

RETINOID COMPOSITIONS AND METHODS OF USE

CROSS-REFERENCE

[001] This application claims the benefit of Australian Application Serial Number 2024900129 filed on January 19, 2024, the entirety of which is hereby incorporated by reference herein.

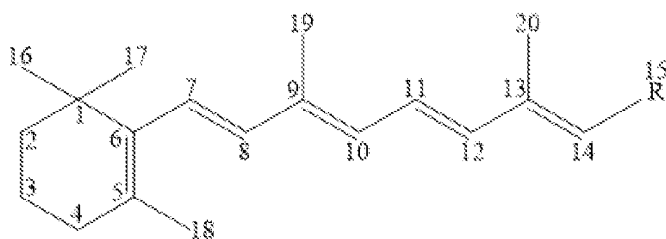
SUMMARY

[002] Retinoid such as vitamin A can be used for treating diseases or conditions such as eye diseases or conditions. For example, by administering retinoid to a subject, lipofuscin abundance in the subject is decreased, thereby treating eye diseases or conditions associated with lipofuscin or N-retinyl-N-retinylidene ethanolamine (A2E) accumulation in the eyes of the subject. Retinoid can also be used for non-medical uses, such as for aesthetic, cosmetic, or supplement purposes.

[003] However, the use of retinoid has drawbacks. For example, administering an excessive dose of retinoid to the subject can lead to hypervitaminosis in the subject. On the other hand, formulation of retinoid to ensure sufficient bioavailability of the retinoid delivered to the site of need in the subject remains an ongoing challenge. For example, retinoid is not readily soluble in an aqueous environment, which confers difficulty in formulating and administering the retinoid to a subject.

[004] Accordingly, there remains a need for compositions and methods for delivering the retinoid to the subject in a quantity to ensure sufficient bioavailability. There also remains a need for compositions and methods utilizing the retinoid for treating a disease or condition or for non-medical (e.g., aesthetic, cosmetic, or supplement) use.

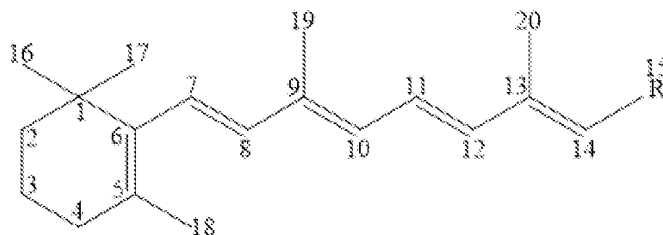
[005] Aspects disclosed herein provide a composition comprising: a retinoid comprising a



structure of Formula I:

; a lipid

excipient; and a surfactant, wherein the retinoid is present in the composition at a percentage (w/w) of about 0.1% to about 90%. In some embodiments, the retinoid comprises a structure of



Formula I:

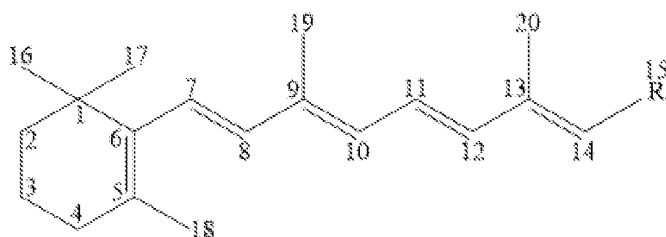
, wherein each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 or at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums (19, 19, 19-trideutero retinoid) or is at the position 20 comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums and at the position 20 comprising substituting three hydrogens with three deuteriums. In some embodiments, the 19, 19, 19-trideutero retinoid comprises a 19, 19, 19-trideutero retinoid analog. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid ester. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid acetate. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 and at the position 20, wherein the position 19 comprises substituting three hydrogens with three deuteriums and the position 20 comprises substituting three hydrogens with three deuteriums (19, 19, 19, 20, 20, 20-hexadeutero retinoid). In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero

retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid ester. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid acetate. In some embodiments, the composition comprises from about 1.0 mg to about 5.0 mg of the retinoid. In some embodiments, the composition comprises from about 2.0 mg to about 3.0 mg of the retinoid. In some embodiments, the composition comprises about 2.5 mg of the retinoid. In some embodiments, the lipid excipient comprises an omega-3 fatty acid. In some embodiments, the omega-3 fatty acid comprises eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA). In some embodiments, the omega-3 fatty acid comprises EPA and DHA. In some embodiments, the composition comprises from about 100 mg to about 500 mg of the EPA. In some embodiments, the composition comprises from about 200 mg to about 400 mg of the EPA. In some embodiments, the composition comprises about 300 mg of the EPA. In some embodiments, the composition comprises from about 50 mg to about 200 mg of the DHA. In some embodiments, the composition comprises from about 100 mg to about 150 mg of the DHA. In some embodiments, the composition comprises about 110 mg of the DHA. In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant. In some embodiments, the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract. In some embodiments, the at least one additional ingredient comprises a turmeric compound. In some embodiments, the at least one additional ingredient comprises a curcuminoid. In some embodiments, the composition comprises from about 20 mg to about 100 mg of the curcuminoid. In some embodiments, the composition comprises about 50 mg of the curcuminoid. In some embodiments, the at least one additional ingredient comprises a carotenoid. In some embodiments, the carotenoid comprises lutein, zeaxanthin, or astaxanthin. In some embodiments, the carotenoid comprises lutein and zeaxanthin. In some embodiments, the composition comprises from about 1 mg to about 100 mg of the lutein. In some embodiments, the composition comprises about 10 mg of the lutein. In some embodiments, the composition comprises from about 1 mg to about 10 mg of the zeaxanthin. In some embodiments, the composition comprises about 2 mg of the zeaxanthin. In some embodiments, the at least one additional ingredient comprises a flavonoid. In some embodiments, the flavonoid comprises anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid. In some embodiments, the amino acid comprises taurine. In some embodiments, the at least one additional ingredient comprises an emulsifier. In some embodiments, the surfactant comprises Tween, Kolliphor, Labrasol, Gelucire, Capmul, polyethylene glycol (PEG), Transcutol, Capryol, or a combination thereof. In some embodiments, the surfactant consists of the Gelucire, the

Capmul, the Tween, and the PEG. In some embodiments, the Gelucire comprises Gelucire 44/14. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Gelucire. In some embodiments, the composition comprises about 0.1 mL of the Gelucire. In some embodiments, the Capmul comprises Capmul MCM. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Capmul. In some embodiments, the composition comprises about 0.1 mL of the Capmul. In some embodiments, the Tween comprises Tween 80. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Tween. In some embodiments, the composition comprises about 0.3 mL of the Tween. In some embodiments, the PEG comprises PEG 400. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the PEG. In some embodiments, the composition comprises about 0.1 mL of the PEG. In some embodiments, the Kolliphor comprises Kolliphor EL. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Kolliphor. In some embodiments, the composition comprises about 0.3 mL of the Kolliphor. In some embodiments, the Transcutol comprises Transcutol HP. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Transcutol. In some embodiments, the composition comprises about 0.1 mL of the Transcutol. In some embodiments, the composition is formulated as a semi-solid. In some embodiments, the composition is formulated as a softgel capsule. In some embodiments, the composition is formulated as a solid dispersion. In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof. In some embodiments, the composition is formulated for an eye administration of a subject. In some embodiments, the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject. In some embodiments, the composition modulates gene expression of a retinal pigment epithelial (RPE) cell. In some embodiments, the composition increases a bioavailability of the retinoid delivered to the RPE cell. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant. In some embodiments, the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject. In some embodiments, the composition does not decrease a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the

surfactant in the subject. In some embodiments, the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject. In some embodiments, the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the stability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the solubility is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%. In some embodiments, the composition further comprises an oil. In some embodiments, the oil comprises corn oil, oleic acid, Maisine cc, or a combination thereof.

[006] Aspects disclosed herein provide methods for treating an eye disease or condition in a subject, the method comprising administering a composition comprising: a retinoid; a lipid excipient; and a surfactant, wherein the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient. In some embodiments, the retinoid comprises a structure of Formula I:



Formula I, wherein each of

numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one

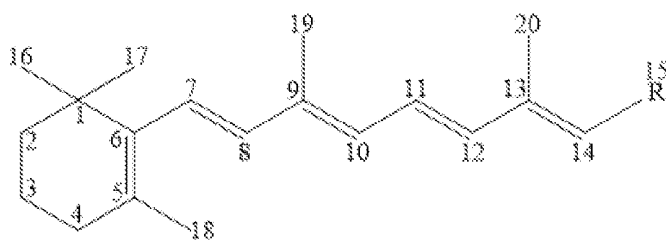
hydrogen with the at least one deuterium is at the position 19 or at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums (19, 19, 19-trideutero retinoid) or is at the position 20 comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums; and at the position 20 comprising substituting three hydrogens with three deuteriums. In some embodiments, the 19, 19, 19-trideutero retinoid comprises a 19, 19, 19-trideutero retinoid analog. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid ester. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid acetate. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 and at the position 20, wherein the position 19 comprises substituting three hydrogens with three deuteriums and the position 20 comprises substituting three hydrogens with three deuteriums (19, 19, 19, 20, 20, 20-hexadeutero retinoid). In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid ester. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid acetate. In some embodiments, the composition comprises from about 1.0 mg to about 5.0 mg of the retinoid. In some embodiments, the composition comprises from about 2.0 mg to about 3.0 mg of the retinoid. In some embodiments, the composition comprises about 2.5 mg of the retinoid. In some embodiments, the lipid excipient comprises an omega-3 fatty acid. In some embodiments, the omega-3 fatty acid comprises eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA). In some embodiments, the omega-3 fatty acid comprises EPA and DHA. In some embodiments, the composition comprises from about 100 mg to about 500 mg of the EPA. In some embodiments, the composition comprises from about 200 mg to about 400 mg of the EPA. In some embodiments, the composition comprises about 300 mg of the EPA. In some embodiments, the composition comprises from about 50 mg to about 200 mg of the DHA. In some embodiments, the composition comprises from about 100 mg to about

150 mg of the DHA. In some embodiments, the composition comprises about 110 mg of the DHA. In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant. In some embodiments, the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract. In some embodiments, the at least one additional ingredient comprises a turmeric compound. In some embodiments, the at least one additional ingredient comprises a curcuminoid. In some embodiments, the composition comprises from about 20 mg to about 100 mg of the curcuminoid. In some embodiments, the composition comprises about 50 mg of the curcuminoid. In some embodiments, the at least one additional ingredient comprises a carotenoid. In some embodiments, the carotenoid comprises lutein, zeaxanthin, or astaxanthin. In some embodiments, the carotenoid comprises lutein and zeaxanthin. In some embodiments, the composition comprises from about 1 mg to about 100 mg of the lutein. In some embodiments, the composition comprises about 10 mg of the lutein. In some embodiments, the composition comprises from about 1 mg to about 10 mg of the zeaxanthin. In some embodiments, the composition comprises about 2 mg of the zeaxanthin. In some embodiments, the at least one additional ingredient comprises a flavonoid. In some embodiments, the flavonoid comprises anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid. In some embodiments, the amino acid comprises taurine. In some embodiments, the at least one additional ingredient comprises an emulsifier. In some embodiments, the surfactant comprises Tween, Kolliphor, Labrasol, Gelucire, Capmul, polyethylene glycol (PEG), Transcutol, Capryol, or a combination thereof. In some embodiments, the surfactant consists of the Gelucire, the Capmul, the Tween, and the PEG. In some embodiments, the Gelucire comprises Gelucire 44/14. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Gelucire. In some embodiments, the composition comprises about 0.1 mL of the Gelucire. In some embodiments, the Capmul comprises Capmul MCM. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Capmul. In some embodiments, the composition comprises about 0.1 mL of the Capmul. In some embodiments, the Tween comprises Tween 80. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Tween. In some embodiments, the composition comprises about 0.3 mL of the Tween. In some embodiments, the PEG comprises PEG 400. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the PEG. In some embodiments, the composition comprises about 0.1 mL of the PEG. In some embodiments, the Kolliphor comprises Kolliphor EL. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Kolliphor. In some embodiments, the composition

comprises about 0.3 mL of the Kolliphor. In some embodiments, the Transcutol comprises Transcutol HP. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Transcutol. In some embodiments, the composition comprises about 0.1 mL of the Transcutol. In some embodiments, the composition is formulated as a semi-solid. In some embodiments, the composition is formulated as a softgel capsule. In some embodiments, the composition is formulated as a solid dispersion. In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof. In some embodiments, the composition is formulated for an eye administration of a subject. In some embodiments, the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject. In some embodiments, the composition modulates gene expression of a retinal pigment epithelial (RPE) cell. In some embodiments, the composition increases a bioavailability of the retinoid delivered to the RPE cell. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant. In some embodiments, the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject. In some embodiments, the composition does not decrease a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject. In some embodiments, the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the stability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the solubility is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about

1% to about 50%. In some embodiments, the composition further comprises an oil. In some embodiments, the oil comprises corn oil, oleic acid, Maisine cc, or a combination thereof. In some embodiments, the eye disease or condition is associated with accumulation of N-retinylidene-N-retinylethanolamine (A2E). In some embodiments, the method further comprises decreasing the accumulation of A2E in the subject. In some embodiments, the eye disease or condition is associated with a retinal pigment epithelial (RPE) cell. In some embodiments, the method further comprises modulating gene expression of the RPE cell. In some embodiments, the gene expression comprises expression of ATP-binding cassette, sub-family A (ABC1), member 4 (ABCA4), elongation of very long chain fatty acids protein 4 (ELOVL4), or a combination thereof. In some embodiments, the eye disease or condition is macular degeneration. In some embodiments, the macular degeneration comprises age-related macular degeneration (AMD), bestrophinopathies, bull's eye maculopathy, central serous retinopathy, Charles Bonnet syndrome (CBS), cone dystrophy, Doyme honeycomb dystrophy, diabetic macular oedema (DMO), macular hole, macular oedema, myopic macular degeneration, pattern dystrophy, pseudoxanthoma elasticum (PXE), punctate inner choroidopathy (PIC), retinal vein occlusion (RVO), Sorsby fundus dystrophy, Stargardt disease, geographic atrophy, or a combination thereof. In some embodiments, the AMD comprises dry AMD. In some embodiments, the AMD comprises early AMD. In some embodiments, the AMD comprises wet AMD.

