cavernosum, intraprostatic, intratesticular, intracartilaginous, intraosseous, intradiscal, intraspinal, intracaudal, intrabursal, intralingival, intraovarian, intrauterine, intraocular, periocular, periodontal, retrobulbar, subarachnoid, subconjunctival, suprachoroidal injection, infusion, implantation, nasal, buccal, sublingual, otic or auricular, ophthalmic, conjunctival, vaginal, rectal, intracervical, endosinusal, laryngeal, oropharyngeal, ureteral, urethral administration, more preferably said lipid nanoparticle is administered intramuscularly, intravenously, intradermally, subcutaneously, intratumorally, intranasally, or by inhalation, most preferably intramuscularly, to a subject in need thereof.

30

35

In another example of the present disclosure, the present disclosure also provides a pharmaceutical composition comprising a lipid nanoparticle of the disclosure, a kit or kit of parts of the disclosure, or the vaccine composition of the disclosure for use in vaccination of a subject comprising an effective dose of mRNA encoding a virus antigen.

40

In another aspect, there is provided a kit or kit of parts, comprising any one of the lipid nanoparticle as defined above, optionally comprising a liquid vehicle for solubilizing, and, optionally, technical instructions providing information on administration and dosage of the components.

- 5 In another aspect, there is provided the use as defined above or a kit or kit of parts as defined above in the manufacture of a medicament, for prevention, prophylaxis, treatment and/or amelioration of a disease selected from infectious diseases including viral, bacterial or protozoological infectious diseases, cancer or tumor diseases.

- 10 In another aspect, there is provided a pharmaceutical composition comprising a lipid nanoparticle as defined above or a kit or kit of parts as defined above for use as a medicament in vaccination of a subject comprising an effective dose of mRNA encoding a virus antigen.

In yet another example of the disclosure, the present disclosure provides improved lyophilizable lipid nanoparticles, which have advantageous physiochemical properties after being lyophilized and reconstituted.

5 In yet another example of the disclosure, the present disclosure provides improved lipid nanoparticles, which have advantageous physiochemical properties after being frozen and thawed.

10 In another aspect, there is provided a lipid nanoparticle comprising a polymer conjugated lipid as defined above, wherein the lipid nanoparticle has a lower PDI and/or lower size upon (i) freezing and thawing or (ii) freeze-drying (lyophilizing) and reconstitution, as compared to a control lipid nanoparticle comprising a PEG-lipid instead said polymer conjugated lipid as defined above.

15 In another aspect, there is provided a method of making a frozen lipid nanoparticle as defined above or a lipid nanoparticle comprising a polymer conjugated lipid as defined above, wherein the lipid nanoparticle upon thawing has a lower PDI and/or lower size as compared to a control lipid nanoparticle comprising a PEG-lipid instead of a polymer conjugated lipid as defined above.

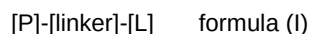
20 In another aspect, there is provided a method of making a lyophilized lipid nanoparticle as defined above or a lipid nanoparticle comprising a polymer conjugated lipid as defined above, wherein the lipid nanoparticle upon reconstitution has a lower PDI and/or lower size as compared to a control lipid nanoparticle comprising a PEG-lipid instead of a polymer conjugated lipid as defined above.

25 In another aspect, there is provided an improved lyophilization process for the preparation of lyophilized lipid nanoparticles as defined above, said process comprising the step of using a polymer conjugated lipid as defined above as excipient instead of a PEG-lipid, wherein the lipid nanoparticle upon reconstitution has a lower PDI and/or lower size as compared to a control lipid nanoparticle comprising a PEG-lipid instead of a polymer conjugated lipid as defined above.

30 In another aspect, there is provided a vaccine composition, comprising a lipid nanoparticle as defined above or a polymer conjugated lipid as defined above.

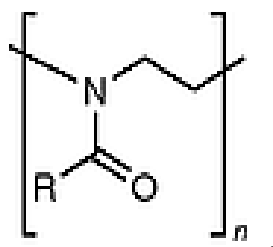
CLAIMS

1. A polymer conjugated lipid according to formula (I):



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

[P] is a heteropolymer moiety or homopolymer moiety, preferably a homopolymer moiety, comprising at least one polyoxazoline (POZ) monomer unit



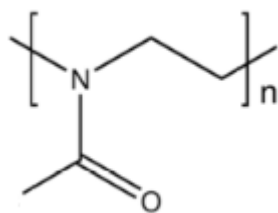
wherein R is C1-9 alkyl or C2-9 alkenyl, preferably C1 or C2 alkyl, and n has a mean value ranging from 45 to 55, preferably n is 50 or wherein n is selected such that the [P] moiety has an average molecular weight of 4.4 kDa, or most preferably 4.3 kDa

[linker] is an optional linker group, and

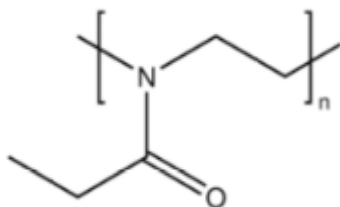
[L] is a lipid moiety.

2. The polymer conjugated lipid of **claim 1**, wherein [P] is a heteropolymer moiety or homopolymer moiety comprising multiple monomer units selected from the group consisting of

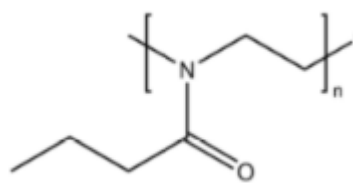
poly(2-methyl-2-oxazoline) (PMOZ)



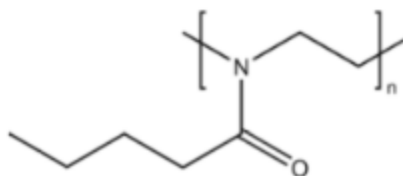
poly(2-ethyl-2-oxazoline) (PEOZ)



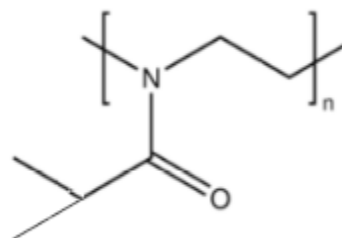
poly(2-propyl-2-oxazoline) (PPOZ)



poly(2-butyl-2-oxazoline) (PBOZ)



poly(2-isopropyl-2-oxazoline) (PIPOZ)



poly(2-methoxymethyl-2-oxazoline) (PMeOMeOx), and

poly(2-dimethylamino-2-oxazoline) (PDMAOx),

preferably wherein [P] is a homopolymer moiety comprising multiple PMOZ or PEOZ monomer units, more preferably wherein [P] comprises or preferably consists of multiple PMOZ monomer units,

wherein

(i) n has a mean value ranging from 45 to 55, preferably n is 50 or wherein

(ii) n is selected such that the [P] moiety has an average molecular weight of 3 kDa to 6 kDa, preferably an average molecular weight of 4.2 kDa to 4.4 kDa, or most preferably 4.3 kDa.

3. The polymer conjugated lipid of any one of **claim 1 to claim 2**, wherein the polymer conjugated lipid is selected from the group consisting of a POZ-monoacylglycerol conjugate, POZ-diacylglycerol conjugate, a POZ-dialkyloxypropyl conjugate, a POZ-steroid or POZ-sterol conjugate, a POZ-phospholipid conjugate, a POZ-ceramide conjugate, and a mixture thereof.

4. The polymer conjugated lipid of any one of **claim 1 to claim 3**, wherein
(i) the lipid moiety [L] comprises at least one straight or branched, saturated or unsaturated alkyl chain containing from 6 to 30 carbon atoms, preferably wherein the lipid moiety [L] comprises at least one straight or branched saturated alkyl chain,

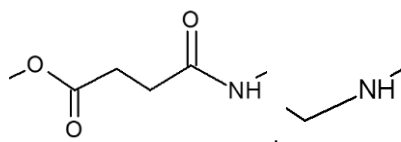
wherein the alkyl chain is optionally interrupted by one or more biodegradable group(s) and/or optionally comprises one terminal biodegradable group, wherein the biodegradable group is selected from the group consisting of but not limited to a pH-sensitive moiety, an alkyl or alkenyl moiety (C₁₋₉ alkyl or C₂₋₉ alkenyl), a zwitterionic linker, non-ester containing linker moieties and ester-containing linker moieties (—C(O)O— or —OC(O)—), amido (—C(O)NH—), disulfide (—S—S—), carbonyl (—C(O)—), ether (—O—), thioether (—S—), oxime (e.g., —C(H)=N—O— or —O—N=C(H)—), carbamate (—NHC(O)O—), urea (—NHC(O)NH—

), succinyl $(-\text{O})\text{CCH}_2\text{CH}_2\text{C}(\text{O})-$, succinamidyl $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})\text{NH}-)$, $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})-)$, $-\text{C}(\text{R}^5)=\text{N}-$, $-\text{N}=\text{C}(\text{R}^5)-$, $-\text{C}(\text{R}^5)=\text{N}-\text{O}-$, $-\text{O}-\text{N}=\text{C}(\text{R}^5)-$, $-\text{O}-\text{C}(\text{O})\text{O}-$, $-\text{C}(\text{O})\text{N}(\text{R}^5)-$, $-\text{N}(\text{R}^5)\text{C}(\text{O})-$, $-\text{C}(\text{S})(\text{NR}^5)-$, $(\text{NR}^5)\text{C}(\text{S})-$, $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{N}(\text{R}^5)-$, $-\text{C}(\text{O})\text{S}-$, $-\text{SC}(\text{O})-$, $-\text{C}(\text{S})\text{O}-$, $-\text{OC}(\text{S})-$, $-\text{OSi}(\text{R}^5)_2\text{O}-$, $-\text{C}(\text{O})(\text{CR}^3\text{R}^4)\text{C}(\text{O})\text{O}-$, or $-\text{OC}(\text{O})(\text{CR}^3\text{R}^4)\text{C}(\text{O})-$, carbonate $(-\text{OC}(\text{O})\text{O}-)$, nitrogen (N), succinoyl, succinate, phosphate esters $(-\text{O}-\text{O}-\text{POH}-\text{O}-)$, cyclic compound, heterocyclic compound, piperidine, pyrazine, pyridine, piperazine, and sulfonate esters, as well as combinations thereof, wherein R^3 , R^4 and R^5 are, independently H or alkyl (e.g. C_1 - C_4 alkyl), or (ii) the lipid moiety [L] comprises ditetradecylamin, preferably wherein the linker group [linker] is $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})-)$.

5. The polymer conjugated lipid of any one of **claim 1 to claim 4**, wherein the lipid moiety [L] comprises at least one, preferably two, straight or branched, saturated or unsaturated alkyl chain comprising 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 carbon atoms, preferably in the range of 10 to 20 carbon atoms, more preferably in the range of 12 to 18 carbon atoms, even more preferably 14, 16 or 18 carbon atoms, even more preferably 16 or 18 carbon atoms, most preferably 14 carbon atoms, wherein all selections are independent of one another.

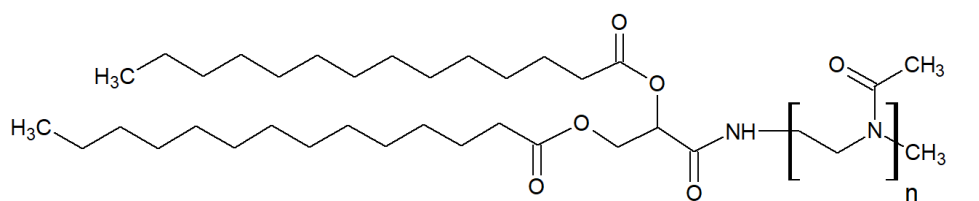
6. The polymer conjugated lipid of any one of **claim 1 to claim 5**, wherein the linker group [linker] is selected from the group consisting of but not limited to a pH-sensitive moiety, a peptide or amid bond $(-\text{CO}-\text{NH}-)$, an alkyl or alkenyl moiety (C_{1-9} alkyl or C_{2-9} alkenyl), a zwitterionic linker, non-ester containing linker moieties and ester-containing linker moieties $(-\text{C}(\text{O})\text{O}-$ or $-\text{OC}(\text{O})-)$, amido $(-\text{C}(\text{O})\text{NH}-)$, disulfide $(-\text{S}-\text{S}-)$, carbonyl $(-\text{C}(\text{O})-)$, ether $(-\text{O}-)$, thioether $(-\text{S}-)$, oxime (e.g., $-\text{C}(\text{H})=\text{N}-\text{O}-$ or $-\text{O}-\text{N}=\text{C}(\text{H})-$), carbamate $(-\text{NHC}(\text{O})\text{O}-)$, urea $(-\text{NHC}(\text{O})\text{NH}-)$, succinyl $(-\text{O})\text{CCH}_2\text{CH}_2\text{C}(\text{O})-$, succinamidyl $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})\text{NH}-)$, $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})-)$, $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})\text{O}-)$, $-\text{C}(\text{R}^5)=\text{N}-$, $-\text{N}=\text{C}(\text{R}^5)-$, $-\text{C}(\text{R}^5)=\text{N}-\text{O}-$, $-\text{O}-\text{N}=\text{C}(\text{R}^5)-$, $-\text{O}-\text{C}(\text{O})\text{O}-$, $-\text{C}(\text{O})\text{N}(\text{R}^5)-$, $-\text{N}(\text{R}^5)\text{C}(\text{O})-$, $-\text{C}(\text{S})(\text{NR}^5)-$, $(\text{NR}^5)\text{C}(\text{S})-$, $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{N}(\text{R}^5)-$, $-\text{C}(\text{O})\text{S}-$, $-\text{SC}(\text{O})-$, $-\text{C}(\text{S})\text{O}-$, $-\text{OC}(\text{S})-$, $-\text{OSi}(\text{R}^5)_2\text{O}-$, $-\text{C}(\text{O})(\text{CR}^3\text{R}^4)\text{C}(\text{O})\text{O}-$, or $-\text{OC}(\text{O})(\text{CR}^3\text{R}^4)\text{C}(\text{O})-$, carbonate $(-\text{OC}(\text{O})\text{O}-)$, nitrogen (N), succinoyl, succinate, phosphate esters $(-\text{O}-\text{O}-\text{POH}-\text{O}-)$, and sulfonate esters, as well as combinations thereof, wherein R^3 , R^4 and R^5 are, independently H or alkyl (e.g. C_1 - C_4 alkyl), preferably wherein the linker group [linker] is selected from the group consisting of $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})-)$, a peptide bond or amid bond $(-\text{CO}-\text{NH}-)$, $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})\text{O}-)$, and $-\text{NH}-\text{CH}_2-$.

7. The polymer conjugated lipid of any one of **claim 1 to claim 6**, wherein the linker group [linker] comprises an amide linker moiety, preferably an ester linker moiety, or wherein the linker group [linker] comprises

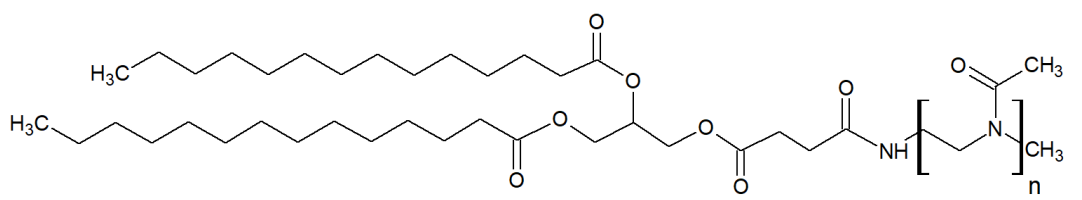


, succinate, a peptide or amid bond $(-\text{CO}-\text{NH}-)$, an amine, or a secondary amine, most preferably wherein the linker group [linker] comprises $(-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{C}(\text{O})-)$.

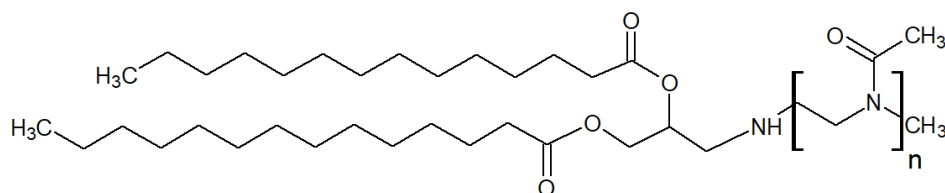
8. The polymer conjugated lipid of any one of **claim 1 to claim 7**, wherein the polymer conjugated lipid is selected from the group consisting of "PMOZ 1":



“PMOZ 2”:

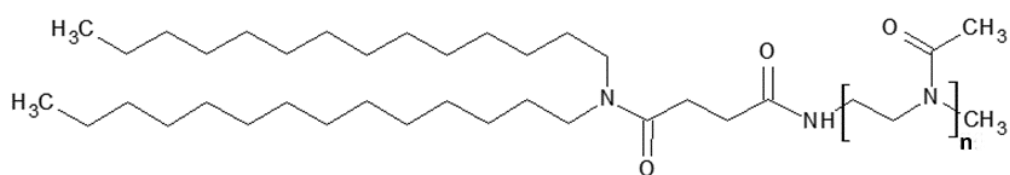


“PMOZ 3”:

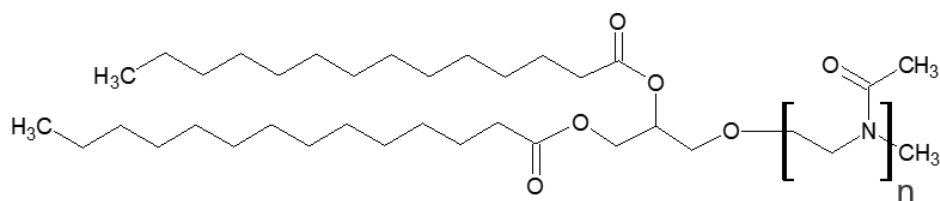


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“PMOZ 4”:



and “PMOZ 5”:



, most preferably the

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polymer conjugated lipid is “PMOZ 4”;

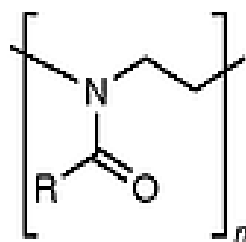
whereby n has a mean value ranging from 2 to 200, preferably from 20 to 100, more preferably from 24 to 26, even more preferably 100, or further even more preferably from 45 to 50, most preferably 50 or

wherein n is selected such that the [P] moiety has an average molecular weight of 3 kDa to 6 kDa, preferably has an average molecular weight of 4.2 kDa to 4.4 kDa, or most preferably 4.3 kDa;

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most preferably wherein the polymer conjugated lipid of any one of **claim 1 to claim 7** is “PMOZ 4” with n having a mean value from 45 to 50, most preferably 50.

9. A lipid nanoparticle comprising a homopolymer moiety comprising at least one polyoxazoline (POZ) monomer unit



wherein R is C₁-C₉ alkyl or C₂-C₉ alkenyl, preferably C₁ or C₂ alkyl, and n has a mean value ranging from 45 to 55, preferably n is 50 or wherein n is selected such that the [P] moiety has an average molecular weight of 4.2 kDa to 4.4 kDa, or most preferably 4.3 kDa,

preferably, wherein the homopolymer moiety comprising multiple monomer units comprises poly(2-methyl-2-oxazoline) (PMOZ), poly(2-ethyl-2-oxazoline) (PEOZ), poly(2-propyl-2-oxazoline) (PPOZ), poly(2-butyl-2-oxazoline) (PBOZ), poly(2-isopropyl-2-oxazoline) (PIPOZ), poly(2-methoxymethyl-2-oxazoline) (PMeOMeOx), or poly(2-dimethylamino-2-oxazoline) (PDMAOx), more preferably the polymer conjugated lipid according to any one of **claim 1 to claim 8**.

10. The lipid nanoparticle of **claim 9**, wherein the lipid nanoparticle further comprises a cationic or ionizable lipid; and/or

wherein the lipid nanoparticles

(i) do not comprise a polyethylene glycol-(PEG)-lipid conjugate or a conjugate of PEG and a lipid-like material, and preferably do not comprise PEG; and/or

(ii) do not comprise a polymer conjugated lipid according to any one of **claim 1 to claim 8** comprising a sulphur group (–S–), a terminating nucleophile, and/or being covalently coupled to a biologically active ingredient being a nucleic acid compound selected from the group consisting of RNA, 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; and/or

wherein the cationic or ionizable lipid preferably carries a net positive charge at physiological pH, more preferably wherein the cationic or ionizable lipid comprises a tertiary nitrogen group or quaternary nitrogen group; and/or

wherein the lipid nanoparticle further comprises a phospholipid, wherein preferably the phospholipid is a zwitterionic compound selected from, but not limited to the group of 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (DPhyPE; 1,2-di-(3,7,11,15-tetramethylhexadecanoyl)-sn-glycero-3-phosphoethanolamine), 1,2-diphytanoyl-sn-glycero-3-phosphocholine (DPhyPC), 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC; dioleoylphosphatidylcholine), 1,2-Dipalmitoyl-sn-glycero-3-phosphocholine (DPPC; dipalmitoylphosphatidylcholine), 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), phosphatidylethanolamines, distearoylphosphatidylcholines, dioleoyl-phosphatidylethanolamine (DOPEA), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE), palmitoyl-oleoylphosphatidylcholine (POPC), palmitoyl-oleoyl-phosphatidylethanolamine (POPE), 1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamine (DPPE), dioleoyl-phosphatidylethanolamine 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate (DOPE-mal), 1,2-Dimyristoyl-sn-glycero-3-phosphoethanolamine (DMPE), 1,2-Dilinoleoyl-sn-glycero-3-phosphoethanolamine (DLoPE), distearoyl-phosphatidylethanolamine (DSPE), 1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine (POPE), 1,2-Dilauroyl-sn-glycero-3-phosphoethanolamine (DLPE), 16-O-monomethylphosphoethanolamine, 16-O-dimethyl phosphatidylethanolamine, 1,2-Dierucoyl-sn-glycero-3-phosphoethanolamine (DEPE), 18-1-trans phosphatidylethanolamine, 1-stearoyl-2-oleoylphosphatidylethanolamine (SOPE), 1,2-Disqualoyl-sn-glycero-3-phosphoethanolamine (DSQPE), 1,2-dielaidoyl-sn-glycero-3-phosphoethanolamine (transDOPE), 1-Stearoyl-2-linoleoyl-sn-glycero-3-

phosphoethanolamine (SLPE), 1-tridecanoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1-oleoyl-2-hydroxy-sn-glycero-3-phospho-L-serine (sodium salt), 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-L-serine (sodium salt) (POPS), 1-1-stearoyl-2-oleoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1,2-dioleoyl-sn-glycero-3-phospho-L-serine (sodium salt) (DOPS), 1,2-distearoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1,2-diphytanoyl-sn-glycero-3-phospho-L-serine (sodium salt), 1-O-hexadecanoyl-2-O-(9Z-octadecenyl)-sn-glycero-3-phosphoethanolamine, 1,2-distearoyl-sn-glycero-3-phosphatidylcholine or 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-di-O-phytanoyl-sn-glycero-3-phosphoethanolamine, 1-palmitoyl-2-cholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (PChemsPC), 1,2-dicholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (DChemsPC), 2-((2,3-bis(oleoyloxy)propyl)dimethylammonio)ethyl hydrogen phosphate (DOCP), 2-((2,3-bis(oleoyloxy)propyl)dimethylammonio)ethyl ethyl phosphate (DOCPE), and 1-O-octadecyl-2-O-methyl-sn-glycero-3-phosphocholine (Edelfosine), preferably wherein the phospholipid is DSPC or DPhyPE, most preferably DPhyPE; and/or

wherein the lipid nanoparticle further comprises a sterol or steroid, preferably selected from the group consisting of cholesterol, cholesteryl hemisuccinate (CHEMS) and a derivate thereof, preferably wherein the lipid nanoparticle further comprises cholesterol; and/or

wherein preferably the lipid nanoparticle comprises

(i) an amount of 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(ii) preferably an amount of 5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**,

(iii) more preferably an amount of 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

based upon a mol-percentage of the composition of 100% of all lipid components or excipients; and/or

wherein the polymer conjugated lipid is a PMOZ-lipid according to any one of **claim 1 to claim 8**.

11. The lipid nanoparticle of **claim 9 or claim 10**, wherein the lipid nanoparticle comprises excipients selected from ratios selected from the group consisting of

(i) 59 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 29.3 mol% cholesterol, 10 mol% neutral lipid and 1.7 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(ii) 59 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 28.5 mol% cholesterol, 10 mol% neutral lipid and 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(iii) 59 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 28.3 mol% cholesterol, 10 mol% DSPC or DPhyPE, preferably DPhyPE, 1 mol% DHPC, and 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(iv) 49 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 29.3 mol% cholesterol, 10 mol% DSPC or DPhyPE, preferably DPhyPE, 10 mol% DHPC, and 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(v) 47.4 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of **C1 to C27** as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 40.9 mol%

cholesterol, 10 mol% DSPC or DPhyPE, preferably DPhyPE, and 1.7 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

and

most preferably

5 (vi) 59 mol% C24 as listed in Table 1, 28.5 mol% cholesterol, 10 mol% DPhyPE and 2.5 mol% “PMOZ 4”,

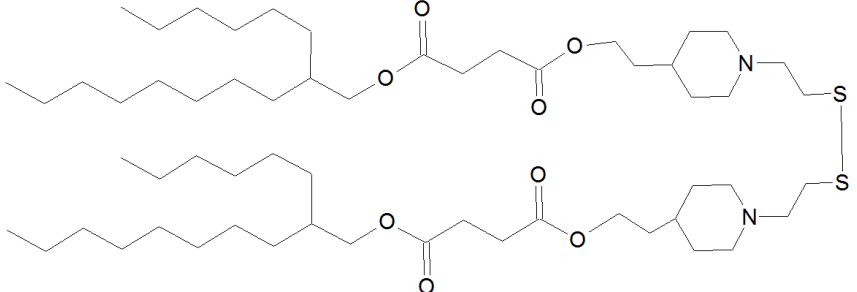
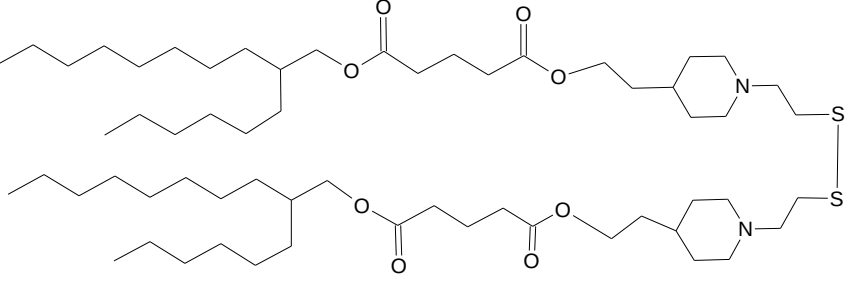
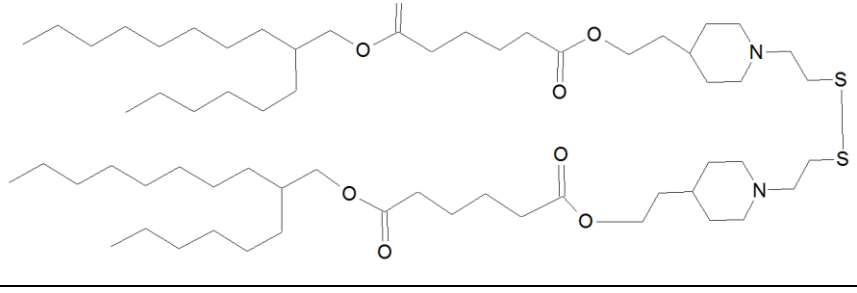
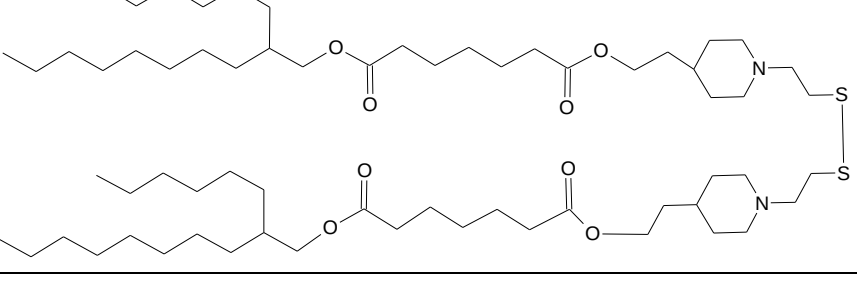
wherein n of the polymer-conjugated lipid has a mean value ranging from 45 to 55, preferably n is 50 or