[007] Aspects disclosed herein provide use of a composition, comprising contacting a subject with the composition, the composition comprising: a retinoid; a lipid excipient; and a surfactant, wherein the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient, and wherein the use is a non-medical use. In some embodiments, the retinoid comprises a structure of Formula I:



, wherein each of numbers 1

through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), or R₅ (COO-glucuronide). In some embodiments, the position of the

carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 or at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums (19, 19, 19-trideutero retinoid) or is at the position 20 comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums; and at the position 20 comprising substituting three hydrogens with three deuteriums. In some embodiments, the 19, 19, 19-trideutero retinoid comprises a 19, 19, 19-trideutero retinoid analog. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid ester. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid acetate. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 and at the position 20, wherein the position 19 comprises substituting three hydrogens with three deuteriums and the position 20 comprises substituting three hydrogens with three deuteriums (19, 19, 19, 20, 20, 20-hexadeutero retinoid). In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid ester. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid acetate. In some embodiments, the composition comprises from about 1.0 mg to about 5.0 mg of the retinoid. In some embodiments, the composition comprises from about 2.0 mg to about 3.0 mg of the retinoid. In some embodiments, the composition comprises about 2.5 mg of the retinoid. In some embodiments, the lipid excipient comprises an omega-3 fatty acid. In some embodiments, the omega-3 fatty acid comprises EPA or DHA. In some embodiments, the omega-3 fatty acid comprises EPA and DHA. In some embodiments, the composition comprises from about 100 mg to about 500 mg of the EPA. In some embodiments, the composition comprises from about 200 mg to about 400 mg of the EPA. In some embodiments, the composition comprises about 300 mg of the EPA. In

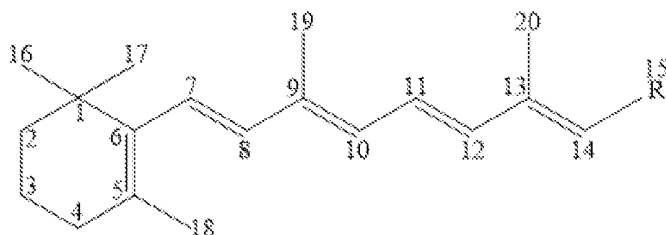
some embodiments, the composition comprises from about 50 mg to about 200 mg of the DHA. In some embodiments, the composition comprises from about 100 mg to about 150 mg of the DHA. In some embodiments, the composition comprises about 110 mg of the DHA. In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant. In some embodiments, the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract. In some embodiments, the at least one additional ingredient comprises a turmeric compound. In some embodiments, the at least one additional ingredient comprises a curcuminoid. In some embodiments, the composition comprises from about 20 mg to about 100 mg of the curcuminoid. In some embodiments, the composition comprises about 50 mg of the curcuminoid. In some embodiments, the at least one additional ingredient comprises a carotenoid. In some embodiments, the carotenoid comprises lutein, zeaxanthin, or astaxanthin. In some embodiments, the composition comprises from about 1 mg to about 100 mg of the lutein. In some embodiments, the composition comprises about 10 mg of the lutein. In some embodiments, the composition comprises from about 1 mg to about 10 mg of the zeaxanthin. In some embodiments, the composition comprises about 2 mg of the zeaxanthin. In some embodiments, the at least one additional ingredient comprises a flavonoid. In some embodiments, the flavonoid comprises anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid. In some embodiments, the amino acid comprises taurine. In some embodiments, the at least one additional ingredient comprises an emulsifier. In some embodiments, the surfactant comprises Tween, Kolliphor, Labrasol, Gelucire, Capmul, PEG, Transcutol, Capryol, or a combination thereof. In some embodiments, the surfactant consists of the Gelucire, the Capmul, the Tween, and the PEG. In some embodiments, the Gelucire comprises Gelucire 44/14. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Gelucire. In some embodiments, the composition comprises about 0.1 mL of the Gelucire. In some embodiments, the Capmul comprises Capmul MCM. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Capmul. In some embodiments, the composition comprises about 0.1 mL of the Capmul. In some embodiments, the Tween comprises Tween 80. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Tween. In some embodiments, the composition comprises about 0.3 mL of the Tween. In some embodiments, the PEG comprises PEG 400. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the PEG. In some embodiments, the composition comprises about 0.1 mL of the PEG. In some embodiments, the Kolliphor comprises Kolliphor EL. In some embodiments, the composition comprises from about 0.05 mL

to about 0.5 mL of the Kolliphor. In some embodiments, the composition comprises about 0.3 mL of the Kolliphor. In some embodiments, the Transcutol comprises Transcutol HP. In some embodiments, the composition comprises from about 0.05 mL to about 0.5 mL of the Transcutol. In some embodiments, the composition comprises about 0.1 mL of the Transcutol. In some embodiments, the composition is formulated as a semi-solid. In some embodiments, the composition is formulated as a softgel capsule. In some embodiments, the composition is formulated as a solid dispersion. In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof. In some embodiments, the composition is formulated for an eye administration of a subject. In some embodiments, the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject. In some embodiments, the composition modulates gene expression of a retinal pigment epithelial (RPE) cell. In some embodiments, the composition increases a bioavailability of the retinoid delivered to the RPE cell. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant. In some embodiments, the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the stability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject. In some embodiments, the composition does not decrease a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject. In some embodiments, the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the solubility is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%. In some

embodiments, the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%. In some embodiments, the composition comprises an oil. In some embodiments, the oil comprises corn oil, oleic acid, Maisine cc, or a combination thereof. In some embodiments, the use is an aesthetic use. In some embodiments, the use is a cosmetic use. In some embodiments, the use is a supplement use. In some embodiments, the use does not treat a disease or condition. In some embodiments, the composition is formulated for transdermal delivery of the retinoid to the subject. In some embodiments, the composition is formulated as a semi-solid. In some embodiments, the composition is formulated as a softgel capsule. In some embodiments, the composition is formulated as a solid dispersion. In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof. In some embodiments, the composition is formulated as a supplement.

[008] In various embodiments disclosed herein, a composition is provided comprising: a retinoid; and a lipid excipient wherein the retinoid is present in the composition at a percentage (w/w) of about 0.1% to about 90%.

[009] In some embodiments, the retinoid comprises a structure of Formula I:



wherein each of numbers 1

through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R_1 (CH_2OH or retinol), R_2 (CH_2O -fatty acid or retinyl ester), R_3 (CHO or retinal), R_4 (COOH or retinoic acid), R_5 (COO -glucuronide), or R_6 ($\text{CH}_2\text{OCHOCH}_3$ or retinyl acetate). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-

trideutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 14 and at the position 20, wherein the position 14 comprises substituting one hydrogen with one deuterium and the position 20 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradeutero retinoid). In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetraideutero retinoid analog. In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinoid ester. In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 14 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadeutero retinoid). In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinoid analog. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid ester. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid acetate.

[0010] In some embodiments, the composition is formulated as a semi-solid.

[0011] In some embodiments, the composition is formulated as a softgel capsule.

[0012] In some embodiments, the composition is formulated as a solid dispersion.

[0013] In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.

[0014] In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant. In some embodiments, the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract. In some embodiments, the at least one additional ingredient comprises a fatty acid. In some embodiments, the fatty acid comprises omega-3 fatty acid. In some embodiments, the at least one additional ingredient comprises a carotenoid. In some embodiments, the carotenoid comprises lutein, zeaxanthin, or astaxanthin. In some embodiments, the at least one additional ingredient comprises a flavonoid. In some embodiments, the flavonoid comprises anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid. In some embodiments, the amino acid comprises taurine.

[0015] In some embodiments, the composition is formulated for an eye administration of a subject.

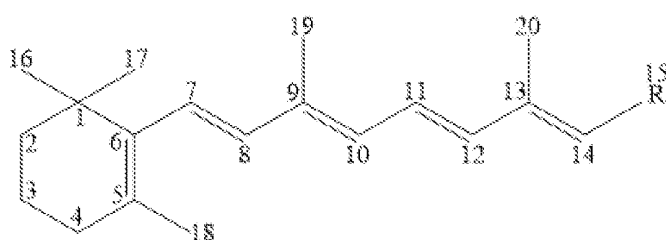
[0016] In some embodiments, the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject.

[0017] In some embodiments, the composition modulates gene expression of a retinal pigment epithelial (RPE) cell. In some embodiments, the composition increases the bioavailability of the retinoid delivered to the RPE cell.

[0018] In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%.

[0019] In various embodiments disclosed herein, a method for treating an eye disease or condition in a subject is provided, comprising administering a composition comprising: a retinoid; and a lipid excipient, wherein the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient.

[0020] In some embodiments, the retinoid comprises a structure of Formula I:



Formula I, wherein each of

numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a

20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 14 and at the position 20, wherein the position 14 comprises substituting one hydrogen with one deuterium and the position 20 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradutero retinoid). In some embodiments, the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid analog. In some embodiments, the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid ester. In some embodiments, the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 12 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadeutero retinoid). In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinoid analog. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid ester. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid acetate.

[0021] In some embodiments, the composition is formulated as a semi-solid.

[0022] In some embodiments, the composition is formulated as a softgel capsule.

[0023] In some embodiments, the composition is formulated as a solid dispersion.

[0024] In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.

[0025] In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant. In some embodiments, the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract. In some embodiments, the at least one additional ingredient comprises a fatty acid. In some embodiments, the fatty acid comprises omega-3 fatty acid. In some embodiments, the at least one additional ingredient comprises a carotenoid. In some embodiments, the carotenoid comprises lutein, zeaxanthin, or astaxanthin. In some embodiments, the at least one additional ingredient comprises a flavonoid. In some embodiments, the flavonoid comprises anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid. In some

embodiments, the amino acid comprises taurine. In some embodiments, the composition is formulated for an eye administration of a subject.

[0026] In some embodiments, the eye disease or condition is associated with accumulation of N-retinylidene-N-retinylethanolamine (A2E).

[0027] In some embodiments, the method further comprises decreasing the accumulation of A2E in the subject.

[0028] In some embodiments, the eye disease or condition is associated with a retinal pigment epithelial (RPE) cell. In some embodiments, the method further comprises modulating gene expression of the RPE cell.

[0029] In some embodiments, the gene expression comprises expression of ATP-binding cassette, sub-family A (ABC1), member 4 (ABCA4), elongation of very long chain fatty acids protein 4 (ELOVL4), or a combination thereof.

[0030] In some embodiments, the eye disease or condition is macular degeneration.

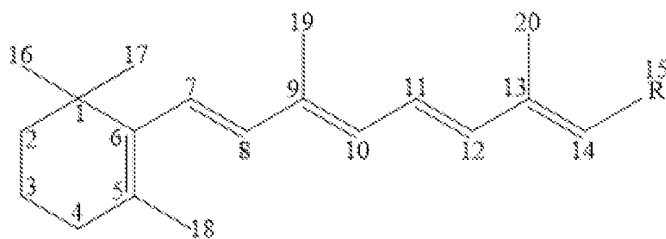
[0031] In some embodiments, the macular degeneration comprises age-related macular degeneration (AMD), bestrophinopathies, bull's eye maculopathy, central serous retinopathy, Charles Bonnet syndrome (CBS), cone dystrophy, Doyme honeycomb dystrophy, diabetic macular oedema (DMO), macular hole, macular oedema, myopic macular degeneration, pattern dystrophy, pseudoxanthoma elasticum (PXE), punctate inner choroidopathy (PIC), retinal vein occlusion (RVO), Sorsby fundus dystrophy, Stargardt disease, geographic atrophy, or a combination thereof. In some embodiments, the AMD comprises dry AMD. In some embodiments, the AMD comprises early AMD. In some embodiments, the AMD comprises wet AMD.

[0032] In some embodiments, the lipid excipient increases the bioavailability of the retinoid in the subject by at least 50% compared to the second bioavailability of the retinoid formulated with the excipient that is different from the lipid excipient.

[0033] In some embodiments, the lipid excipient increases the bioavailability of the retinoid in the subject by 100% compared to the second bioavailability of the retinoid formulated with the excipient that is different from the lipid excipient. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%.

[0034] In various embodiments disclosed herein, a use of a composition is provided, comprising contacting a subject with the composition, the composition comprising: a retinoid; and a lipid excipient, wherein the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient, and wherein the use is a non-medical use.

[0035] In some embodiments, the retinoid comprises a structure of Formula I:



Formula I, wherein each of

numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), or R₅ (COO-glucuronide). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 14 and at the position 20, wherein the position 14 comprises substituting one hydrogen with one deuterium and the position 20 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradeutero retinoid). In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinoid analog. In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinoid ester. In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 12 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three

hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadeutero retinoid). In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinoid analog. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid ester. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid acetate.

[0036] In some embodiments, the use is an aesthetic use. In some embodiments, the use is a cosmetic use. In some embodiments, the use is a supplement use.

[0037] In some embodiments, the use does not treat a disease or condition.

[0038] In some embodiments, the composition is formulated for transdermal delivery of the retinoid to the subject.

[0039] In some embodiments, the composition is formulated as a semi-solid.

[0040] In some embodiments, the composition is formulated as a softgel capsule.

[0041] In some embodiments, the composition is formulated as a solid dispersion.

[0042] In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.

[0043] In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant. In some embodiments, the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract. In some embodiments, the at least one additional ingredient comprises a fatty acid. In some embodiments, the fatty acid comprises omega-3 fatty acid. In some embodiments, the at least one additional ingredient comprises a carotenoid. In some embodiments, the carotenoid comprises lutein, zeaxanthin, or astaxanthin. In some embodiments, the at least one additional ingredient comprises a flavonoid. In some embodiments, the flavonoid comprises anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid. In some embodiments, the amino acid comprises taurine.

[0044] In some embodiments, the retinoid is present in the composition at a percentage (w/w) of about 1% to about 50%. In some embodiments, the lipid excipient increases the bioavailability of the retinoid in the subject by 100% compared to the second bioavailability of the retinoid formulated with the excipient that is different from the lipid excipient. In some embodiments, the composition is formulated as a supplement.

INCORPORATION BY REFERENCE

[0045] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or

patent application was specifically and individually indicated to be incorporated by reference. To the extent publications and patents or patent applications incorporated by reference contradict the disclosure contained in the specification, the specification is intended to supersede and/or take precedence over any such contradictory material.

BRIEF DESCRIPTION OF THE DRAWINGS

[0046] The novel features of the disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the disclosure are utilized, and the accompanying drawings (also “Figure” and “FIG.” herein), of which:

[0047] **Fig. 1** illustrates a graph showing linearity of an Ultra Performance Liquid Chromatography (UPLC) method for assay analysis as disclosed herein.

[0048] **Fig. 2** illustrates images showing appearance of first round lipid formulations for F01-F17.

[0049] **Fig. 3** illustrates images showing dilution appearance of first round lipid formulations without retinol-d6, diluted with simulated gastric fluid (SGF) and FaSSIF.

[0050] **Fig. 4** illustrates images showing dilution appearance of first round lipid formulations with retinol-d6, diluted with SGF and FaSSIF.

[0051] **Fig. 5** illustrates images showing appearance of second round of lipid formulations.

[0052] **Fig. 6** illustrates images showing dilution appearance of second round lipid formulations without retinol-d6. In a dilution study without retinol-d6 but with lutein, zeaxanthin and curcuminoid, F22 showed good PDI. F18-F22 showed suspension with coarse particle state after diluted with simulated gastric fluid (SGF) and FaSSIF. The PSD results were significantly impacted by the presence of insoluble substances, resulting in multiple peaks and poor data quality. Consequently, in following dilution study involving retinol-d6, lutein, zeaxanthin, and curcuminoid were excluded to avoid their influence.

[0053] **Fig. 7** illustrates appearance of F23 and dilution appearance of second round lipid formulations with retinol-d6.

[0054] **Fig. 8** illustrates graphs showing an overlay of placebo and standard (STD) solution.

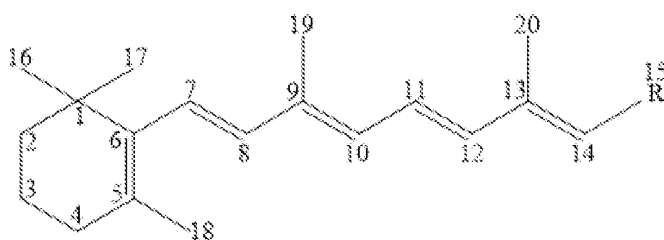
[0055] **Fig. 9** illustrates time-course measurements of the plasma concentration of retinol-d3 for a 24-hour duration.

[0056] The novel features of the disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be

obtained by reference to the following detailed description that sets forth illustrative embodiments.

DETAILED DESCRIPTION

[0057] Retinoid can treat a variety of diseases or conditions. For example, retinoid can be administered to a subject with retinal deficiency. Such retinal deficiency can manifest into eye diseases or conditions. Retinoid can also be used for non-medical uses such as for aesthetic, cosmetic, or supplement use. However, frequent or excessive administration of retinoid can lead to toxicity such as hypervitaminosis A syndrome, where the symptoms of retinoid toxicity can include changes in lipid metabolism, liver damage, nausea, vomiting, blurred vision, or bone damage. Accordingly, as described herein, in some aspects, is a composition comprising: a retinoid; and a lipid excipient. In some embodiments, the retinoid is present in the composition at a percentage (weight per weight or w/w) of about 10% to about 90%. In some embodiments, the retinoid is present in the composition at a percentage (weight per weight or w/w) of about 1% to about 50%. In some embodiments, the retinoid comprises a structure of Formula I:



Formula I, where each number denotes a position of a carbon covalently linked to at least one hydrogen, where at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the position of the

carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 14 and at the position 20, wherein the position 14 comprises substituting one hydrogen with one deuterium and the position 20 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradеuterо retinoid). In some embodiments, the 14, 20, 20, 20-tetradеuterо retinoid comprises a 14, 20, 20, 20-tetradеuterо retinoid analog. In some embodiments, the 14, 20, 20, 20-tetradеuterо retinoid comprises a 14, 20, 20, 20-tetradеuterо retinoid ester. In some embodiments, the 14, 20, 20, 20-tetradеuterо retinoid comprises a 14, 20, 20, 20-tetradеuterо retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 12 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadeuterо retinoid). In some embodiments, the 12, 14, 20, 20, 20-pentadeuterо retinoid comprises a 12, 14, 20, 20, 20-pentadeuterо retinoid analog. In some embodiments, the 12, 14, 20, 20, 20-pentadeuterо retinoid analog comprises a 12, 14, 20, 20, 20-pentadeuterо retinoid ester. In some embodiments, the 12, 14, 20, 20, 20-pentadeuterо retinoid analog comprises a 12, 14, 20, 20, 20-pentadeuterо retinoid acetate. In some embodiments, the retinoid described herein comprises retinol-d6. In some embodiments, the retinoid described herein consists of retinol-d6. In some embodiments, the retinoid described herein comprises Vitamin A-d6. In some embodiments, the retinoid described herein consists of Vitamin A-d6. In some embodiments, the retinoid described herein comprises retinol-d3. In some embodiments, the retinoid described herein consists of retinol-d3. In some embodiments, the retinoid described herein comprises Vitamin A-d3. In some embodiments, the retinoid described herein consists of Vitamin A-d3.

[0058] In some embodiments, the composition is formulated for treating an eye disease or condition described herein. In some embodiments, the composition is formulated with a lipid excipient partially due the retinoid being a fat-soluble molecule. In some embodiments, the composition comprising the retinoid can comprise an oil-based capsule (e.g., softgel capsule). In some embodiments, the composition comprises an additional excipient for increasing water solubility or retinoid bioavailability. For example, hydroxypropyl- β -cyclodextrin (HPBCD) or nanoparticle (e.g., lipid nanoparticle, nanomicelle, nanocapsule, nanosphere, or a combination thereof) can be added to the composition to increase: the abundance of the retinoid in the composition or retinoid bioavailability in the subject upon administration of the composition to the subject. In some embodiments, the composition comprises a retinoid comprising a deuterated retinoid. In some embodiments, the composition comprises at least one additional ingredient. In

some embodiments, the at least one additional ingredient is an antioxidant. In some embodiments, the composition is an oil-based formulation (e.g., a softgel capsule). In some embodiments, the composition is a lipid-based formulation (e.g., lipid nanoparticle, amorphous solid dispersion, or lipid polymer mix). Example 1 provides non-limiting examples of manufacturing and components of the composition described herein. In some embodiments, the composition can be any one of the formulations as illustrated in **Table 6** (e.g., any one of F01-F17). For example, as illustrated in **Table 6**, in some embodiments, the composition can be formulation F01, F02, F03, F04, F05, F06, F07, F08, F09, F10, F11, F12, F13, F14, F15, F16, or F17. In some embodiments, the composition can be any one of the formulations as illustrated in **Table 9** (e.g., any one of F18-F22). For example, as illustrated in **Table 9**, in some embodiments, the composition can be formulation F18, F19, F20, F21, or F22.

[0059] Described herein, in some aspects, is a method for treating an eye disease or condition in a subject. In some embodiments, the method comprises administering a composition comprising: a retinoid; and a lipid excipient. In some embodiments, the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient. In some embodiments, the lipid excipient increases a bioavailability of the retinoid in the subject by 100% compared to a bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient. In some embodiments, the increased bioavailability of the retinoid increases therapeutic efficacy for treating the eye disease or condition. In some embodiments, the increased bioavailability of the retinoid decreases retinoid toxicity in the subject. In some embodiments, the retinoid (e.g., deuterated vitamin A or vitamin A derivative), when administered to the subject, can decrease the formation or abundance of vitamin A dimer in the subject. In some embodiments, the retinoid (e.g., deuterated vitamin A or vitamin A derivative), when administered to the subject, can decrease the formation or abundance of lipofuscin in the subject. In some embodiments, the retinoid (e.g., deuterated vitamin A or vitamin A derivative), when administered to the subject, can decrease the formation or abundance of N-retinylidene-N-retinylethanolamine (A2E), a toxic compound that accumulates in the retinal pigment epithelial (RPE) cells of the eye. A2E is formed as a byproduct of the visual cycle, where retinaldehyde (a derivative of vitamin A) reacts with phosphatidylethanolamine in the RPE cells for regulating the visual cycle and maintaining the health of the retina. Retinoid can decrease the formation or abundance of A2E through several mechanisms, including regulation of the visual cycle. Retinoid is an essential component of the visual cycle, which is the process by which light is converted into electrical signals in the retina. By modulating this cycle, retinoid can influence the

generation of toxic byproducts like A2E. In addition, retinoid exhibits antioxidant properties that can help neutralize free radicals and decrease oxidative stress in cells. Oxidative stress is linked to the formation of A2E and other harmful compounds in the retina. Also, retinoids can influence the function and metabolism of retinal pigment epithelial cells. By maintaining the proper function of these cells, retinoid can potentially reduce the accumulation of A2E. Additionally, retinoid can modulate gene expression of enzymes involved in the formation of A2E in RPE cells. In some embodiments, the gene expression comprises expression of ATP-binding cassette, sub-family A (ABC1), member 4 (ABCA4), elongation of very long chain fatty acids protein 4 (ELOVL4), or a combination thereof. In some embodiments, the eye disease or condition to be treated by a composition described herein includes macular degeneration such as age-related macular degeneration (AMD).

[0060] Described herein, in some aspects, is a use of a composition described herein. In some embodiments, the use is a non-medical use. In some embodiments, the use is not a method of treatment use. In some embodiments, the use of the composition does not treat an eye disease or condition described herein. In some embodiments, the use is an aesthetic use. In some embodiments, the use is a cosmetic use. In some embodiments, the use is a supplement use.