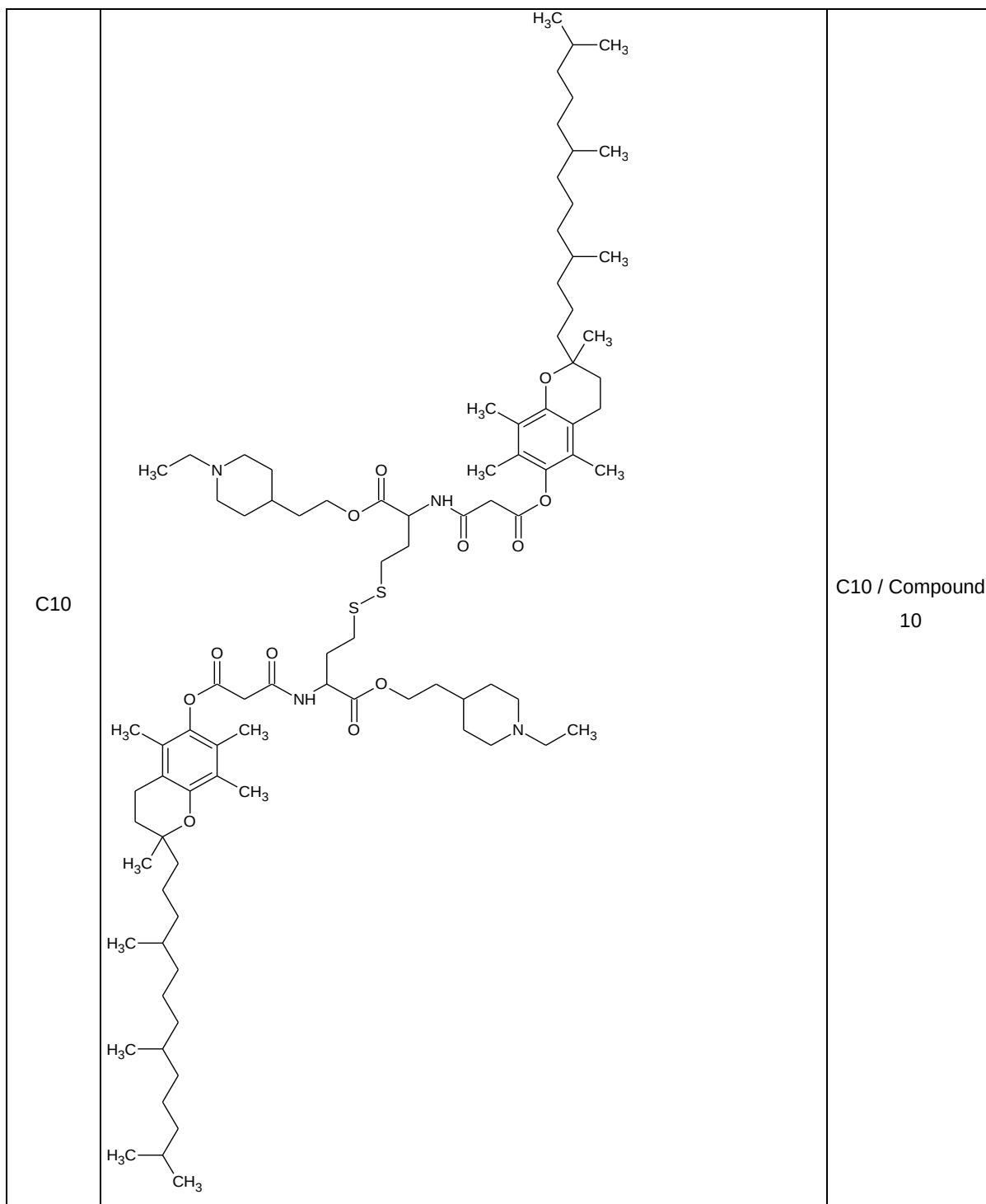
wherein n is selected such that the polymer moiety has an average molecular weight of 4.2 kDa to 4.4 kDa,

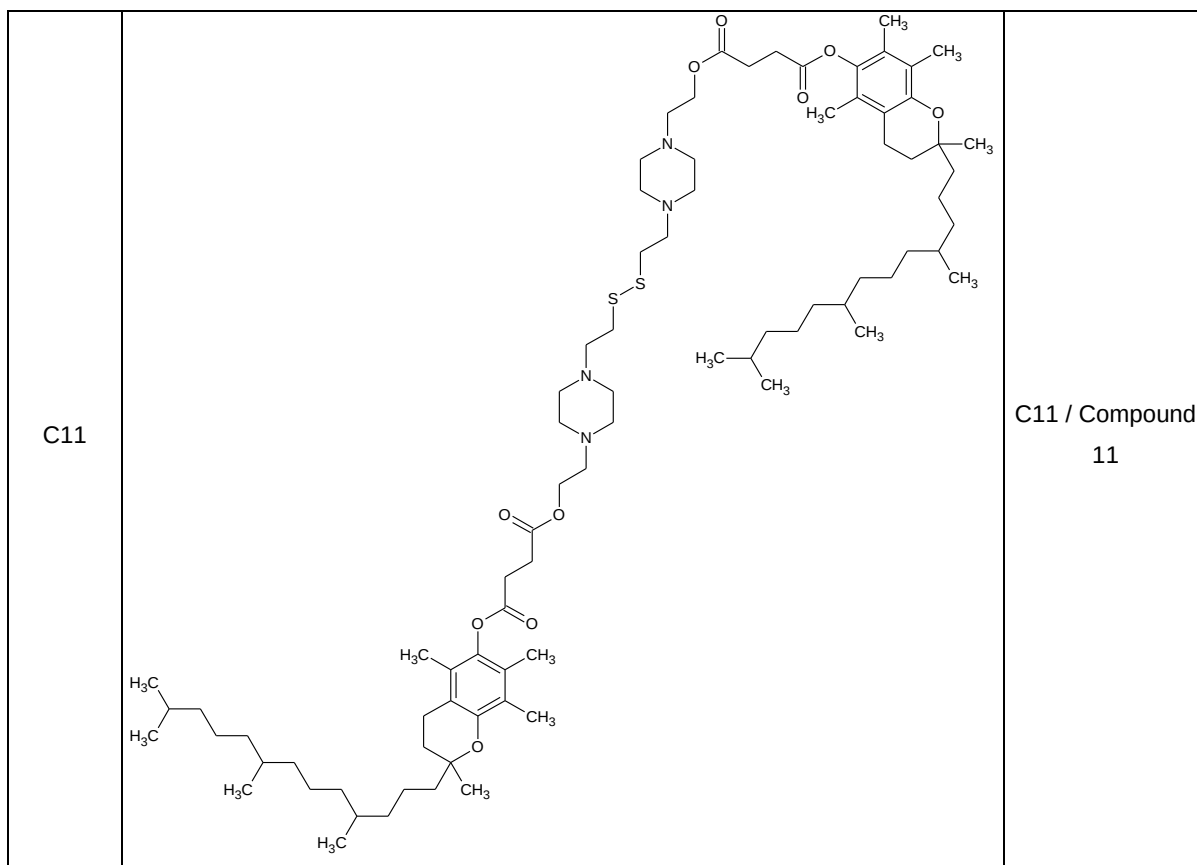
or most preferably 4.3 kDa,

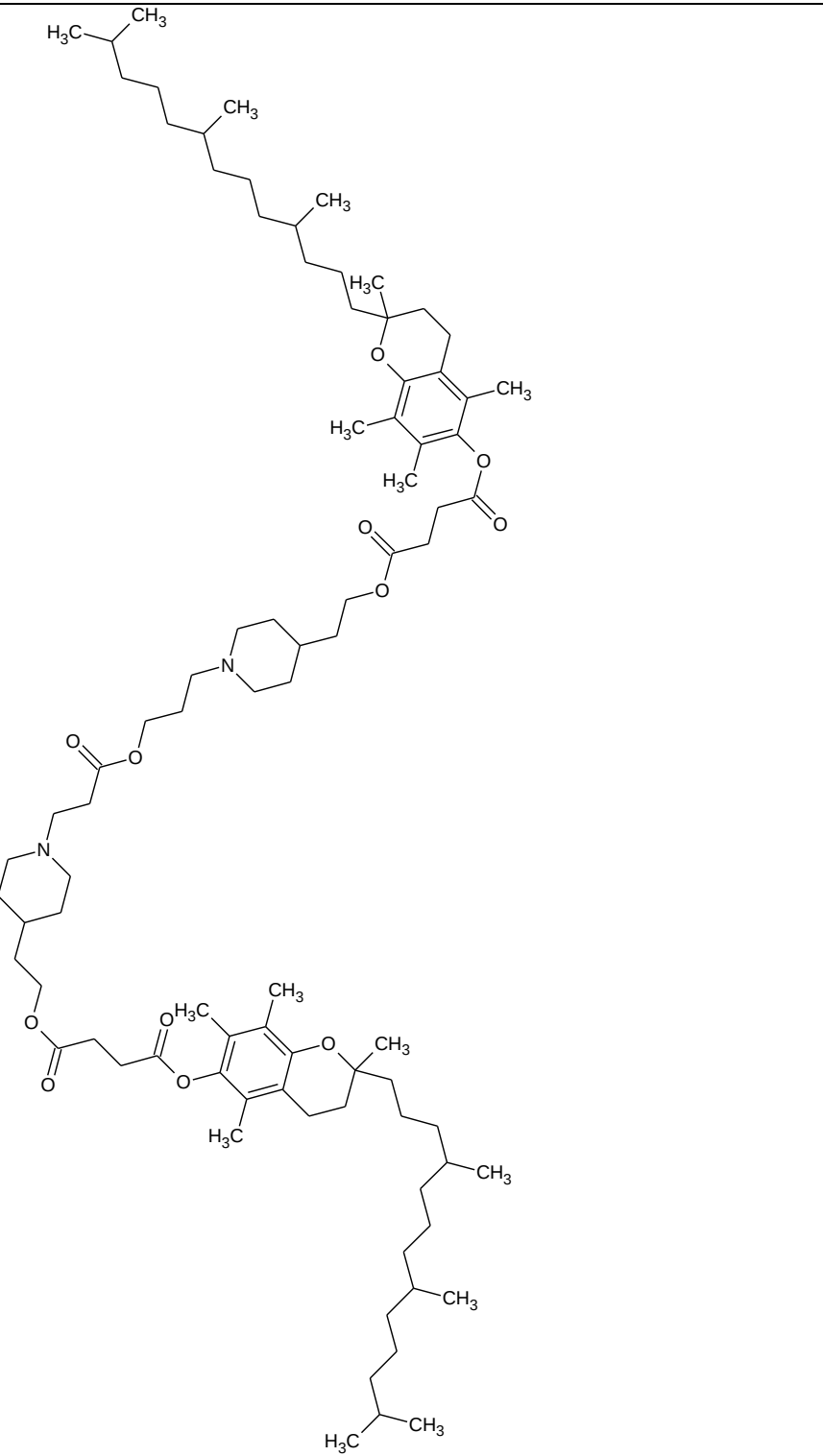
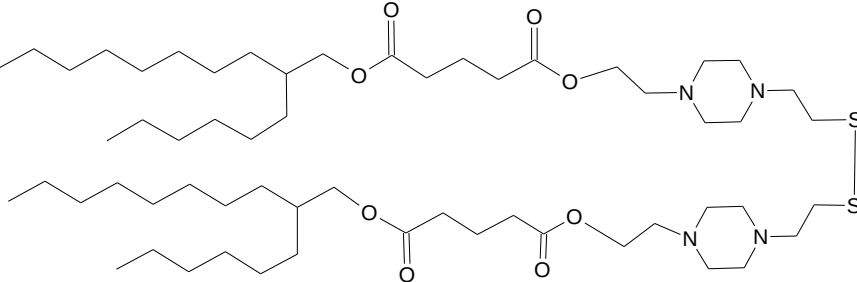
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Table 1:

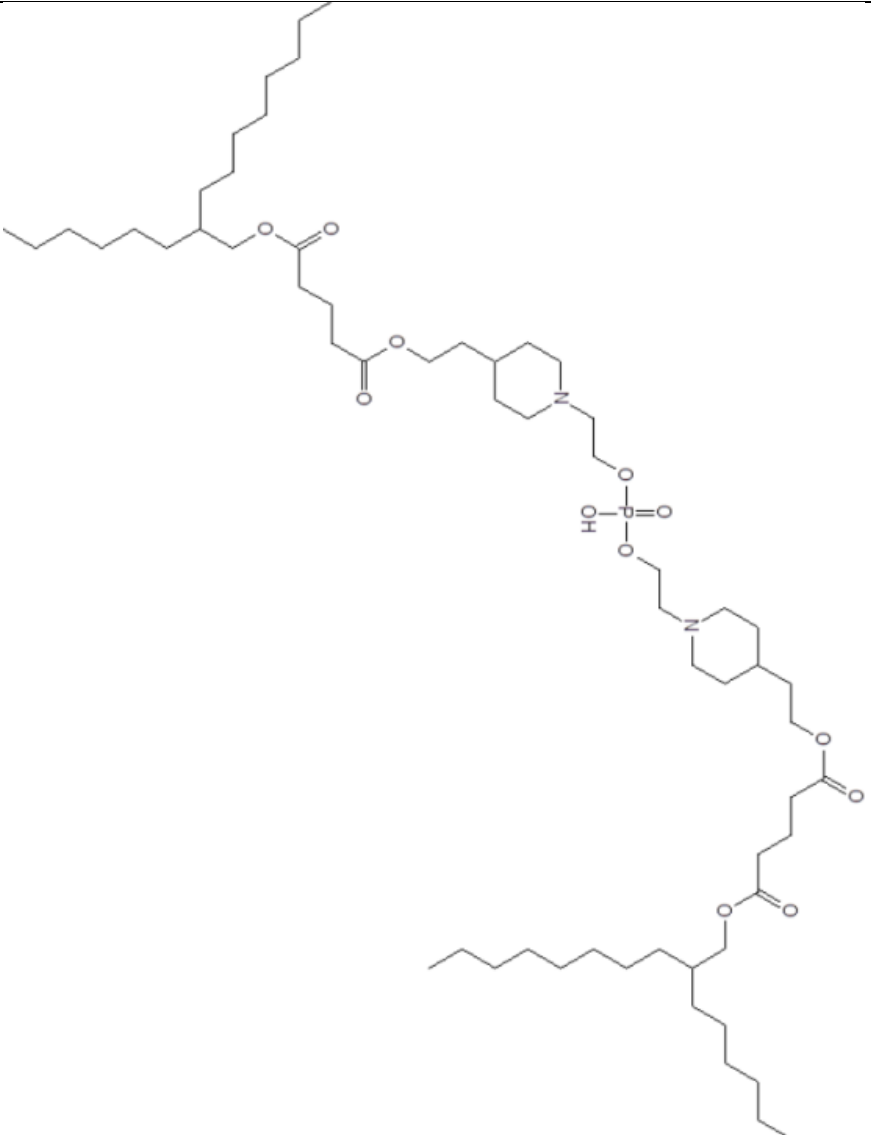
Cationic Lipid Compound No.	Structure	Name
C1		HEXA-C4DE-PipSS
C2		HEXA-C5DE-PipSS (GN02-lipid)
C3		HEXA-C6DE-PipSS
C4		HEXA-C7DE-PipSS

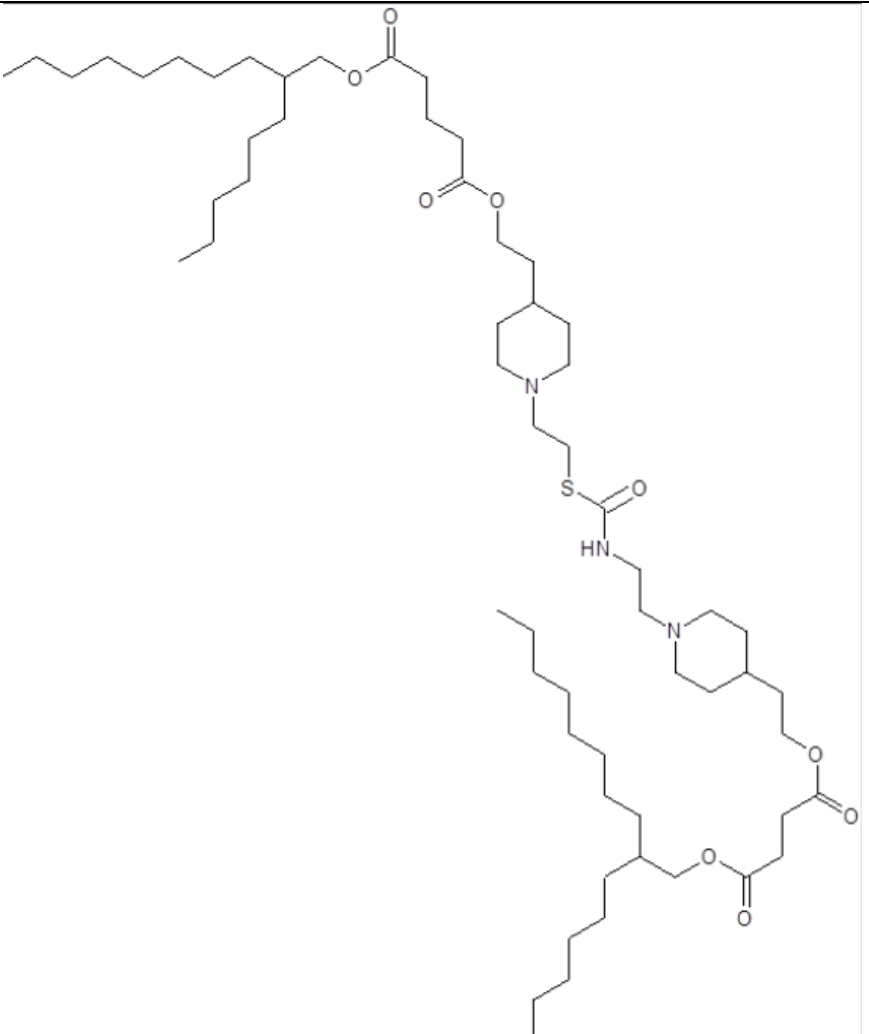


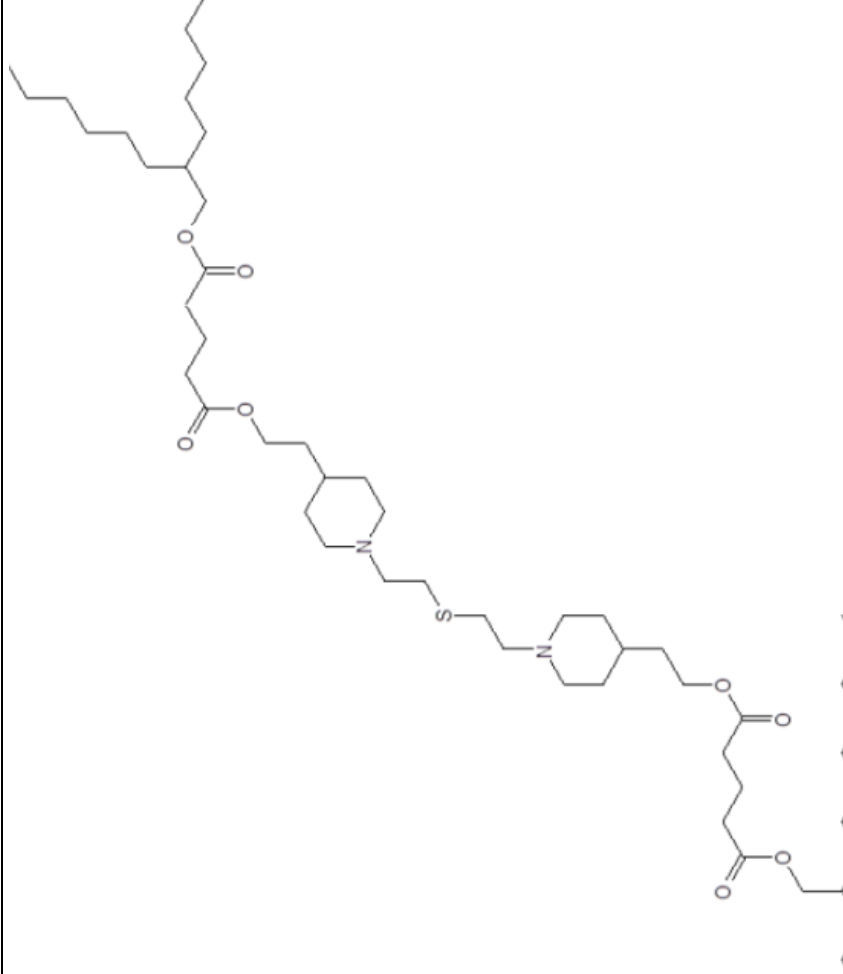


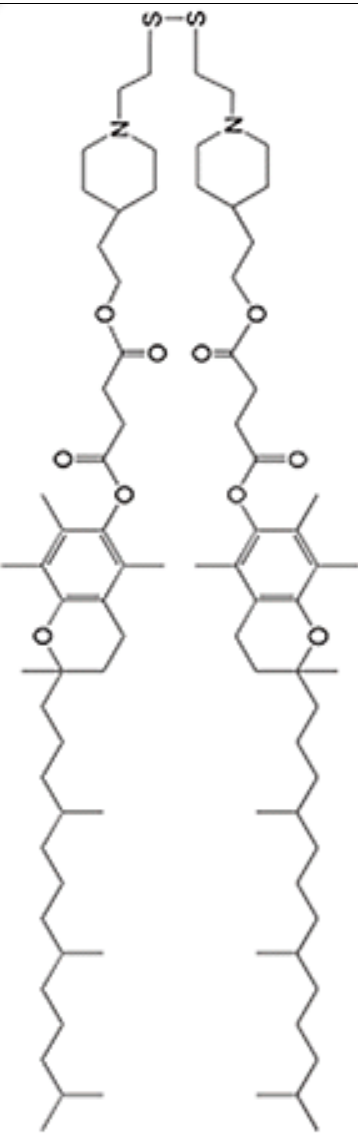
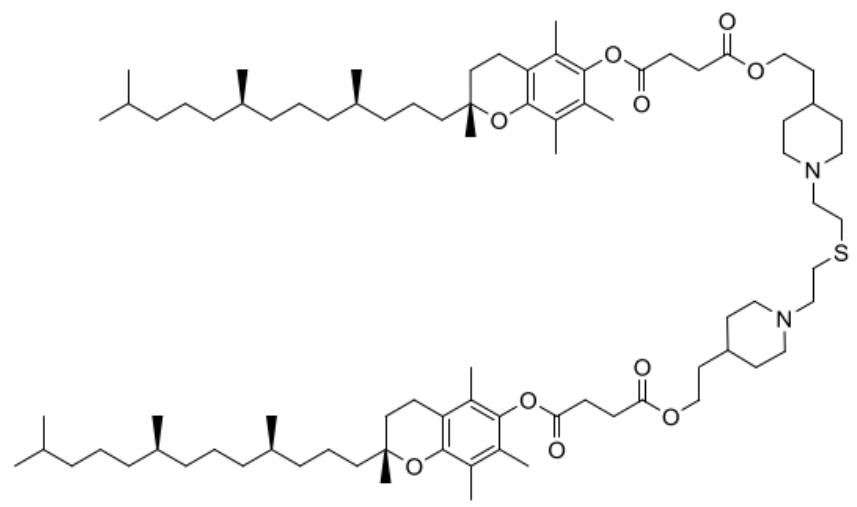
C12		C12 / Compound 12
C13		HEXA-C5DE- PipAZSS

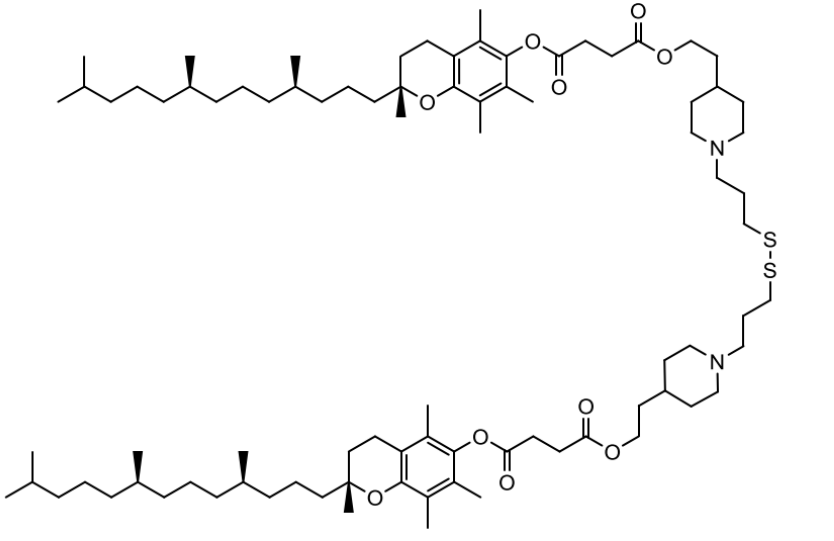
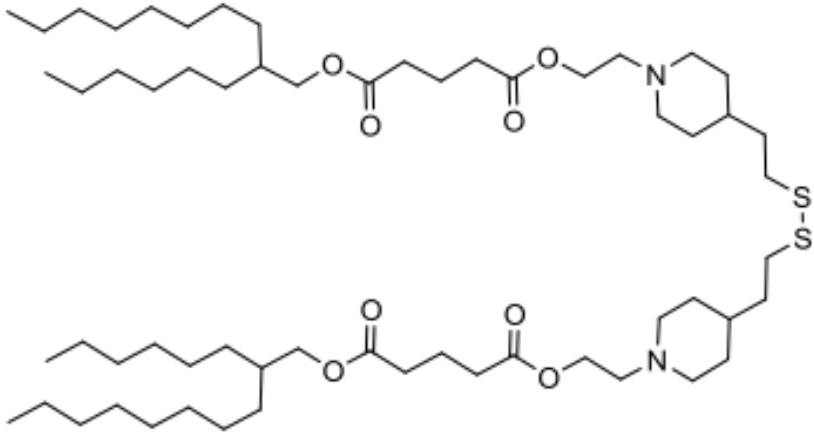
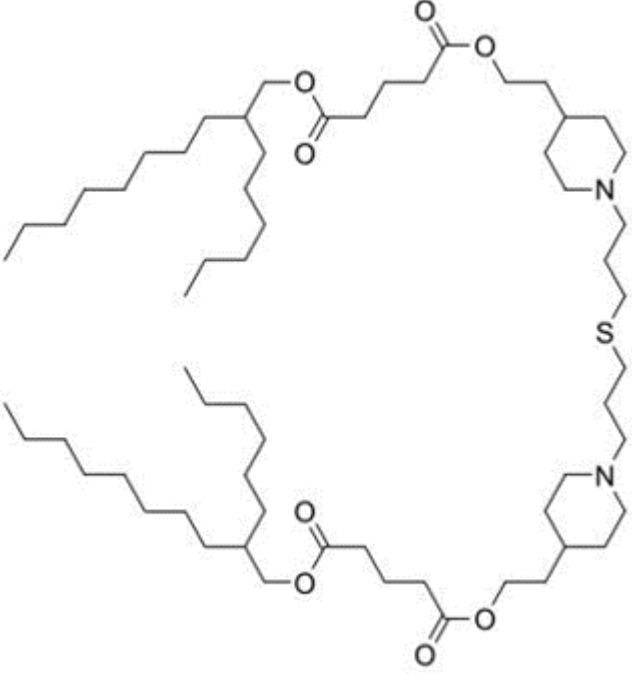
C14		HEXACA-C5DE-PipSS
C15		HEXA-C5DE-PipC3SS
C16		C16-HEXA-C5DE-PipSS
C17		DPhy-HEXA-C5DE-PipSS
C18		2DPhy-C5DE-PipSS
C19		Vit E-C5DE-Pip-TEN

C20	 <p>The chemical structure represents a surfactant molecule. It features a central phosphate group, $\text{HO}-\text{P}(=\text{O})(\text{O}^-)-\text{O}-$, which is linked to two piperidine rings. The first piperidine ring is connected to a 2-hexyloxyethyl chain, which is further linked to a 5-decylpentanoate chain. The second piperidine ring is connected to a 2-(5-decylpentanoate)ethyl chain. The decyl chains are represented by zigzag lines.</p>	HEXA-C5DE-Pip- Phosphate
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C21	 <p>The chemical structure is a symmetrical molecule. It features a central thiocarbamate group, S-C(=O)-NH-, where the sulfur atom is double-bonded to a carbon atom, which is single-bonded to a nitrogen atom. This central nitrogen is connected to two identical side chains. Each side chain consists of a 4-(2-ethoxyethyl)piperidine ring. The piperidine ring is connected to the central nitrogen via its 4-position. The 2-position of the piperidine ring is connected to a 2-ethoxyethyl group, which is $\text{-CH}_2\text{-CH}_2\text{-O-C(=O)-CH}_2\text{-CH}_2\text{-}$. The terminal ethyl group of this side chain is $\text{-CH}_2\text{-CH}_3$. The overall structure is symmetrical about the central thiocarbamate group.</p>	HEXA-C5DE-Pip- Thiocarbamate
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C22		HEXA-C5DE-Pip- Thioether
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C23		COATSOME® SS-EC
C24		THIOETHER or VitE-C4DE- Piperidine- Thioether

C25		<p>“C3SS” or “VitE-C4DE-Piperidine-C3SS”</p>
C26		<p>HEXA-C5DE-inverted-PipSS</p>
C27		<p>HEXA-C5DE-Pip-C3 thioether or HEXA-C5DE-piperidine-C3 thioether</p>

12. The lipid nanoparticle of any one of **claim 9 to claim 11**, wherein the polymer conjugated lipid of **claim 1 to claim 8** inhibits aggregation of the lipid nanoparticles.
13. The lipid nanoparticle of any one of **claim 9 to claim 12**, further comprising a biologically active ingredient.
14. The lipid nanoparticle of **claim 13**, wherein the biologically active ingredient is a nucleic acid compound selected from the group consisting of RNA, 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 chemically modified mRNA or chemically unmodified mRNA.
15. The lipid nanoparticle of any one of **claim 9 to claim 14**, wherein the mRNA is associated with the lipid nanoparticle, preferably wherein the mRNA is encapsulated in the lipid nanoparticle; and/or wherein the lipid nanoparticles comprise the mRNA at an amount such as to achieve an N/P ratio in the range of 5 to 20, more preferably 10 to 18, even more preferably 12 to 16, most preferably 14; and/or wherein the lipid nanoparticle is a sterile solid composition for reconstitution with a sterile liquid carrier, and wherein the lipid nanoparticle 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 wherein the lipid nanoparticle is a sterile liquid composition, and wherein the lipid nanoparticles have a mean hydrodynamic diameter as determined by dynamic laser scattering from 50 nm to 300 nm, or from 60 nm to 250 nm, or from 60 nm to 200 nm, or from 70 to 200 nm, or from 75 nm to 160, or from 85 nm to 140 nm, or from 90 nm to 130 nm, or from 50 nm to 120 nm; and/or wherein the lipid nanoparticles exhibit a zeta potential in the range of -50 mV to +50 mV, preferably in the range of -25 mV to +25 mV, more preferably in the range of -10 mV to +10 mV, most preferably in the range of -5 mV to +5 mV; and/or wherein the mRNA compound is a mono-, bi-, or multicistronic mRNA; and/or wherein the mRNA compound comprises at least one chemical modification, wherein the chemical modification preferably is 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, most preferably wherein the base modification preferably is selected from the group consisting of pseudouridine (psi or ψ), N1-methylpseudouridine (N1MPU, N1Mpsi or N1M ψ), 1-ethylpseudouracil, 2-thiouracil (s2U), 4-thiouracil, 5-methylcytosine, 5-methyluracil, 5-methoxyuracil, and any combination thereof; and/or wherein the mRNA compound comprises a coding region encoding a peptide or protein, wherein the coding region exhibits a sequence modification, 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, compared with the coding region of the corresponding wild-type mRNA, the
 - G/C content of the coding region is increased;
 - C content of the coding region is increased;
 - codon usage in the coding region is adapted to the human codon usage; and/or
 - codon adaptation index (CAI) is increased or maximized in the coding region.
16. The lipid nanoparticle of any one of **claim 9 to claim 15**, wherein the mRNA compound further comprises
 - a) a 5'-CAP structure, preferably m7GpppN, more preferably CAP1 or m7G(5')ppp(5')(2'OMeA)pG;

b) optionally 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) a coding sequence;

e) at least one 3'-UTR element;

f) at least one poly(A) sequence;

g) at least one poly(C) sequence;

or any combinations of these.

17. The lipid nanoparticle of any one of **claim 9 to claim 16**, 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 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 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, preferably a mutated alpha-globin 3'-UTR (SEQ ID NO:11/12), more preferably a HSD17B4 5'-UTR (SEQ ID NO:21/22) and a PSMB3 3'-UTR (SEQ ID NO:19/20); and/or 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)pG and m7G(5')ppp(5')(2'OMeG)pG;
 - 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, most preferably according to SEQ ID NO:22 (HSD17B4);
 - 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, most preferably according to SEQ ID NO:20 (PSMB3);
 - 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.

18. The lipid nanoparticle of any one of **claim 9 to claim 17**, 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, tumor 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 use 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 use 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 use in the treatment of cancer or tumor diseases;
 - (iv) therapeutic proteins for use in hormone replacement therapy;
 - (v) therapeutic proteins for use in reprogramming somatic cells into pluri- or omnipotent stem cells;
 - (vi) therapeutic proteins for use as adjuvant or immunostimulation;
 - (vii) therapeutic proteins being a therapeutic antibody;
 - (viii) therapeutic proteins being a gene editing agent; and
 - (ix) therapeutic proteins for use in treating or preventing a liver disease selected from the group consisting of liver fibrosis, liver cirrhosis and liver cancer.
19. The lipid nanoparticle of **claim 18 subitem (a)**, wherein the at least one coding sequence encoding a pathogenic antigen is selected from the group consisting of a bacterial, viral, fungal and protozoal antigen.
20. The lipid nanoparticle of **claim 19**, wherein the at least one coding sequence encoding a pathogenic antigen
 - (i) is derived from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV), Bunyavirales virus, Cytomegalovirus (CMV), Dengue viruses (DENV-1, DENV-2, DENV-3 and DENV-4), Ebola virus, Epstein-Barr virus (EBV), 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 (ExPEC), Lassa mammarenavirus (LASV), MERS coronavirus, Mycobacterium tuberculosis, Nipah virus, Norovirus, Rabies virus, Respiratory Syncytial virus (RSV), Rhinovirus, Rota virus, Vaccinia virus, Yellow Fever virus (YFV), Zika virus (ZIKV), Chlamydia trachomatis (i.e. bacterium chlamydia causing chlamydia), or Malaria parasite (e.g. Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, or Plasmodium ovale); and/or
 - (ii) is derived from a structural protein, an accessory protein, or a replicase protein from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV), or an immunogenic fragment or immunogenic variant of any of these; and/or
 - (iii) is derived from a spike protein (S), an envelope protein (E), a membrane protein (M) or a nucleocapsid protein (N) from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV), or an immunogenic fragment or immunogenic variant of any of these, preferably wherein the spike protein (S) comprises or consists of spike protein fragment S1 or spike protein fragment S2, more preferably spike protein fragment S1, or an immunogenic fragment or immunogenic variant thereof (e.g. receptor binding domain (RBD), critical neutralisation domain (CND)); and/or
 - (iv) is derived from a pre-fusion stabilized spike protein (S) (S_{stab}) from a SARS coronavirus 2 (SARS-CoV-2), nCoV-2019 coronavirus, SARS coronavirus (SARS-CoV) comprising at least one pre-fusion stabilizing mutation.

21. Use of the lipid nanoparticle of any one of **claim 9 to claim 20** in the manufacture of a medicament
(i) in the treatment or prophylaxis of infectious diseases; cancer or tumor 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 the treatment of metabolic or endocrine disorders;
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 lipid nanoparticle is to be administered via local or locoregional injection,
infusion or implantation, in particular intradermal, subcutaneous, intramuscular, intracameral,
subconjunctival, suprachoroidal injection, subretinal, subtenon, retrobulbar, topical, posterior juxtasceral
administration, or intrapulmonary inhalation, interstitial, locoregional, intravitreal, intratumoral, intralymphatic,
intranodal, intra-articular, intrasynovial, periarticular, intraperitoneal, intra-abdominal, intracardiac,
intralesional, intrapericardial, intraventricular, intrapleural, perineural, intrathoracic, epidural, intradural,
peridural, intrathecal, intramedullary, intracerebral, intracavernous, intracorporus cavernosum,
intraprostatic, intratesticular, intracartilaginous, intraosseous, intradiscal, intraspinal, intracaudal, intrabursal,
intraingival, intraovarian, intrauterine, intraocular, periocular, periodontal, retrobulbar, subarachnoid,
subconjunctival, suprachoroidal injection, infusion, implantation, nasal, buccal, sublingual, otic or auricular,
ophthalmic, conjunctival, vaginal, rectal, intracervical, endosinusial, laryngeal, oropharyngeal, ureteral,
urethral administration, more preferably said lipid nanoparticle is administered intramuscularly,
intravenously, intradermally, subcutaneously, intratumorally, intranasally, or by inhalation, most preferably
intramuscularly, to a subject in need thereof.
22. A kit or kit of parts, comprising any one of the lipid nanoparticle of **claim 9 to claim 20**, optionally comprising
a liquid vehicle for solubilizing, and, optionally, technical instructions providing information on administration
and dosage of the components.
23. The lipid nanoparticle of any one of **claim 9 to claim 20** or the kit or kit of parts of **claim 22** for use in *in vivo*
drug delivery, preferably for use in delivering a nucleic acid, preferably a mRNA.
24. The lipid nanoparticle of any one of **claim 9 to claim 20** or the kit or kit of parts of **claim 22** for use as a
medicament.
25. The lipid nanoparticle of claim 24 for use in the manufacture of a vaccine.
26. Use of **claim 25** or a kit or kit of parts of **claim 22** in the manufacture of a medicament, for prevention,
prophylaxis, treatment and/or amelioration of a disease selected from infectious diseases including viral,
bacterial or protozoological infectious diseases, cancer or tumor diseases.
27. A pharmaceutical composition comprising a lipid nanoparticle of any one of **claim 9 to claim 20** or a kit or
kit of parts of **claim 22** for use as a medicament in vaccination of a subject comprising an effective dose of
mRNA encoding a virus antigen.
28. The lipid nanoparticle of **claim 9 or claim 10**, wherein the lipid nanoparticle comprises excipients selected
from ratios selected from the group consisting of