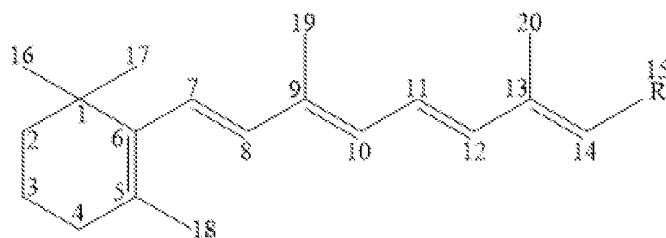
Compositions

[0061] Described herein, in some aspects, is a composition comprising a retinoid. In some embodiments, the composition comprises the retinoid and a lipid excipient. In some embodiments, the composition comprises the retinoid, the lipid excipient, and a surfactant. In some embodiments, the composition comprising the lipid excipient and the surfactant increases bioavailability, solubility, stability, or a combination thereof compared to formulating the retinoid in a comparable composition in absence of the lipid excipient or the surfactant. In some embodiments, the composition comprising the lipid excipient and the surfactant increases bioavailability, solubility, stability, or a combination thereof compared to formulating the retinoid in a comparable composition in absence of the lipid excipient and the surfactant.

[0062] In some embodiments, the retinoid is present in the composition at a percentage (w/w) from about 10% to about 90%. In some embodiments, the bioavailability of the retinoid (e.g., the abundance of the retinoid delivered to the site of need in a subject upon administration of the composition) is increased compared to a bioavailability of the retinoid formulated in absence of the lipid excipient. In some embodiments, the lipid excipient increases the bioavailability of the retinoid by at least 10%, at least 20%, at least 50%, at least two fold, at least five fold, or at least ten fold.

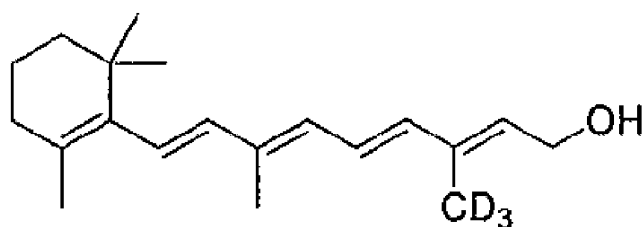
[0063] In some embodiments, the retinoid comprises a vitamin A derivative. In some embodiments, the vitamin A derivative comprises a deuterated vitamin A. In some embodiments, the vitamin A derivative is a deuterated vitamin A. In some embodiments, the deuterated vitamin A comprises a substitution of a hydrogen with a deuterium. In some embodiments, the deuterated vitamin A comprises a substitution of one or more hydrogens with one or more deuterium. In some embodiments, the deuterated vitamin A comprises a substitution of two or more hydrogens with two or more deuteriums. In some embodiments, the deuterated vitamin A comprises a substitution of three or more hydrogens with three or more deuteriums. In some embodiments, the deuterated vitamin A comprises a substitution of four or more hydrogens with four or more deuterium. In some embodiments, the deuterated vitamin A comprises a substitution of five or more hydrogens with five or more deuteriums. In some embodiments, the deuterated vitamin A comprises a substitution of six or more hydrogens with six or more deuteriums. In some embodiments, the deuterated vitamin A comprises a substitution of seven or more hydrogens with seven or more deuteriums. In some embodiments, the deuterated vitamin A comprises a substitution of eight or more hydrogens with eight or more deuteriums. In some embodiments, the deuterated vitamin A comprises a substitution of a hydrogen with a deuterium, wherein the substituted hydrogen is covalently linked to a carbon of the deuterated vitamin A. In some embodiments, the deuterated vitamin A comprises two or more substitutions of a hydrogen with a deuterium, wherein the two or more substituted hydrogens are covalently linked to two or more carbons of the deuterated vitamin A. In some embodiments, the vitamin A derivative comprises retinyl ester, retinol, retinaldehyde, retinoic acid, or a combination thereof. In some embodiments, the vitamin A derivative comprises a synthetic retinoid such as adapalene.

[0064] In some embodiments, the retinoid is present in the composition at a percentage (weight per weight or w/w) of about 10% to about 90%. In some embodiments, the retinoid is present in the composition at a percentage (weight per weight or w/w) of about 1% to about 50%. In some embodiments, the retinoid comprises a structure of Formula I:



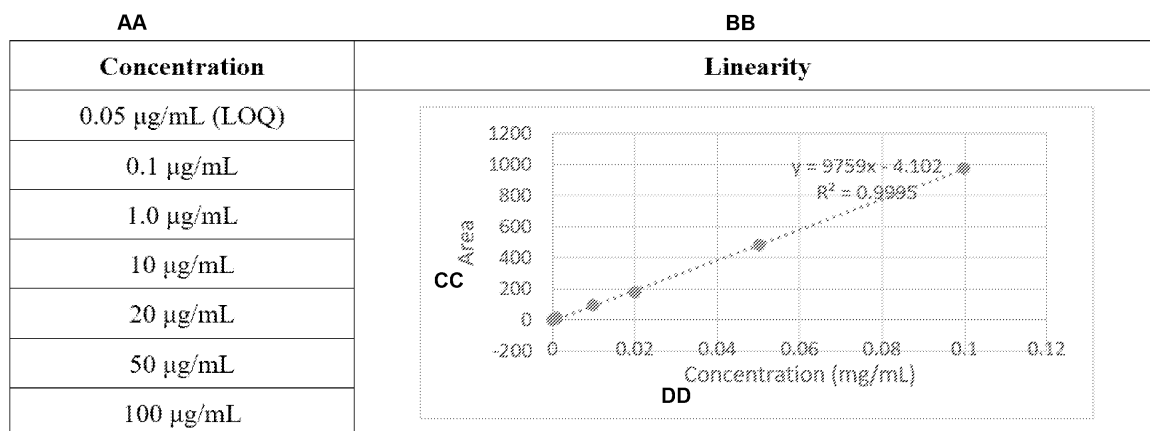
Formula I, wherein each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one

deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate). In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinol. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinol ester. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinol acetate. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinal. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero pro-vitamin A carotenoid. In some embodiments, the retinoid comprises a structure of:



[0065] In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 19 or at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums (19, 19, 19-trideutero retinoid) or at the position 20 comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums and at the position 20 comprising substituting three hydrogens with three deuteriums.

Fig. 1



AA Concentration CC Superficie
BB Linéarité DD Concentration (mg/mL)

embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinol acetate. In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinol ester. In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero retinal. In some embodiments, the 14, 20, 20, 20-tetradeutero retinoid comprises a 14, 20, 20, 20-tetradeutero pro-vitamin A carotenoid.

[0068] In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 12 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadeutero retinoid). In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinoid analog. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinoid ester. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinoid acetate. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinol. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinol ester. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinol acetate. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinal. In some embodiments, the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero pro-vitamin A carotenoid.

[0069] In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 19. In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 19, comprising substituting three hydrogens with three deuteriums (19, 19, 19-trideutero retinoid). In some embodiments, the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 10 and at the position 19, wherein the position 10 comprises substituting one hydrogen with one deuterium and the position 19 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradeutero retinoid). In some embodiments, the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero retinoid analog. In some embodiments, the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero retinoid ester. In some embodiments, the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero retinoid acetate. In some embodiments, the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero retinol. In some embodiments,

the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero retinol ester. In some embodiments, the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero retinol acetate. In some embodiments, the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero retinal. In some embodiments, the 10, 19, 19, 19-tetradeutero retinoid comprises a 10, 19, 19, 19-tetradeutero pro-vitamin A carotenoid.

[0070] In some embodiments, the retinoid comprising the structure of Formula I comprises substituting one hydrogen with one deuterium. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least one hydrogen with at least one deuterium. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting two hydrogens with two deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least two hydrogens with at least two deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting three hydrogens with three deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least three hydrogens with at least three deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting four hydrogens with four deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least four hydrogens with at least four deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting five hydrogens with five deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least five hydrogens with at least five deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting six hydrogens with six deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least six hydrogens with at least six deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting seven hydrogens with seven deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least seven hydrogens with at least seven deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting eight hydrogens with eight deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least eight hydrogens with at least eight deuteriums. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting one hydrogen with one tritium. In some embodiments, the retinoid comprising the structure of Formula I comprises substituting at least one hydrogen with at least one tritium.

[0071] In some embodiments, the retinoid described herein comprises a derivative or analog of retinoic acid. In some embodiments, the retinoid comprises tretinoin (all-trans retinoic acid). In

some embodiments, the retinoid comprises adapalene. In some embodiments, the retinoid comprises tazarotene. In some embodiments, the retinoid comprises trifarotene. In some embodiments, the retinoid comprises alitretinoin. In some embodiments, the retinoid comprises bexarotene. In some embodiments, the retinoid comprises isotretinoin. In some embodiments, the retinoid comprises retinyl palmitate. In some embodiments, the retinoid comprises a 9-cis retinal analog (e.g., QLT091001). In some embodiments, the retinoid comprises tamibarotene. In some embodiments, the retinoid comprises acitretin. In some embodiments, the retinoid comprises tararotene.

[0072] In some embodiments, the composition, when administered to a subject, confers therapeutic efficacy to the subject for treating a disease or condition in the subject. In some embodiments, the disease or condition is associated with lipofuscin. In some embodiments, the disease or condition is associated with accumulation of lipofuscin. In some embodiments, the disease or condition is associated with presence or abundance of lipofuscin in the retinal pigment epithelial (RPE) cell. In some embodiments, the disease or condition is associated with N-retinylidene-N-retinylethanolamine (A2E). In some embodiments, the disease or condition is associated with accumulation of A2E. In some embodiments, the disease or condition is associated with a RPE cell. In some embodiments, the disease or condition is associated with the presence or abundance of A2E in the RPE cell. In some embodiments, the disease or condition is macular degeneration. Non-limiting examples of the macular degeneration includes age-related macular degeneration (AMD), bestrophinopathies, bull's eye maculopathy, central serous retinopathy, Charles Bonnet syndrome (CBS), cone dystrophy, Doyne honeycomb dystrophy, diabetic macular oedema (DMO), macular hole, macular oedema, myopic macular degeneration, pattern dystrophy, pseudoxanthoma elasticum (PXE), punctate inner choroidopathy (PIC), retinal vein occlusion (RVO), Sorsby fundus dystrophy, or Stargardt disease.

[0073] In some embodiments, the composition decreases accumulation of vitamin A dimer in the subject. In some embodiments, the composition decreases accumulation of lipofuscin in the subject. In some embodiments, the composition modulates one or more gene expressions of a gene associated with lipofuscin accumulation in the subject. In some embodiments, the composition decreases accumulation of A2E in the subject. In some embodiments, the composition modulates one or more gene expressions of a gene associated with A2E accumulation or retinoic acid metabolism in the subject. In some embodiments, the composition increases the bioavailability of the retinoid delivered to the RPE cell in the subject. In some embodiments, the composition decreases toxicity associated with retinoid in the subject. For example, the subject, when administered with a composition described herein, does not exhibit or

does exhibit decreased retinoid toxicity compared to if the subject is administered with retinoid in other formulations.

[0074] In some embodiments, the composition comprises at least one lipid excipient. In some embodiments, the at least one lipid excipient comprises oil dissolving or encapsulating the retinoid. In some embodiments, the at least one lipid excipient comprises lipid. For example, the lipid excipient may be a lipid for formulating the composition as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof. In some embodiments, the at least one lipid excipient comprises an omega-3 fatty acid. In some embodiments, the omega-3 fatty acid comprises eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA). In some embodiments, the composition comprises the omega-3 fatty acid comprising EPA and DHA. In some embodiments, the composition comprises EPA at about 50 milligrams (mg) to about 1,000 mg. In some embodiments, the composition comprises EPA at about 50 mg to about 100 mg, about 50 mg to about 200 mg, about 50 mg to about 250 mg, about 50 mg to about 300 mg, about 50 mg to about 350 mg, about 50 mg to about 400 mg, about 50 mg to about 450 mg, about 50 mg to about 500 mg, about 50 mg to about 750 mg, or about 50 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 100 mg to about 200 mg, about 100 mg to about 250 mg, about 100 mg to about 300 mg, about 100 mg to about 350 mg, about 100 mg to about 400 mg, about 100 mg to about 450 mg, about 100 mg to about 500 mg, about 100 mg to about 750 mg, or about 100 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 200 mg to about 250 mg, about 200 mg to about 300 mg, about 200 mg to about 350 mg, about 200 mg to about 400 mg, about 200 mg to about 450 mg, about 200 mg to about 500 mg, about 200 mg to about 750 mg, or about 200 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 250 mg to about 300 mg, about 250 mg to about 350 mg, about 250 mg to about 400 mg, about 250 mg to about 450 mg, about 250 mg to about 500 mg, about 250 mg to about 750 mg, or about 250 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 300 mg to about 350 mg, about 300 mg to about 400 mg, about 300 mg to about 450 mg, about 300 mg to about 500 mg, about 300 mg to about 750 mg, or about 300 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 350 mg to about 400 mg, about 350 mg to about 450 mg, about 350 mg to about 500 mg, about 350 mg to about 750 mg, or about 350 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 400 mg to about 450 mg, about 400 mg to about 500 mg, about 400 mg to about 750 mg, or about 400 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 450 mg to about 500 mg, about 450 mg to about 750 mg, or about 450 mg to about 1,000 mg. In some embodiments, the composition

comprises EPA at about 500 mg to about 750 mg, about 500 mg to about 1,000 mg, or about 750 mg to about 1,000 mg. In some embodiments, the composition comprises EPA at about 50 mg, about 100 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 750 mg, or about 1,000 mg. In some embodiments, the composition comprises EPA at least about 50 mg, at least about 100 mg, at least about 200 mg, at least about 250 mg, at least about 300 mg, at least about 350 mg, at least about 400 mg, at least about 450 mg, at least about 500 mg, or at least about 750 mg. In some embodiments, the composition comprises EPA at most about 100 mg, at most about 200 mg, at most about 250 mg, at most about 300 mg, at most about 350 mg, at most about 400 mg, at most about 450 mg, at most about 500 mg, at most about 750 mg, or at most about 1,000 mg.