(i) 59 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 29.3 mol% cholesterol, 10 mol% neutral lipid and 1.7 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(ii) 59 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 28.5 mol% cholesterol, 10 mol% neutral lipid and 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(iii) 59 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 28.3 mol% cholesterol, 10 mol% DSPC or DPhyPE, preferably DPhyPE, 1 mol% DHPC, and 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

(iv) 49 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of C1 to C24 as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 29.3 mol% cholesterol, 10 mol% DSPC or DPhyPE, preferably DPhyPE, 10 mol% DHPC, and 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

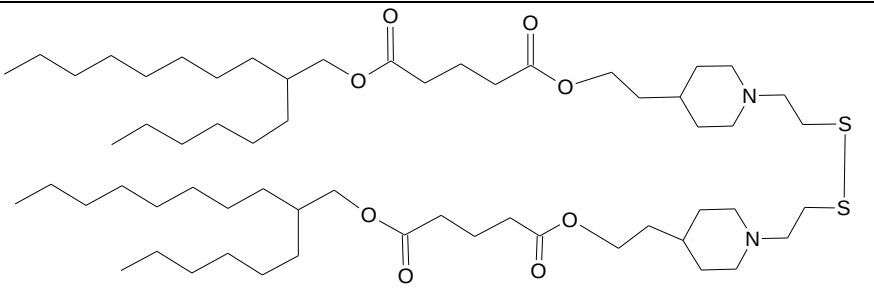
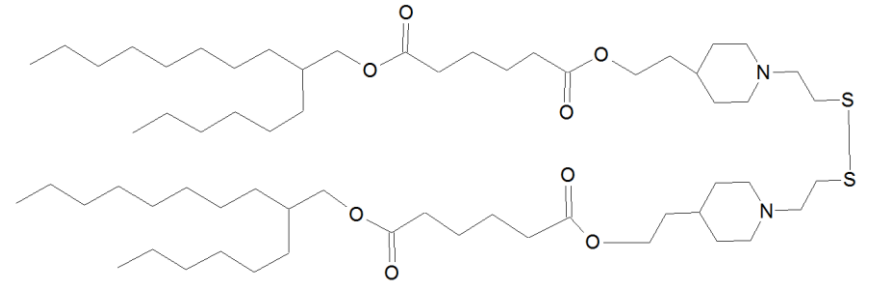
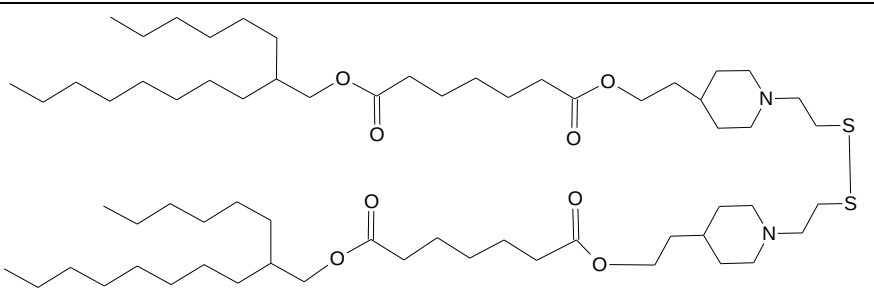
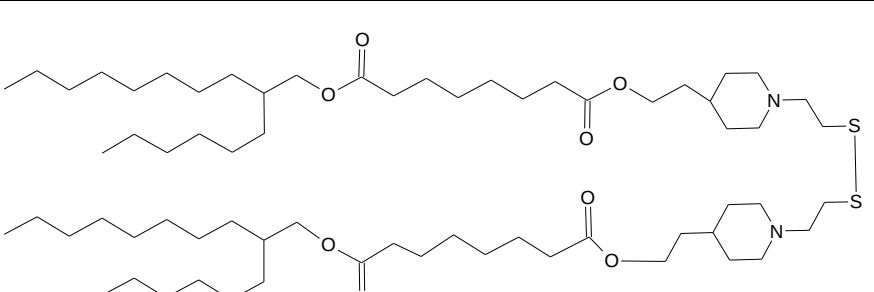
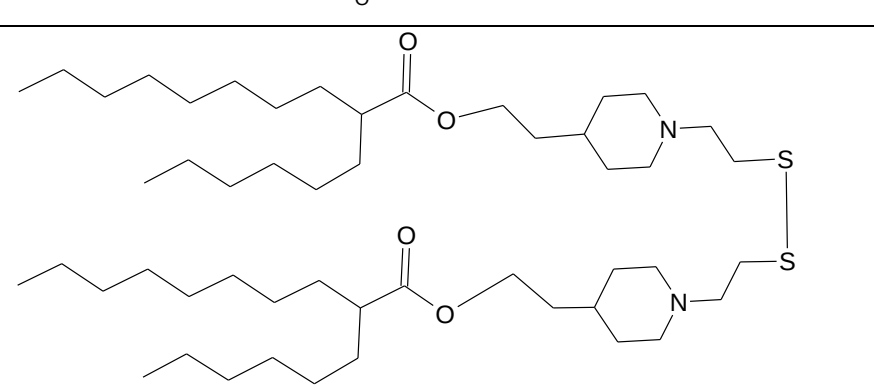
(v) 47.4 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of **C1 to C27** as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 40.9 mol% cholesterol, 10 mol% DSPC or DPhyPE, preferably DPhyPE, and 1.7 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;

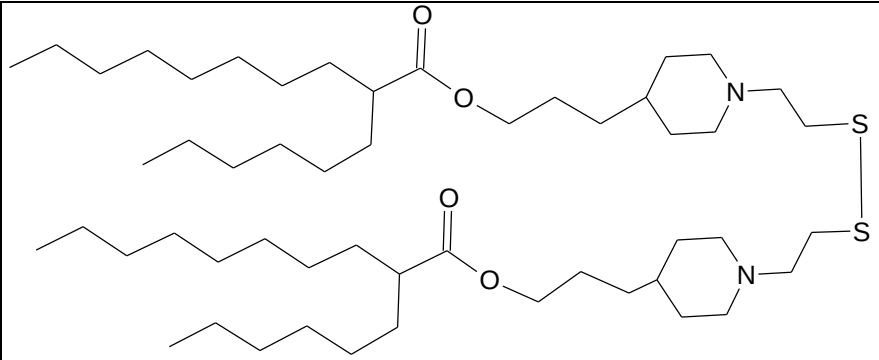
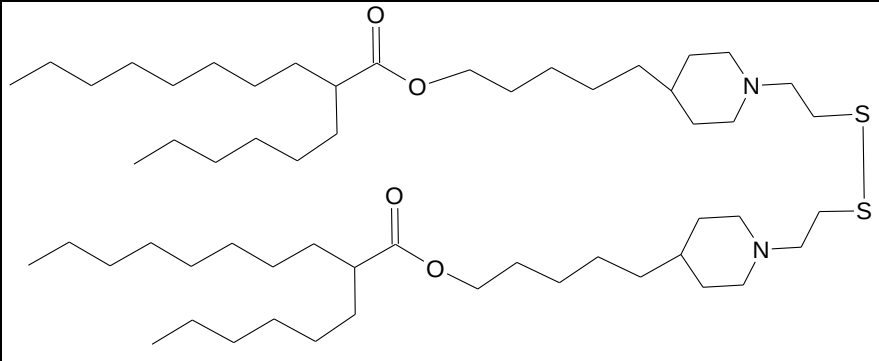
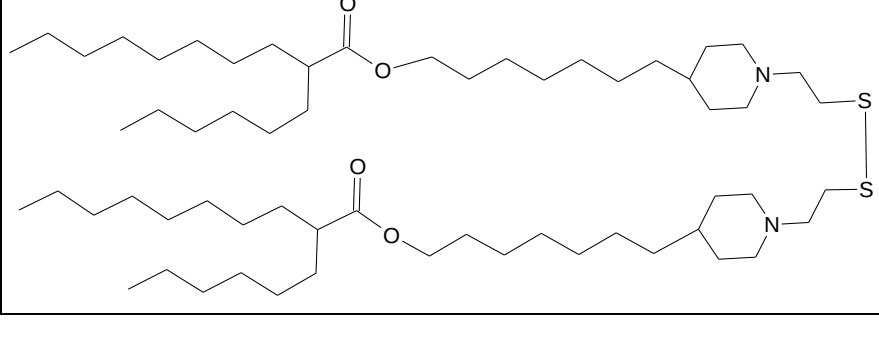
(vi) 47.4 mol% cationic or ionizable lipid, preferably one of the ionizable lipid structures of **C1 to C27** as listed in Table 1, more preferably the ionizable lipid structure C24 as listed in Table 1, 40.1 mol% cholesterol, 10 mol% DSPC and 2.5 mol% of the polymer conjugated lipid of any one of **claim 1 to claim 8**;
and most preferably

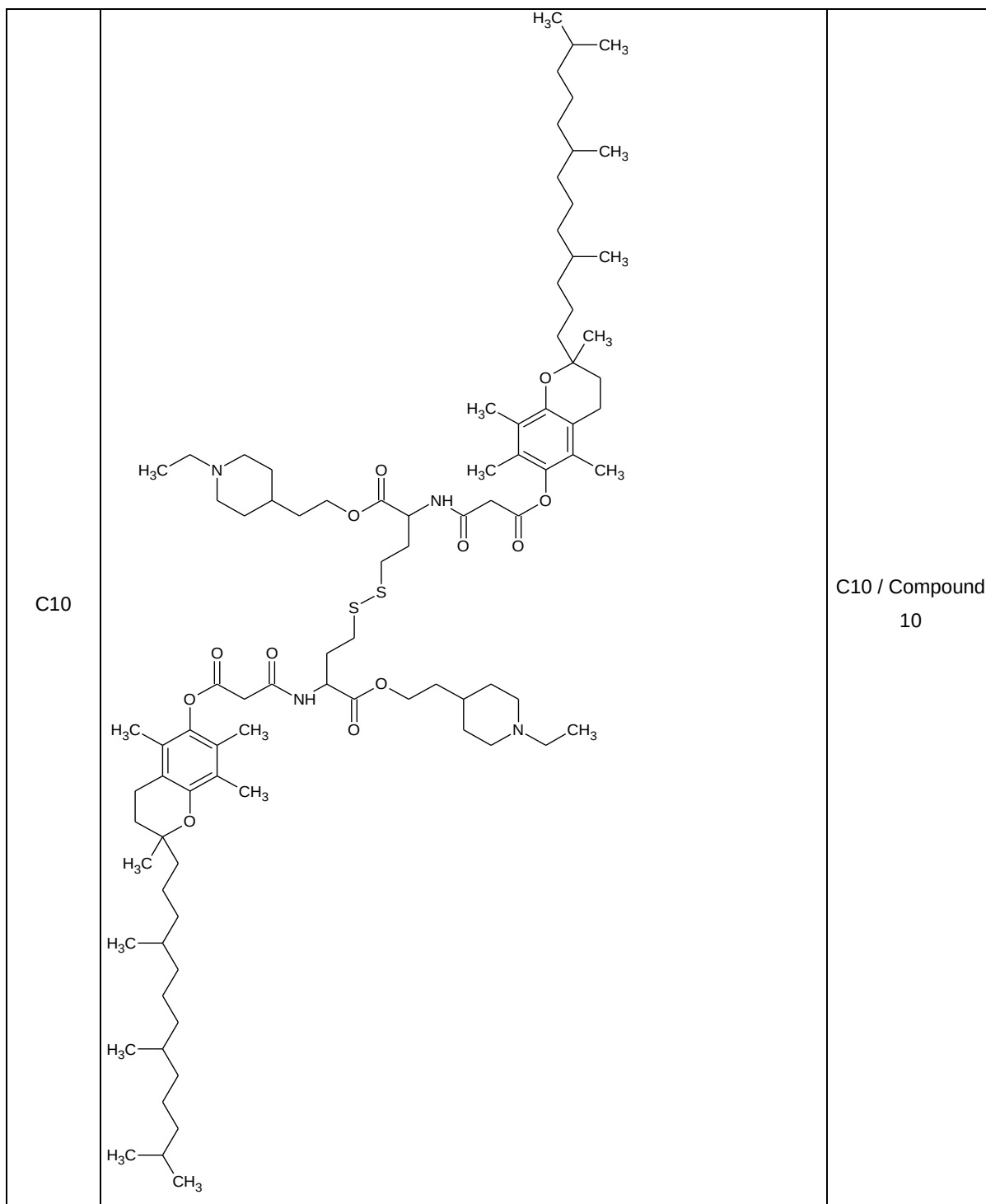
(vii) 59 mol% C24 as listed in Table 1, 28.5 mol% cholesterol, 10 mol% DPhyPE and 2.5 mol% "PMOZ 4", wherein n of the polymer-conjugated lipid has a mean value ranging from 45 to 55, preferably n is 50 or wherein n is selected such that the polymer moiety has an average molecular weight of 4.2 kDa to 4.4 kDa, or most preferably 4.3 kDa,