[0075] In some embodiments, the composition comprises DHA at about 50 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 50 mg to about 110 mg, about 50 mg to about 120 mg, about 50 mg to about 130 mg, about 50 mg to about 140 mg, about 50 mg to about 150 mg, about 50 mg to about 200 mg, about 50 mg to about 250 mg, about 50 mg to about 300 mg, about 50 mg to about 350 mg, about 50 mg to about 400 mg, or about 50 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 110 mg to about 120 mg, about 110 mg to about 130 mg, about 110 mg to about 140 mg, about 110 mg to about 150 mg, about 110 mg to about 200 mg, about 110 mg to about 250 mg, about 110 mg to about 300 mg, about 110 mg to about 350 mg, about 110 mg to about 300 mg, or about 110 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 120 mg to about 130 mg, about 120 mg to about 140 mg, about 120 mg to about 150 mg, about 120 mg to about 200 mg, about 120 mg to about 250 mg, about 120 mg to about 300 mg, about 120 mg to about 350 mg, about 120 mg to about 400 mg, or about 120 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 130 mg to about 140 mg, about 130 mg to about 150 mg, about 130 mg to about 200 mg, about 130 mg to about 250 mg, about 130 mg to about 300 mg, about 130 mg to about 350 mg, about 130 mg to about 400 mg, or about 130 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 140 mg to about 150 mg, about 140 mg to about 200 mg, about 140 mg to about 250 mg, about 140 mg to about 300 mg, about 140 mg to about 350 mg, about 140 mg to about 400 mg, or about 140 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 150 mg to about 200 mg, about 150 mg to about 250 mg, about 150 mg to about 300 mg, about 150 mg to about 350 mg, about 150 mg to about 400 mg, or about 150 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 200 mg to about 250 mg, about 200 mg to about 300 mg, about 200 mg to about 350 mg, about 200 mg to about 400 mg, or about 200

mg to about 500 mg. In some embodiments, the composition comprises DHA at about 250 mg to about 300 mg, about 250 mg to about 350 mg, about 250 mg to about 400 mg, or about 250 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 300 mg to about 350 mg, about 300 mg to about 400 mg, or about 300 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 350 mg to about 400 mg or about 350 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 400 mg to about 500 mg. In some embodiments, the composition comprises DHA at about 50 mg, about 110 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, or about 500 mg. In some embodiments, the composition comprises DHA at least about 50 mg, at least about 110 mg, at least about 120 mg, at least about 130 mg, at least about 140 mg, at least about 150 mg, at least about 200 mg, at least about 250 mg, at least about 300 mg, at least about 350 mg, at least about 400 mg, or at least about 500 mg. In some embodiments, the composition comprises DHA at most about 50 mg, at most about 110 mg, at most about 120 mg, at most about 130 mg, at most about 140 mg, at most about 150 mg, at most about 200 mg, at most about 250 mg, at most about 300 mg, at most about 350 mg, at most about 400 mg, or at most about 500 mg.

[0076] In some embodiments, the composition is formulated as a semi-solid. In some embodiments, the composition is formulated as a softgel capsule. In some embodiments, the composition is formulated as a solid dispersion. In some embodiments, the composition is formulated for oral delivery of the retinoid. In some embodiments, the composition is formulated as an eyedrop. In some embodiments, the composition is formulated for topical or transdermal delivery of the retinoid. In some embodiments, the composition comprising the retinoid can be formulated for local administration to the eye or for systemic administration such as intravenous, intramuscular, subcutaneous, enteral, parenteral or oral administration. In some embodiments, the composition can be formulated with an additional ophthalmologically agent such as an isotonicizing agent; a buffering agent; a surfactant, or a preservative. In some embodiments, the pH of the composition is within the range acceptable to ophthalmologic formulations such as about a pH 4 to a pH 8. In some embodiments, the composition is formulated for a slow release or timed-release of the retinoid. For example, the composition can be formulated for delayed release or sustained release of the retinoid to deliver retinoid over the course of one or more of the dosing time periods. Such composition can decrease or eliminate the need for repeated administrations.

[0077] In some embodiments, the composition described herein can be formulated for delivering of the retinoid to the subject. Example 1 illustrates non-limiting examples of the manufacturing of the composition. In some embodiments, the composition described herein can be formulated

as an oil based capsule, wherein the retinoid can be dissolved in a carrier oil. Non-limiting examples of the carrier oil include soybean oil, sunflower oil, safflower oil, or fish oil. The choice of carrier oil can modulate the stability, bioavailability, or shelf life of the retinoid. In some embodiments, the retinoid can be mixed with the carrier oil. In some embodiments, this mixture can then be encapsulated within a softgel capsule shell made of gelatin or other suitable materials. In some embodiments, the composition can further include an additional excipient for increasing water solubility or retinoid bioavailability. For example, hydroxypropyl- β -cyclodextrin (HPBCD) or nanoparticle (e.g., lipid nanoparticle, nanomicelle, nanocapsule, or nanosphere) can be added to the composition. The inclusion of HPBCD can increase water solubility of the retinoid. In some embodiments, the composition can also be formulated as a polymer or dispersion, wherein the composition includes hydroxypropyl cellulose, hydroxypropyl methylcellulose hypromellose phthalate, polyvinylpyrrolidone-vinyl acetate, hypromellose-acetate-succinate, or a combination of any mixture thereof. In some embodiments, the polymer or the dispersion can be further processed by fast evaporation, spray-drying, precipitation, or melt extrusion to obtain an amorphous state of the composition. In some embodiments, the composition described herein can also be formulated as a liquid capsule, an oil-in-water emulsion, or a lipid matrix. In some embodiments, the composition can be formulated as a solid dispersion. For example, the retinoid can be incorporated into poly(lactic-co-glycolic)(PLGA) millicylindrical implants.

[0078] In some embodiments, the composition is formulated for non-medical use. In some embodiments, the composition does not treat a disease or condition. For example, the composition can be used for aesthetic or cosmetic purpose. In some embodiments, the composition is a supplement.

[0079] In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant. Non-limiting example of the antioxidant includes vitamin C, vitamin E, zinc, grape seed extract, or a combination thereof. In some embodiments, the at least one additional ingredient comprises a fatty acid such as omega-3 fatty acid. In some embodiments, the at least one additional ingredient comprises a carotenoid. Non-limiting example of the carotenoid includes lutein, zeaxanthin, astaxanthin, or a combination thereof. In some embodiments, the at least one additional ingredient comprises a flavonoid such as anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid such as taurine. In some embodiments, the composition comprises at least one additional ingredient comprising an antioxidant, a fatty acid, a carotenoid, a flavonoid, an amino acid, or a combination thereof. In some embodiments, the

composition comprises at least one additional ingredient comprising two or more of an antioxidant, a fatty acid, a carotenoid, a flavonoid, and an amino acid. In some embodiments, the composition comprises at least one additional ingredient comprising an antioxidant, a fatty acid, a carotenoid, a flavonoid, and an amino acid.

[0080] In some embodiments, the composition comprises at least one additional ingredient comprising a turmeric compound. In some embodiments, the turmeric compound comprises a curcuminoid. In some embodiments, the composition comprises curcuminoid at about 10 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 10 mg to about 110 mg, about 10 mg to about 20 mg, about 10 mg to about 30 mg, about 10 mg to about 50 mg, about 10 mg to about 100 mg, about 10 mg to about 150 mg, about 10 mg to about 200 mg, about 10 mg to about 250 mg, about 10 mg to about 300 mg, about 10 mg to about 300 mg, or about 10 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 20 mg to about 30 mg, about 20 mg to about 50 mg, about 20 mg to about 100 mg, about 20 mg to about 150 mg, about 20 mg to about 200 mg, about 20 mg to about 250 mg, about 20 mg to about 300 mg, about 20 mg to about 400 mg, or about 20 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 30 mg to about 50 mg, about 30 mg to about 100 mg, about 30 mg to about 150 mg, about 30 mg to about 200 mg, about 30 mg to about 250 mg, about 30 mg to about 300 mg, about 30 mg to about 400 mg, or about 30 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 50 mg to about 100 mg, about 50 mg to about 150 mg, about 50 mg to about 200 mg, about 50 mg to about 250 mg, about 50 mg to about 300 mg, about 50 mg to about 400 mg, or about 50 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 100 mg to about 150 mg, about 100 mg to about 200 mg, about 100 mg to about 250 mg, about 100 mg to about 300 mg, about 100 mg to about 400 mg, or about 100 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 150 mg to about 200 mg, about 150 mg to about 250 mg, about 150 mg to about 300 mg, about 150 mg to about 400 mg, or about 150 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 200 mg to about 250 mg, about 200 mg to about 300 mg, about 200 mg to about 400 mg, or about 200 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 250 mg to about 300 mg, about 250 mg to about 400 mg, about 250 mg to about 500 mg, about 300 mg to about 400 mg, or about 300 mg to about 500 mg. In some embodiments, the composition comprises curcuminoid at about 10 mg, about 20 mg, about 30 mg, about 40 mg, about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, or about 500 mg. In some embodiments, the composition comprises

curcuminoid at least about 10 mg, at least about 20 mg, at least about 30 mg, at least about 40 mg, at least about 50 mg, at least about 100 mg, at least about 150 mg, at least about 200 mg, at least about 250 mg, at least about 300 mg, at least about 400 mg, or at least about 500 mg. In some embodiments, the composition comprises curcuminoid at most about 10 mg, at most about 20 mg, at most about 30 mg, at most about 400 mg, at most about 50 mg, at most about 100 mg, at most about 150 mg, at most about 200 mg, at most about 250 mg, at most about 300 mg, at most about 400 mg, or at most about 500 mg.

[0081] In some embodiments, the composition comprises at least one additional ingredient comprising a carotenoid. In some embodiments, the carotenoid comprises lutein, zeaxanthin, or astaxanthin. In some embodiments, the composition comprises lutein at about 0.5 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 0.5 mg to about 1 mg, about 0.5 mg to about 2 mg, about 0.5 mg to about 5 mg, about 0.5 mg to about 10 mg, about 0.5 mg to about 20 mg, about 0.5 mg to about 30 mg, about 0.5 mg to about 40 mg, or about 0.5 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 1 mg to about 2 mg, about 1 mg to about 5 mg, about 1 mg to about 10 mg, about 1 mg to about 20 mg, about 1 mg to about 30 mg, about 1 mg to about 40 mg, or about 1 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 2 mg to about 5 mg, about 2 mg to about 10 mg, about 2 mg to about 20 mg, about 2 mg to about 30 mg, about 2 mg to about 40 mg, or about 2 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 5 mg to about 10 mg, about 5 mg to about 20 mg, about 5 mg to about 30 mg, about 5 mg to about 40 mg, or about 5 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 10 mg to about 20 mg, about 10 mg to about 30 mg, about 10 mg to about 40 mg, or about 10 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 20 mg to about 30 mg, about 20 mg to about 40 mg, or about 20 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 30 mg to about 40 mg or about 30 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 40 mg to about 50 mg. In some embodiments, the composition comprises lutein at about 0.5 mg, about 1 mg, about 2 mg, about 5 mg, about 10 mg, about 20 mg, about 30 mg, about 40 mg, or about 50 mg. In some embodiments, the composition comprises lutein at least about 0.5 mg, at least about 1 mg, at least about 2 mg, at least about 5 mg, at least about 10 mg, at least about 20 mg, at least about 30 mg, at least about 40 mg, or at least about 50 mg. In some embodiments, the composition comprises lutein at most about 1 mg, at most about 2 mg, at most about 5 mg, at most about 10 mg, at most about 20 mg, at most about 30 mg, at most about 40 mg, or at most about 50 mg.

[0082] In some embodiments, the composition comprises zeaxanthin at about 0.5 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 0.5 mg to about 1 mg, about 0.5 mg to about 2 mg, about 0.5 mg to about 5 mg, about 0.5 mg to about 10 mg, about 0.5 mg to about 20 mg, about 0.5 mg to about 30 mg, about 0.5 mg to about 40 mg, or about 0.5 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 1 mg to about 2 mg, about 1 mg to about 5 mg, about 1 mg to about 10 mg, about 1 mg to about 20 mg, about 1 mg to about 30 mg, about 1 mg to about 40 mg, or about 1 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 2 mg to about 5 mg, about 2 mg to about 10 mg, about 2 mg to about 20 mg, about 2 mg to about 30 mg, about 2 mg to about 40 mg, or about 2 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 5 mg to about 10 mg, about 5 mg to about 20 mg, about 5 mg to about 30 mg, about 5 mg to about 40 mg, or about 5 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 10 mg to about 20 mg, about 10 mg to about 30 mg, about 10 mg to about 40 mg, or about 10 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 20 mg to about 30 mg, about 20 mg to about 40 mg, or about 20 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 30 mg to about 40 mg or about 30 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 40 mg to about 50 mg. In some embodiments, the composition comprises zeaxanthin at about 0.5 mg, about 1 mg, about 2 mg, about 5 mg, about 10 mg, about 20 mg, about 30 mg, about 40 mg, or about 50 mg. In some embodiments, the composition comprises zeaxanthin at least about 0.5 mg, at least about 1 mg, at least about 2 mg, at least about 5 mg, at least about 10 mg, at least about 20 mg, at least about 30 mg, at least about 40 mg, or at least about 50 mg. In some embodiments, the composition comprises zeaxanthin at most about 1 mg, at most about 2 mg, at most about 5 mg, at most about 10 mg, at most about 20 mg, at most about 30 mg, at most about 40 mg, or at most about 50 mg.

[0083] In some embodiments, the composition comprises a surfactant. Non-limiting examples of the surfactant can include Tween, Kolliphor, Labrasol, Gelucire, Capmul, polyethylene glycol (PEG), Transcutol, Capryol, or a combination thereof. In some embodiments, the composition comprises the surfactant comprising Gelucire (e.g., Gelucire 44/14). In some embodiments, the composition comprises Gelucire at about 0.01 milliliters (mL) to about 5 mL. In some embodiments, the composition comprises Gelucire at about 0.01 mL to about 0.05 mL, about 0.01 mL to about 0.1 mL, about 0.01 mL to about 0.5 mL, about 0.01 mL to about 1 mL, about 0.01 mL to about 2 mL, about 0.01 mL to about 3 mL, about 0.01 mL to about 4 mL, or about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 0.05

mL to about 0.1 mL, about 0.05 mL to about 0.5 mL, about 0.05 mL to about 1 mL, about 0.05 mL to about 2 mL, about 0.05 mL to about 3 mL, about 0.05 mL to about 4 mL, or about 0.05 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 0.1 mL to about 0.5 mL, about 0.1 mL to about 1 mL, about 0.1 mL to about 2 mL, about 0.1 mL to about 3 mL, about 0.1 mL to about 4 mL, or about 0.1 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 0.5 mL to about 1 mL, about 0.5 mL to about 2 mL, about 0.5 mL to about 3 mL, about 0.5 mL to about 4 mL, or about 0.5 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 1 mL to about 2 mL, about 1 mL to about 3 mL, about 1 mL to about 4 mL, or about 1 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 2 mL to about 3 mL, about 2 mL to about 4 mL, or about 2 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 3 mL to about 4 mL or about 3 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 4 mL to about 5 mL. In some embodiments, the composition comprises Gelucire at about 0.01 mL, about 0.05 mL, about 0.1 mL, about 0.5 mL, about 1 mL, about 2 mL, about 3 mL, about 4 mL, or about 5 mL. In some embodiments, the composition comprises Gelucire at least about 0.01 mL, at least about 0.05 mL, at least about 0.1 mL, at least about 0.5 mL, at least about 1 mL, at least about 2 mL, at least about 3 mL, at least about 4 mL, or at least about 5 mL. In some embodiments, the composition comprises Gelucire at most about 0.05 mL, at most about 0.1 mL, at most about 0.5 mL, at most about 1 mL, at most about 2 mL, at most about 3 mL, at most about 4 mL, or at most about 5 mL.

[0084] In some embodiments, the composition comprises the surfactant comprising Capmul (e.g., Capmul MCM). In some embodiments, the composition comprises Capmul at about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 0.01 mL to about 0.05 mL, about 0.01 mL to about 0.1 mL, about 0.01 mL to about 0.5 mL, about 0.01 mL to about 1 mL, about 0.01 mL to about 2 mL, about 0.01 mL to about 3 mL, about 0.01 mL to about 4 mL, or about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 0.05 mL to about 0.1 mL, about 0.05 mL to about 0.5 mL, about 0.05 mL to about 1 mL, about 0.05 mL to about 2 mL, about 0.05 mL to about 3 mL, about 0.05 mL to about 4 mL, or about 0.05 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 0.1 mL to about 0.5 mL, about 0.1 mL to about 1 mL, about 0.1 mL to about 2 mL, about 0.1 mL to about 3 mL, about 0.1 mL to about 4 mL, or about 0.1 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 0.5 mL to about 1 mL, about 0.5 mL to about 2 mL, about 0.5 mL to about 3 mL, about 0.5 mL to about 4 mL, or about 0.5 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 1 mL to about 2

mL, about 1 mL to about 3 mL, about 1 mL to about 4 mL, or about 1 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 2 mL to about 3 mL, about 2 mL to about 4 mL, or about 2 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 3 mL to about 4 mL or about 3 mL to above 5 mL. In some embodiments, the composition comprises Capmul at about 4 mL to about 5 mL. In some embodiments, the composition comprises Capmul at about 0.01 mL, about 0.05 mL, about 0.1 mL, about 0.5 mL, about 1 mL, about 2 mL, about 3 mL, about 4 mL, or about 5 mL. In some embodiments, the composition comprises Capmul at least about 0.01 mL, at least about 0.05 mL, at least about 0.1 mL, at least about 0.5 mL, at least about 1 mL, at least about 2 mL, at least about 3 mL, at least about 4 mL, or at least about 5 mL. In some embodiments, the composition comprises Capmul at most about 0.05 mL, at most about 0.1 mL, at most about 0.5 mL, at most about 1 mL, at most about 2 mL, at most about 3 mL, at most about 4 mL, or at most about 5 mL.

[0085] In some embodiments, the composition comprises the surfactant comprising Tween (e.g., Tween 80). In some embodiments, the composition comprises Tween at about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 0.01 mL to about 0.05 mL, about 0.01 mL to about 0.1 mL, about 0.01 mL to about 0.3 mL, about 0.01 mL to about 0.5 mL, about 0.01 mL to about 1 mL, about 0.01 mL to about 2 mL, about 0.01 mL to about 3 mL, about 0.01 mL to about 4 mL, or about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 0.05 mL to about 0.1 mL, about 0.05 mL to about 0.3 mL, about 0.05 mL to about 0.5 mL, about 0.05 mL to about 1 mL, about 0.05 mL to about 2 mL, about 0.05 mL to about 3 mL, about 0.05 mL to about 4 mL, or about 0.05 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 0.1 mL to about 0.3 mL, about 0.1 mL to about 0.5 mL, about 0.1 mL to about 1 mL, about 0.1 mL to about 2 mL, about 0.1 mL to about 3 mL, about 0.1 mL to about 4 mL, or about 0.1 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 0.3 mL to about 0.5 mL, about 0.3 mL to about 1 mL, about 0.3 mL to about 2 mL, about 0.3 mL to about 3 mL, about 0.3 mL to about 4 mL, or about 0.3 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 0.5 mL to about 1 mL, about 0.5 mL to about 2 mL, about 0.5 mL to about 3 mL, about 0.5 mL to about 4 mL, or about 0.5 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 1 mL to about 2 mL, about 1 mL to about 3 mL, about 1 mL to about 4 mL, or about 1 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 2 mL to about 3 mL, about 2 mL to about 4 mL, or about 2 mL to about 5 mL. In some embodiments, the composition comprises Tween at or about 3 mL to about 4 mL or about 3 mL to about 5 mL. In some embodiments, the composition comprises Tween at about 4 mL to about

5 mL. In some embodiments, the composition comprises Tween at about 0.01 mL, about 0.05 mL, about 0.1 mL, about 0.3 mL, about 0.5 mL, about 1 mL, about 2 mL, about 3 mL, about 4 mL, or about 5 mL. In some embodiments, the composition comprises Tween at least about 0.01 mL, at least about 0.05 mL, at least about 0.1 mL, at least about 0.3 mL, at least about 0.5 mL, at least about 1 mL, at least about 2 mL, at least about 3 mL, at least about 4 mL, or at least about 5 mL. In some embodiments, the composition comprises Tween at most about 0.05 mL, at most about 0.1 mL, at most about 0.3 mL, at most about 0.5 mL, at most about 1 mL, at most about 2 mL, at most about 3 mL, at most about 4 mL, or at most about 5 mL.

[0086] In some embodiments, the composition comprises the surfactant comprising PEG (e.g., PEG 400). In some embodiments, the composition comprises PEG at about 0.01 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 0.01 mL to about 0.05 mL, about 0.01 mL to about 0.1 mL, about 0.01 mL to about 0.3 mL, about 0.01 mL to about 0.5 mL, about 0.01 mL to about 1 mL, about 0.01 mL to about 2 mL, about 0.01 mL to about 3 mL, about 0.01 mL to about 4 mL, or about 0.01 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 0.05 mL to about 0.1 mL, about 0.05 mL to about 0.3 mL, about 0.05 mL to about 0.5 mL, about 0.05 mL to about 1 mL, about 0.05 mL to about 2 mL, about 0.05 mL to about 3 mL, about 0.05 mL to about 4 mL, or about 0.05 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 0.1 mL to about 0.3 mL, about 0.1 mL to about 0.5 mL, about 0.1 mL to about 1 mL, about 0.1 mL to about 2 mL, about 0.1 mL to about 3 mL, about 0.1 mL to about 4 mL, or about 0.1 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 0.3 mL to about 0.5 mL, about 0.3 mL to about 1 mL, about 0.3 mL to about 2 mL, about 0.3 mL to about 3 mL, about 0.3 mL to about 4 mL, or about 0.3 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 0.5 mL to about 1 mL, about 0.5 mL to about 2 mL, about 0.5 mL to about 3 mL, about 0.5 mL to about 4 mL, or about 0.5 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 1 mL to about 2 mL, about 1 mL to about 3 mL, about 1 mL to about 4 mL, or about 1 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 2 mL to about 3 mL, about 2 mL to about 4 mL, or about 2 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 3 mL to about 4 mL or about 3 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 4 mL to about 5 mL. In some embodiments, the composition comprises PEG at about 0.01 mL, about 0.05 mL, about 0.1 mL, about 0.3 mL, about 0.5 mL, about 1 mL, about 2 mL, about 3 mL, about 4 mL, or about 5 mL. In some embodiments, the composition comprises PEG at least about 0.01 mL, at least about 0.05 mL, at least about 0.1 mL, at least about 0.3 mL, at least about 0.5 mL, at least about 1 mL,

at least about 2 mL, at least about 3 mL, at least about 4 mL, or at least about 5 mL. In some embodiments, the composition comprises PEG at most about 0.05 mL, at most about 0.1 mL, at most about 0.3 mL, at most about 0.5 mL, at most about 1 mL, at most about 2 mL, at most about 3 mL, at most about 4 mL, or at most about 5 mL.