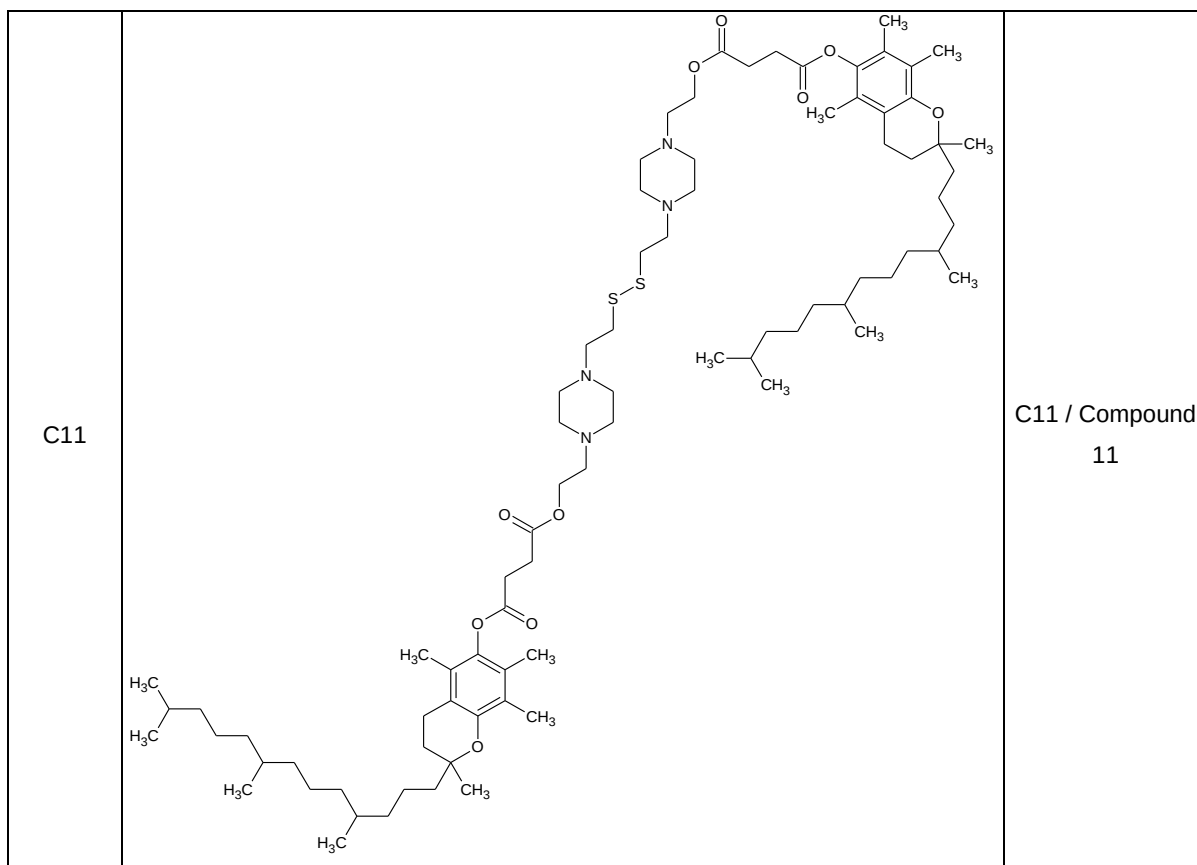
Table 1:

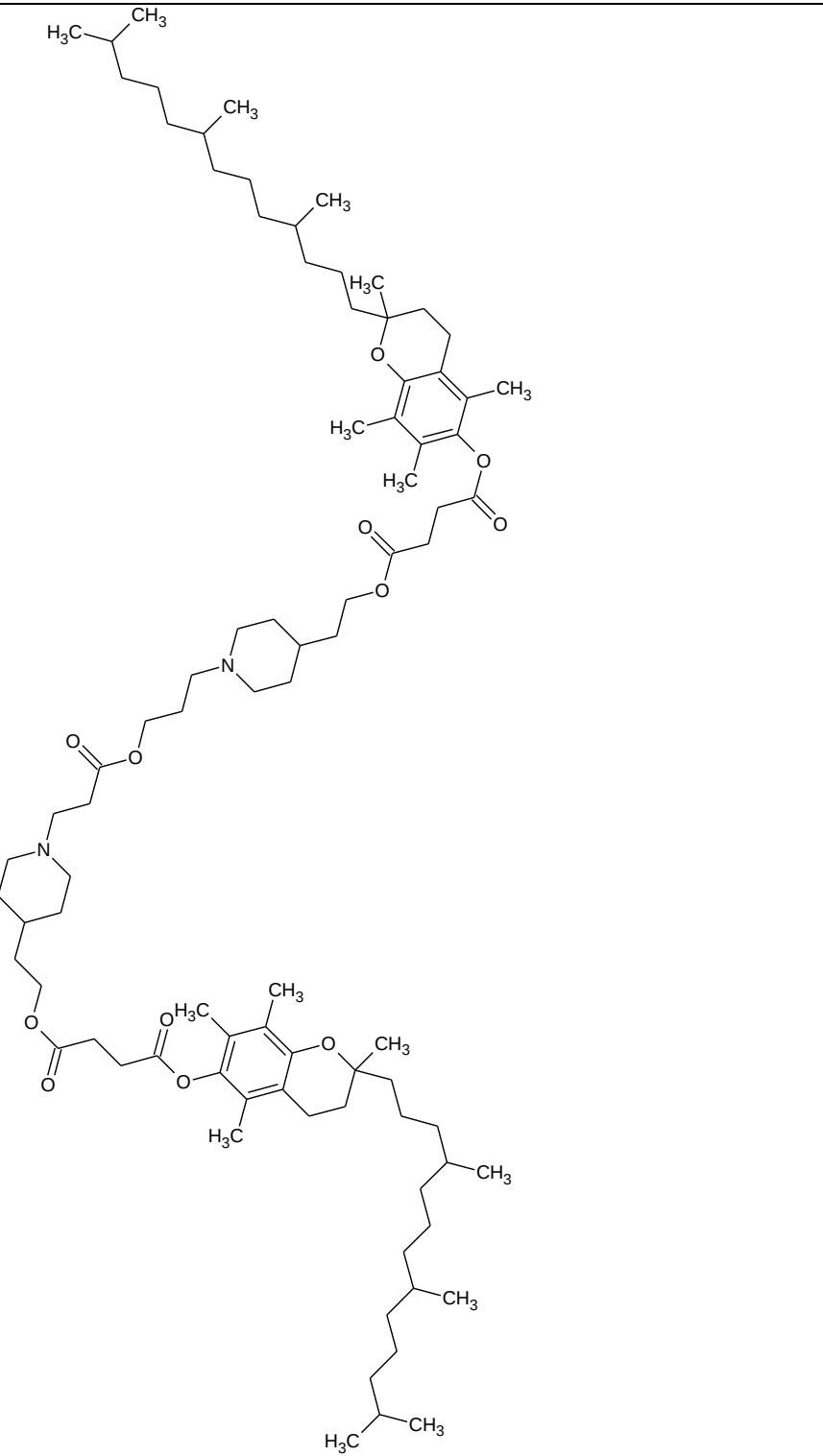
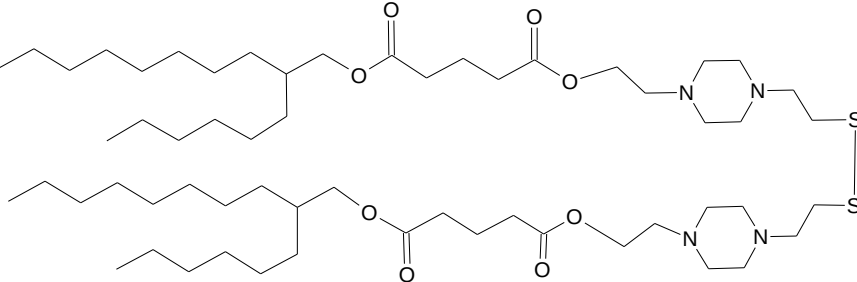
Cationic Lipid Compound No.	Structure	Name
C1		HEXA-C4DE-PipSS

C2		HEXA-C5DE-PipSS (GN02-lipid)
C3		HEXA-C6DE-PipSS
C4		HEXA-C7DE-PipSS
C5		HEXA-C8DE-PipSS
C6		HEXACA -C3ME-PipSS