[0087] In some embodiments, the composition comprises the surfactant comprising Kolliphor (e.g., Kolliphor EL). In some embodiments, the composition comprises Kolliphor at about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 0.01 mL to about 0.05 mL, about 0.01 mL to about 0.1 mL, about 0.01 mL to about 0.3 mL, about 0.01 mL to about 0.5 mL, about 0.01 mL to about 1 mL, about 0.01 mL to about 2 mL, about 0.01 mL to about 3 mL, about 0.01 mL to about 4 mL, or about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 0.05 mL to about 0.1 mL, about 0.05 mL to about 0.3 mL, about 0.05 mL to about 0.5 mL, about 0.05 mL to about 1 mL, about 0.05 mL to about 2 mL, about 0.05 mL to about 3 mL, about 0.05 mL to about 4 mL, or about 0.05 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 0.1 mL to about 0.3 mL, about 0.1 mL to about 0.5 mL, about 0.1 mL to about 1 mL, about 0.1 mL to about 2 mL, about 0.1 mL to about 3 mL, about 0.1 mL to about 4 mL, or about 0.1 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 0.3 mL to about 0.5 mL, about 0.3 mL to about 1 mL, about 0.3 mL to about 2 mL, about 0.3 mL to about 3 mL, about 0.3 mL to about 4 mL, or about 0.3 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 0.5 mL to about 1 mL, about 0.5 mL to about 2 mL, about 0.5 mL to about 3 mL, about 0.5 mL to about 4 mL, or about 0.5 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 1 mL to about 2 mL, about 1 mL to about 3 mL, about 1 mL to about 4 mL, or about 1 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 2 mL to about 3 mL, about 2 mL to about 4 mL, or about 2 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 3 mL to about 4 mL or about 3 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 4 mL to about 5 mL. In some embodiments, the composition comprises Kolliphor at about 0.01 mL, about 0.05 mL, about 0.1 mL, about 0.3 mL, about 0.5 mL, about 1 mL, about 2 mL, about 3 mL, about 4 mL, or about 5 mL. In some embodiments, the composition comprises Kolliphor at least about 0.01 mL, at least about 0.05 mL, at least about 0.1 mL, at least about 0.3 mL, at least about 0.5 mL, at least about 1 mL, at least about 2 mL, at least about 3 mL, at least about 4 mL, or at least about 5 mL. In some embodiments, the composition comprises Kolliphor at most about 0.05 mL, at most about 0.1

mL, at most about 0.3 mL, at most about 0.5 mL, at most about 1 mL, at most about 2 mL, at most about 3 mL, at most about 4 mL, or at most about 5 mL.

[0088] In some embodiments, the composition comprises the surfactant comprising Transcutol (e.g., Transcutol HP). In some embodiments, the composition comprises Transcutol at about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 0.01 mL to about 0.05 mL, about 0.01 mL to about 0.1 mL, about 0.01 mL to about 0.3 mL, about 0.01 mL to about 0.5 mL, about 0.01 mL to about 1 mL, about 0.01 mL to about 2 mL, about 0.01 mL to about 3 mL, about 0.01 mL to about 4 mL, or about 0.01 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 0.05 mL to about 0.1 mL, about 0.05 mL to about 0.3 mL, about 0.05 mL to about 0.5 mL, about 0.05 mL to about 1 mL, about 0.05 mL to about 2 mL, about 0.05 mL to about 3 mL, about 0.5 mL to about 4 mL, or about 0.05 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 0.1 mL to about 0.3 mL, about 0.1 mL to about 0.5 mL, about 0.1 mL to about 1 mL, about 0.1 mL to about 2 mL, about 0.1 mL to about 3 mL, about 0.1 mL to about 4 mL, or about 0.1 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 0.3 mL to about 0.5 mL, about 0.3 mL to about 1 mL, about 0.3 mL to about 2 mL, about 0.3 mL to about 3 mL, about 0.3 mL to about 4 mL, or about 0.3 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 0.5 mL to about 1 mL, about 0.5 mL to about 2 mL, about 0.5 mL to about 3 mL, about 0.5 mL to about 4 mL, or about 0.5 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 1 mL to about 2 mL, about 1 mL to about 3 mL, about 1 mL to about 4 mL, or about 1 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 2 mL to about 3 mL, about 2 mL to about 4 mL, or about 2 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 3 mL to about 4 mL or about 3 mL or about 5 mL. In some embodiments, the composition comprises Transcutol at about 4 mL to about 5 mL. In some embodiments, the composition comprises Transcutol at about 0.01 mL, about 0.05 mL, about 0.1 mL, about 0.3 mL, about 0.5 mL, about 1 mL, about 2 mL, about 3 mL, about 4 mL, or about 5 mL. In some embodiments, the composition comprises Transcutol at least about 0.01 mL, at least about 0.05 mL, at least about 0.1 mL, at least about 0.3 mL, at least about 0.5 mL, at least about 1 mL, at least about 2 mL, at least about 3 mL, at least about 4 mL, or at least about 5 mL. In some embodiments, the composition comprises Transcutol at most about 0.05 mL, at most about 0.1 mL, at most about 0.3 mL, at most about 0.5 mL, at most about 1 mL, at most about 2 mL, at most about 3 mL, at most about 4 mL, or at most about 5 mL.

[0089] In some embodiments, the composition is formulated for an eye administration of a subject. In some embodiments, the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject. In some embodiments, the composition modulates gene expression of a retinal pigment epithelial (RPE) cell. In some embodiments, the composition increases a bioavailability of the retinoid delivered to the RPE cell compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant. In some embodiments, the bioavailability is increased by at least about 5% to about 5,000%. In some embodiments, the bioavailability is increased by at least about 5% to about 10%, about 5% to about 20%, about 5% to about 30%, about 5% to about 40%, about 5% to about 50%, about 5% to about 100%, about 5% to about 200%, about 5% to about 500%, about 5% to about 1,000%, about 5% to about 5,000%, about 10% to about 20%, about 10% to about 30%, about 10% to about 40%, about 10% to about 50%, about 10% to about 100%, about 10% to about 200%, about 10% to about 500%, about 10% to about 1,000%, about 10% to about 5,000%, about 20% to about 30%, about 20% to about 40%, about 20% to about 50%, about 20% to about 100%, about 20% to about 200%, about 20% to about 500%, about 20% to about 1,000%, about 20% to about 5,000%, about 30% to about 40%, about 30% to about 50%, about 30% to about 100%, about 30% to about 200%, about 30% to about 500%, about 30% to about 1,000%, about 30% to about 5,000%, about 40% to about 50%, about 40% to about 100%, about 40% to about 200%, about 40% to about 500%, about 40% to about 1,000%, about 40% to about 5,000%, about 50% to about 100%, about 50% to about 200%, about 50% to about 500%, about 50% to about 1,000%, about 50% to about 5,000%, about 100% to about 200%, about 100% to about 500%, about 100% to about 1,000%, about 100% to about 5,000%, about 200% to about 500%, about 200% to about 1,000%, about 200% to about 5,000%, about 500% to about 1,000%, about 500% to about 5,000%, or about 1,000% to about 5,000%. In some embodiments, the bioavailability is increased by at least about 5%, about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, about 1,000%, or about 5,000%. In some embodiments, the bioavailability is increased by at least at least about 5%, about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, or about 1,000%. In some embodiments, the bioavailability is increased by at least at most about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, about 1,000%, or about 5,000% compared to the second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant.

[0090] In some embodiments, the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the

surfactant. In some embodiments, the stability is increased by at least about 5% to about 5,000% compared to the second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the stability is increased by at least about 5% to about 10%, about 5% to about 20%, about 5% to about 30%, about 5% to about 40%, about 5% to about 50%, about 5% to about 100%, about 5% to about 200%, about 5% to about 500%, about 5% to about 1,000%, about 5% to about 5,000%, about 10% to about 20%, about 10% to about 30%, about 10% to about 40%, about 10% to about 50%, about 10% to about 100%, about 10% to about 200%, about 10% to about 500%, about 10% to about 1,000%, about 10% to about 5,000%, about 20% to about 30%, about 20% to about 40%, about 20% to about 50%, about 20% to about 100%, about 20% to about 200%, about 20% to about 500%, about 20% to about 1,000%, about 20% to about 5,000%, about 30% to about 40%, about 30% to about 50%, about 30% to about 100%, about 30% to about 200%, about 30% to about 500%, about 30% to about 1,000%, about 30% to about 5,000%, about 40% to about 50%, about 40% to about 100%, about 40% to about 200%, about 40% to about 500%, about 40% to about 1,000%, about 40% to about 5,000%, about 50% to about 100%, about 50% to about 200%, about 50% to about 500%, about 50% to about 1,000%, about 50% to about 5,000%, about 100% to about 200%, about 100% to about 500%, about 100% to about 1,000%, about 100% to about 5,000%, about 200% to about 500%, about 200% to about 1,000%, about 200% to about 5,000%, about 500% to about 1,000%, about 500% to about 5,000%, or about 1,000% to about 5,000%. In some embodiments, the stability is increased by at least about 5%, about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, about 1,000%, or about 5,000%. In some embodiments, the stability is increased by at least at least about 5%, about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, or about 1,000%. In some embodiments, the stability is increased by at least at most about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, about 1,000%, or about 5,000% compared to the second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant.

[0091] In some embodiments, the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the solubility is increased by at least about 5% to about 5,000% compared to the second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the solubility is increased by at least about 5% to about 10%, about 5% to about 20%, about 5% to about 30%, about 5% to about 40%, about 5% to about 50%, about 5% to about 100%, about 5% to about 200%, about 5% to

about 500%, about 5% to about 1,000%, about 5% to about 5,000%, about 10% to about 20%, about 10% to about 30%, about 10% to about 40%, about 10% to about 50%, about 10% to about 100%, about 10% to about 200%, about 10% to about 500%, about 10% to about 1,000%, about 10% to about 5,000%, about 20% to about 30%, about 20% to about 40%, about 20% to about 50%, about 20% to about 100%, about 20% to about 200%, about 20% to about 500%, about 20% to about 1,000%, about 20% to about 5,000%, about 30% to about 40%, about 30% to about 50%, about 30% to about 100%, about 30% to about 200%, about 30% to about 500%, about 30% to about 1,000%, about 30% to about 5,000%, about 40% to about 50%, about 40% to about 100%, about 40% to about 200%, about 40% to about 500%, about 40% to about 1,000%, about 40% to about 5,000%, about 50% to about 100%, about 50% to about 200%, about 50% to about 500%, about 50% to about 1,000%, about 50% to about 5,000%, about 100% to about 200%, about 100% to about 500%, about 100% to about 1,000%, about 100% to about 5,000%, about 200% to about 500%, about 200% to about 1,000%, about 200% to about 5,000%, about 500% to about 1,000%, about 500% to about 5,000%, or about 1,000% to about 5,000%. In some embodiments, the solubility is increased by at least about 5%, about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, about 1,000%, or about 5,000%. In some embodiments, the solubility is increased by at least at least about 5%, about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, or about 1,000%. In some embodiments, the solubility is increased by at least at most about 10%, about 20%, about 30%, about 40%, about 50%, about 100%, about 200%, about 500%, about 1,000%, or about 5,000% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant.

[0092] In some embodiments, the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject. In some embodiments, the composition does not decrease a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject. **Fig. 9** illustrates that the bioavailability of the retinol formulated in a non-limiting example of a composition described herein was not decreased compared to other comparable formulations.

Methods

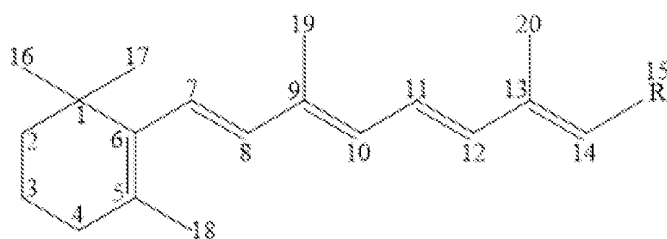
[0093] Described herein, in some aspects, is a method for treating a disease or condition in a subject by administering to the subject a composition described herein. In some embodiments, the disease or condition is associated with retinoic acid deficiency in the subject. In some embodiments, the composition comprising both the retinoid and the lipid excipient increases bioavailability of the retinoid in the subject compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient. In some embodiments, the composition comprising both the retinoid and the lipid excipient increases bioavailability of the retinoid in the subject by at least 10%, at least 20%, at least 50%, at least 100%, or more. In some embodiments, the increased bioavailability of the retinoid in the subject increases the therapeutic efficacy for treating the disease or condition. In some embodiments, the increased bioavailability of the retinoid in the subject decreases the doses of retinoid needed to achieve comparable therapeutic efficacy in the subject. In some embodiments, the method described herein decreases retinoid toxicity in the subject. Example 2 and Example 3 illustrate studies examining the safety and therapeutic efficacy of the composition described herein.

[0094] In some embodiments, the method comprises administering the composition described herein to a subject, where the subject has an eye disease or condition. In some embodiments, the eye disease or condition is associated with accumulation of lipofuscin. In some embodiments, the method decreases accumulation of vitamin A dimer in the subject. In some embodiments, the method decreases accumulation of lipofuscin in the subject. In some embodiments, the eye disease or condition is associated with a retinal pigment epithelial (RPE) cell. In some embodiments, the eye disease or condition is associated with accumulation of lipofuscin in the RPE cell. In some embodiments, the eye disease or condition is associated with accumulation of A2E. In some embodiments, the eye disease or condition is associated with accumulation of A2E in the RPE cell. In some embodiments, the method decreases accumulation of A2E in the subject. In some embodiments, the eye disease or condition is associated with a RPE cell. In some embodiments, the eye disease or condition is macular degeneration. Non-limiting examples of the macular degeneration include age-related macular degeneration (AMD), bestrophinopathies, bull's eye maculopathy, central serous retinopathy, Charles Bonnet syndrome (CBS), cone dystrophy, Doyne honeycomb dystrophy, diabetic macular oedema (DMO), macular hole, macular oedema, myopic macular degeneration, pattern dystrophy, pseudoxanthoma elasticum (PXE), punctate inner choroidopathy (PIC), retinal vein occlusion (RVO), Sorsby fundus dystrophy, Stargardt disease, or a combination thereof. In some embodiments, the eye disease or condition is dry AMD. In some embodiments, the eye disease or condition is early AMD. In some embodiments, the eye disease or condition is wet AMD.