C7		HEXACA-C4ME- PipSS
C8		HEXACA-C6ME- PipSS
C9		HEXACA-C8ME- PipSS

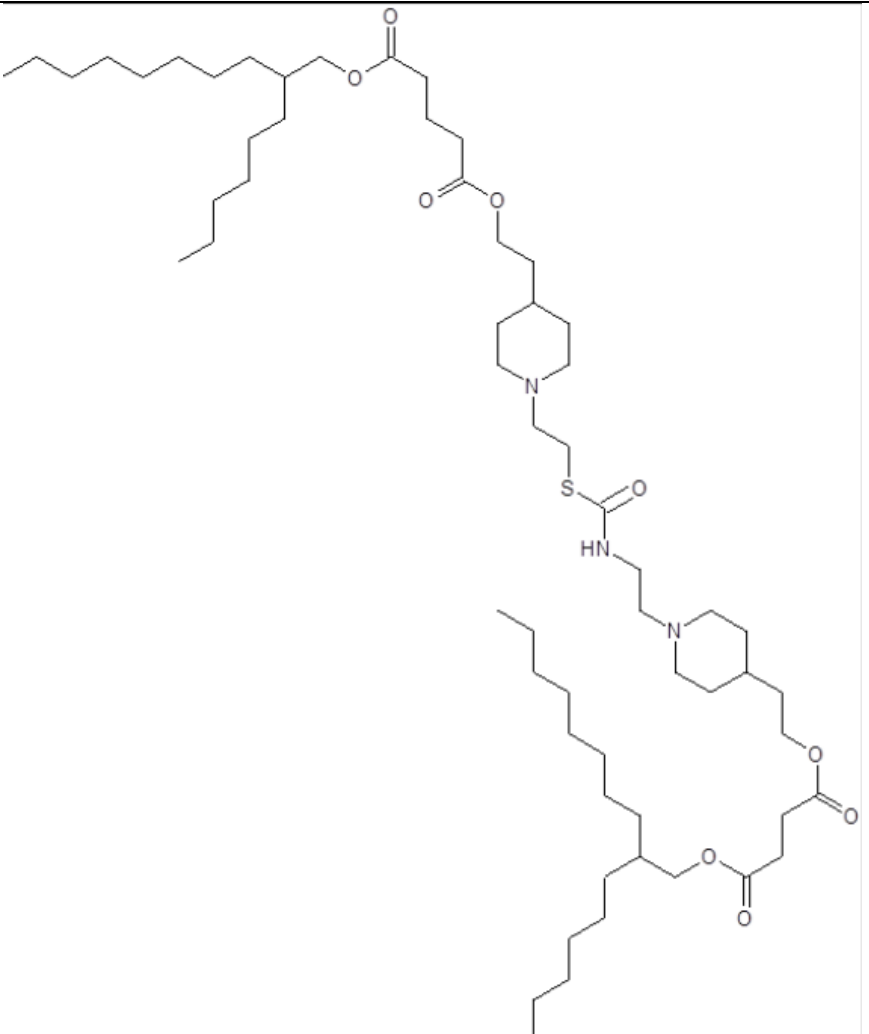


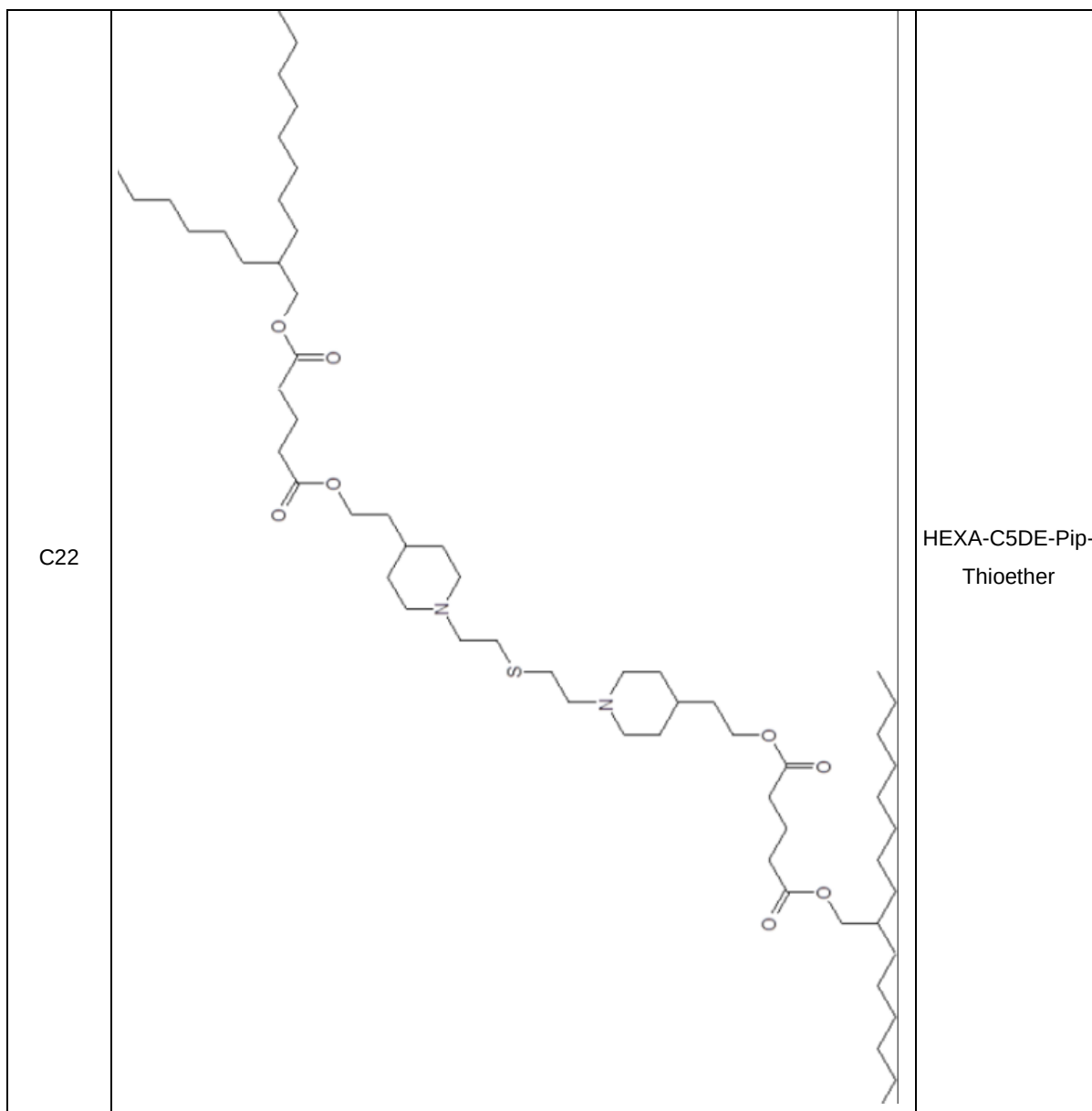


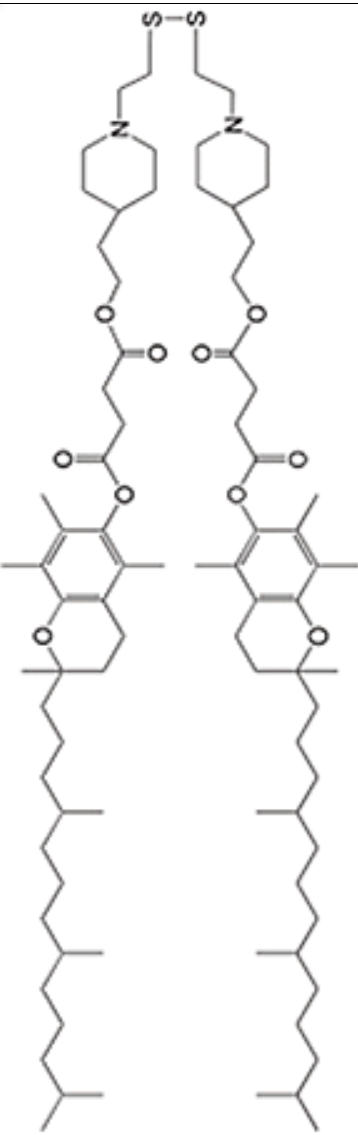
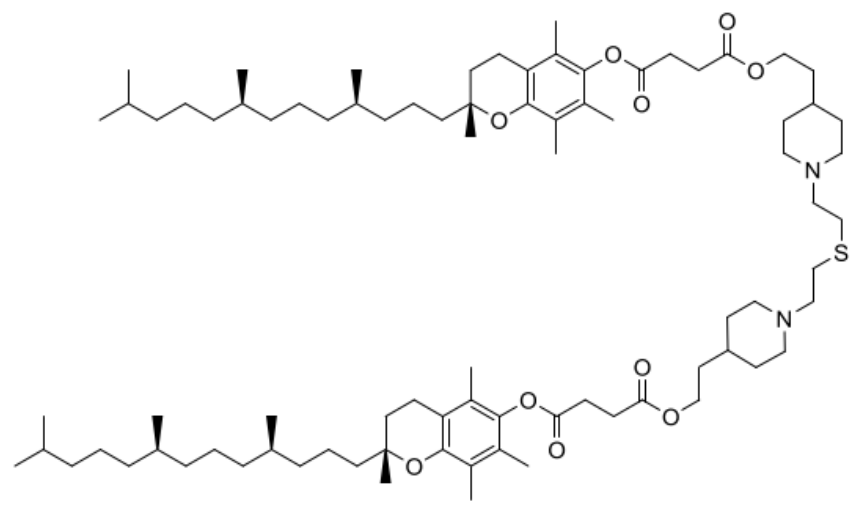
C12		C12 / Compound 12
C13		HEXA-C5DE- PipAZSS

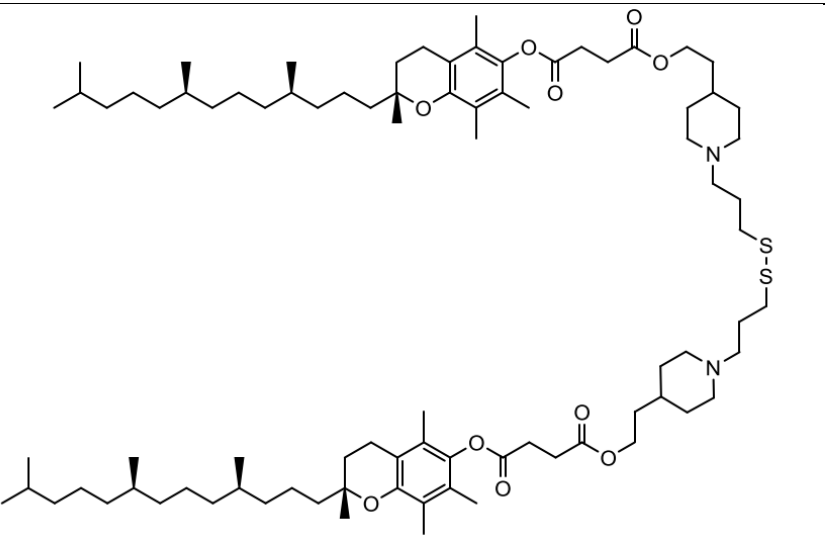
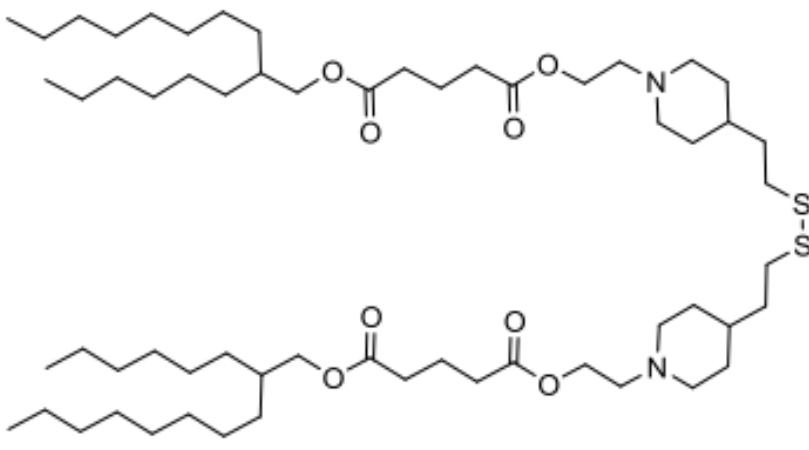
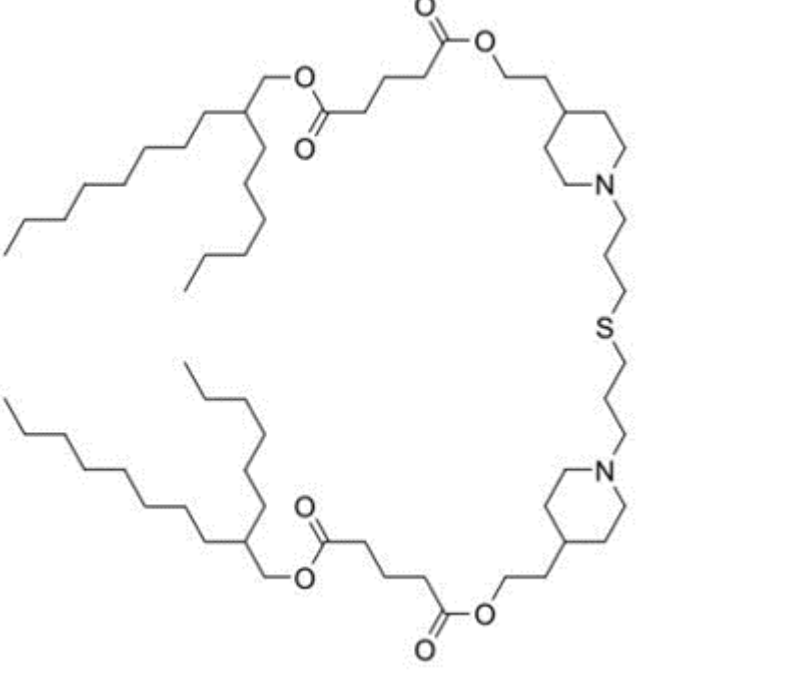
C14		HEXACA-C5DE-PipSS
C15		HEXA-C5DE-PipC3SS
C16		C16-HEXA-C5DE-PipSS
C17		DPhy-HEXA-C5DE-PipSS
C18		2DPhy-C5DE-PipSS
C19		Vit E-C5DE-Pip-TEN

HEXA-C5DE-Pip-
Phosphate

C21	 <p>The chemical structure is a symmetrical molecule. It features a central thiocarbamate group, S-C(=O)-NH-, where the sulfur atom is double-bonded to a carbonyl carbon, which is single-bonded to a nitrogen atom. This central nitrogen is connected to two identical side chains. Each side chain consists of a 4-(2-ethoxyethyl)piperidine ring. The piperidine ring is connected at its 4-position to a 2-ethoxyethyl group. The ethoxy group is further connected to a 2-ethylhexanoate ester moiety. The overall structure is symmetrical about the central thiocarbamate group.</p>	HEXA-C5DE-Pip- Thiocarbamate
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C23		COATSOME® SS-EC
C24		THIOETHER or VitE-C4DE- Piperidine- Thioether

C25		<p>“C3SS” or “VitE-C4DE-Piperidine-C3SS”</p>
C26		<p>HEXA-C5DE-inverted-PipSS</p>
C27		<p>HEXA-C5DE-Pip-C3 thioether or HEXA-C5DE-piperidine-C3 thioether</p>

29. The lipid nanoparticle of **claim 9 or claim 10 or claim 28**, wherein the lipid nanoparticle 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 lipid nanoparticle 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 05:0 PC (1,2-dipentanoyl-sn-glycero-3-phosphocholine), 04:0 PC (1,2-dibutyl-sn-glycero-3-phosphocholine), 06:0 PC (DHPC, 1,2-dihexanoyl-sn-glycero-3-phosphocholine), 07:0 PC (DHPC, 1,2-diheptanoyl-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), preferably 07:0 PC (DHPC, 1,2-diheptanoyl-sn-glycero-3-phosphocholine); and/or wherein the lipid nanoparticles 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 lipid nanoparticle 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 05:0 PC (1,2-dipentanoyl-sn-glycero-3-phosphocholine), 04:0 PC (1,2-dibutyl-sn-glycero-3-phosphocholine), 06:0 PC (DHPC, 1,2-dihexanoyl-sn-glycero-3-phosphocholine), 07:0 PC (DHPC, 1,2-diheptanoyl-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), preferably 07:0 PC (DHPC, 1,2-diheptanoyl-sn-glycero-3-phosphocholine).
30. A lipid nanoparticle comprising a polymer conjugated lipid according to any one of **claim 1 to claim 8**, wherein the lipid nanoparticle has a lower PDI and/or lower size upon (i) freezing and thawing or (ii) freeze-drying (lyophilizing) and reconstitution, as compared to a control lipid nanoparticle comprising a PEG-lipid instead said polymer conjugated lipid according to any one of **claim 1 to claim 8**.
31. A method of making a frozen lipid nanoparticle of any one of **claim 9 or claim 10 or claim 28 or claim 29** or a lipid nanoparticle comprising a polymer conjugated lipid according to any one of **claim 1 to claim 8**, wherein the lipid nanoparticle upon thawing has a lower PDI and/or lower size as compared to a control lipid nanoparticle comprising a PEG-lipid instead of a polymer conjugated lipid according to any one of **claim 1 to claim 8**.
32. A method of making a lyophilized lipid nanoparticle of any one of **claim 9 or claim 10 or claim 28 or claim 29** or a lipid nanoparticle comprising a polymer conjugated lipid according to any one of **claim 1 to claim 8**, wherein the lipid nanoparticle upon reconstitution has a lower PDI and/or lower size as compared to a control lipid nanoparticle comprising a PEG-lipid instead of a polymer conjugated lipid according to any one of **claim 1 to claim 8**.
33. An improved lyophilization process for the preparation of lyophilized lipid nanoparticles of any one of **claim 9 or claim 10 or claim 28 or claim 29**, said process comprising the step of using a polymer conjugated lipid

according to any one of **claim 1** to **claim 8** as excipient instead of a PEG-lipid, wherein the lipid nanoparticle upon reconstitution has a lower PDI and/or lower size as compared to a control lipid nanoparticle comprising a PEG-lipid instead of a polymer conjugated lipid according to any one of **claim 1** to **claim 8**.

- 5 34. A vaccine composition, comprising a lipid nanoparticle of any one of **claim 9** or **claim 10** or **claim 28** or **claim 29** or a polymer conjugated lipid according to any one of **claim 1** to **claim 8**.
- 10 35. A vaccine composition or a lipid nanoparticle of any one of the preceding claims comprising a polymer-conjugated lipid according to any of the preceding claims, wherein the formulation has an increase in LNP mean size of 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less after one or more freeze/thaw cycles as compared to that prior to freeze/thaw cycles; and/or
 15 wherein the formulation has an increase in LNP mean size of 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less after one or more freeze/thaw cycles as compared to that prior to freeze/thaw cycles; and/or
 20 wherein the formulation has an increase in LNP mean size of 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less after lyophilization as compared to that prior to lyophilization; and/or
 25 wherein the formulation has an increase in LNP mean size of 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less after lyophilization as compared to that prior to lyophilization; and/or
 wherein the formulation has an increase in LNP mean size of 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less after dilution as compared to that prior to dilution; and/or
 wherein the formulation has an increase in LNP mean size of 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less after dilution as compared to that prior to dilution; and/or
 wherein the encapsulation efficiency of the formulation is substantially the same after storage at 4 °C or lower for at least one month; and/or
 wherein the LNP mean size of the LNPs is substantially the same after storage at 4 °C or lower for at least one month.