[0095] In some embodiments, the therapeutic efficacy for treating the eye disease or condition can be determined by vision function (e.g., Example 3). In some embodiments, improvements in the subject's visual functions in one or both eyes can be evaluated based on measures of visual field, visual acuity, and retinal sensitivity testing, electroretinograms, dynamic pupillary response, nystagmus, cortical visual function, color vision, visual mobility testing, patient-reported outcomes of quality of life/ability to perform life tasks, or a combination thereof. Improvements in the subject's visual functions in one or both eyes during a therapeutic regimen can be demonstrated by comparing the subject's visual functions of each eye with a baseline measure of the subject's visual functions of each eye prior to the treatment by a therapeutic regimen or by comparing the subject's visual functions of each eye with a comparable human visual system not receiving the treatment.

Uses

[0096] Described herein, in some aspects, is a method of using or a use of a composition described herein. In some embodiments, the use is a non-medical or non-therapeutic use. Example 5 illustrates non-limiting examples of the non-medical or non-therapeutic use. In some embodiments, the use does not treat a disease or condition. For example, the use can be for aesthetic or cosmetic purpose. In some embodiments, the use is an aesthetic use. In some embodiments, the use is a cosmetic use. In some embodiments, the use is a supplement use. In some embodiments, the composition formulated for the non-medical or non-therapeutic use includes a retinoid; a lipid excipient; or a surfactant. In some embodiments, the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient. In some embodiments, the retinoid comprises a structure of Formula I:



. In some embodiments, each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium. In some embodiments, the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), or R₅ (COO-glucuronide). In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is

at the position 10, 12, 14, 19, 20, or a combination thereof. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 or at the position 20. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums (19, 19, 19-trideutero retinoid) or is at the position 20 comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid). Example 4 illustrates efficacy study for the 20, 20, 20-trideutero retinoid described herein. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums; and at the position 20 comprising substituting three hydrogens with three deuteriums. In some embodiments, the 19, 19, 19-trideutero retinoid comprises a 19, 19, 19-trideutero retinoid analog. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid ester. In some embodiments, the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid acetate. In some embodiments, the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid ester. In some embodiments, the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid acetate. In some embodiments, the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 and at the position 20, wherein the position 19 comprises substituting three hydrogens with three deuteriums and the position 20 comprises substituting three hydrogens with three deuteriums (19, 19, 19, 20, 20, 20-hexadeutero retinoid). In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid ester. In some embodiments, the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid acetate.

[0097] In some embodiments, the composition comprises from about 1.0 mg to about 5.0 mg of the retinoid. In some embodiments, the lipid excipient comprises an omega-3 fatty acid. In some embodiments, the omega-3 fatty acid comprises EPA or DHA. In some embodiments, the composition comprises from about 100 mg to about 500 mg of the EPA. In some embodiments, the composition comprises from about 50 mg to about 200 mg of the DHA. In some embodiments, the composition comprises at least one additional ingredient. In some embodiments, the at least one additional ingredient comprises an antioxidant such as vitamin C, vitamin E, zinc, or grape seed extract. In some embodiments, the at least one additional

ingredient comprises a turmeric compound. In some embodiments, the at least one additional ingredient comprises a curcuminoid from about 20 mg to about 100 mg of the curcuminoid. In some embodiments, the at least one additional ingredient comprises a carotenoid such as lutein, zeaxanthin, or astaxanthin. In some embodiments, the composition comprises from about 1 mg to about 100 mg of the lutein. In some embodiments, the composition comprises from about 1 mg to about 10 mg of the zeaxanthin. In some embodiments, the at least one additional ingredient comprises a flavonoid such as anthocyanin. In some embodiments, the at least one additional ingredient comprises an amino acid or an amino acid analog. In some embodiments, the at least one additional ingredient comprises an emulsifier. In some embodiments, the surfactant comprises Tween, Kolliphor, Labrasol, Gelucire, Capmul, PEG, Transcutol, Capryol, or a combination thereof. In some embodiments, the surfactant consists of the Gelucire, the Capmul, the Tween, and the PEG.

[0098] In some embodiments, the use of the composition, where the composition is formulated as a semi-solid. In some embodiments, the composition is formulated as a softgel capsule. In some embodiments, the composition is formulated as a solid dispersion. In some embodiments, the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof. In some embodiments, the composition is formulated for an eye administration of a subject. In some embodiments, the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject. In some embodiments, the composition modulates gene expression of a retinal pigment epithelial (RPE) cell. In some embodiments, the composition increases a bioavailability of the retinoid delivered to the RPE cell. As shown in Example 6, a composition described herein can increase bioavailability or stability of the retinoid. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant. In some embodiments, the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the stability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject. In some embodiments, the composition does not decrease a

bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject. In some embodiments, the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject. In some embodiments, the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the solubility is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%. In some embodiments, the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%. In some embodiments, the composition comprises an oil. In some embodiments, the oil comprises corn oil, oleic acid, Maisine cc, or a combination thereof. In some embodiments, the use described herein is an aesthetic use. In some embodiments, the use described herein is a cosmetic use. In some embodiments, the use described herein is a supplement use. In some embodiments, the use described herein does not treat a disease or condition. In some embodiments, the use described herein comprises administering the composition topically or transdermally to the subject.

[0099] Use of absolute or sequential terms, for example, “will,” “will not,” “shall,” “shall not,” “must,” “must not,” “first,” “initially,” “next,” “subsequently,” “before,” “after,” “lastly,” and “finally,” are not meant to limit scope of the present embodiments disclosed herein but as exemplary.

[00100] As used herein, the singular forms “a,” “an” and “the” are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, to the extent that the terms “including,” “includes,” “having,” “has,” “with,” or variants thereof are used in either the detailed description and/or the claims, such terms are intended to be inclusive in a manner similar to the term “comprising.”

[00101] As used herein, the phrases “at least one,” “one or more,” and “and/or” are open-ended expressions that are both conjunctive and disjunctive in operation. For example, each of the expressions “at least one of A, B and C,” “at least one of A, B, or C,” “one or more of A, B, and C,” “one or more of A, B, or C” and “A, B, and/or C” means A alone, B alone, C alone, A and B together, A and C together, B and C together, or A, B and C together.

[00102] As used herein, “or” may refer to “and,” “or,” or “and/or” and may be used both exclusively and inclusively. For example, the term “A or B” may refer to “A or B,” “A but not B,” “B but not A,” and “A and B”. In some cases, context may dictate a particular meaning.

[00103] Any systems, methods, software, and platforms described herein are modular. Accordingly, terms such as “first” and “second” do not necessarily imply priority, order of importance, or order of acts.

[00104] The term “about” when referring to a number or a numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and the number or numerical range may vary from, for example, from 1% to 15% of the stated number or numerical range. In examples, the term “about” refers to $\pm 10\%$ of a stated number or value.

[00105] The terms “increased”, “increasing”, or “increase” are used herein to generally mean an increase by a statically significant amount. In some aspects, the terms “increased,” or “increase,” mean an increase of at least 10% as compared to a reference level, for example an increase of at least about 10%, at least about 20%, or at least about 30%, or at least about 40%, or at least about 50%, or at least about 60%, or at least about 70%, or at least about 80%, or at least about 90% or up to and including a 100% increase or any increase between 10-100% as compared to a reference level, standard, or control. Other examples of “increase” include an increase of at least 2-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 100-fold, at least 1000-fold or more as compared to a reference level.

[00106] The terms “decreased”, “decreasing”, or “decrease” are used herein generally to mean a decrease by a statistically significant amount. In some aspects, “decreased” or “decrease” means a reduction by at least 10% as compared to a reference level, for example a decrease by at least about 20%, or at least about 30%, or at least about 40%, or at least about 50%, or at least about 60%, or at least about 70%, or at least about 80%, or at least about 90% or up to and including a 100% decrease (e.g., absent level or non-detectable level as compared to a reference level), or any decrease between 10-100% as compared to a reference level. In the context of a marker or symptom, by these terms is meant a statistically significant decrease in such level. The decrease can be, for example, at least 10%, at least 20%, at least 30%, at least 40% or more, and is preferably down to a level accepted as within the range of normal for an individual without a given disease.

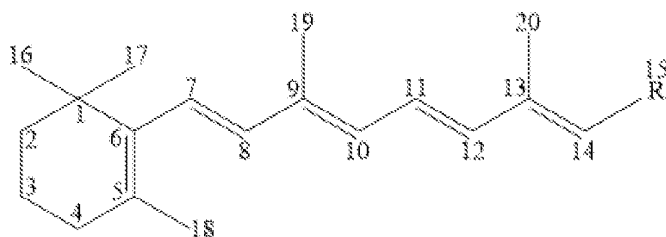
[00107] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. It is not intended that the invention be limited by the specific examples provided within the specification. While the invention has been described with reference to the aforementioned specification, the descriptions and illustrations of the embodiments herein are not meant to be construed in a limiting sense. Numerous variations, changes, and substitutions will

now occur to those skilled in the art without departing from the invention. Furthermore, it shall be understood that all aspects of the invention are not limited to the specific depictions, configurations or relative proportions set forth herein which depend upon a variety of conditions and variables. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is therefore contemplated that the invention shall also cover any such alternatives, modifications, variations or equivalents. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

EMBODIMENTS

[00108] Embodiment 1. A composition comprising: a retinoid; and a lipid excipient, wherein the retinoid is present in the composition at a percentage (w/w) of about 0.1% to about 90%.

[00109] Embodiment 2. The composition of Embodiment 1, wherein the retinoid comprises a structure of Formula I:



wherein each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium.

[00110] Embodiment 3. The composition of Embodiment 2, wherein the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate).

[00111] Embodiment 4. The composition of Embodiment 2, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof.

[00112] Embodiment 5. The composition of Embodiment 4, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20.

[00113] Embodiment 6. The composition of Embodiment 5, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid).

- [00114] Embodiment 7. The composition of Embodiment 6, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog.
- [00115] Embodiment 8. The composition of Embodiment 7, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid ester.
- [00116] Embodiment 9. The composition of Embodiment 7, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid acetate.
- [00117] Embodiment 10. The composition of Embodiment 5, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 14 and at the position 20, wherein the position 14 comprises substituting one hydrogen with one deuterium and the position 20 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradutero retinoid).
- [00118] Embodiment 11. The composition of Embodiment 10, wherein the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid analog.
- [00119] Embodiment 12. The composition of Embodiment 11, wherein the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid ester.
- [00120] Embodiment 13. The composition of Embodiment 11, wherein the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid acetate.
- [00121] Embodiment 14. The composition of Embodiment 5, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 14 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadutero retinoid).
- [00122] Embodiment 15. The composition of Embodiment 14, wherein the 12, 14, 20, 20, 20-pentadutero retinoid comprises a 12, 14, 20, 20, 20-pentadutero retinoid analog.
- [00123] Embodiment 16. The composition of Embodiment 14, wherein the 12, 14, 20, 20, 20-pentadutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadutero retinoid ester.
- [00124] Embodiment 17. The composition of Embodiment 14, wherein the 12, 14, 20, 20, 20-pentadutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadutero retinoid acetate.
- [00125] Embodiment 18. The composition of Embodiment 1, wherein the composition is formulated as a semi-solid.
- [00126] Embodiment 19. The composition of any of Embodiments 1-18, wherein the composition is formulated as a softgel capsule.

[00127] Embodiment 20. The composition of any one of Embodiments 1-17, wherein the composition is formulated as a solid dispersion.

[00128] Embodiment 21. The composition of any one of Embodiments 1-17, wherein the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.

[00129] Embodiment 22. The composition of any one of Embodiments 1-21, wherein the composition comprises at least one additional ingredient.

[00130] Embodiment 23. The composition of Embodiment 22, wherein the at least one additional ingredient comprises an antioxidant.

[00131] Embodiment 24. The composition of Embodiment 23, wherein the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract.

[00132] Embodiment 25. The composition of Embodiment 22, wherein the at least one additional ingredient comprises a fatty acid.

[00133] Embodiment 26. The composition of Embodiment 25, wherein the fatty acid comprises omega-3 fatty acid.

[00134] Embodiment 27. The composition of Embodiment 22, wherein the at least one additional ingredient comprises a carotenoid.

[00135] Embodiment 28. The composition of Embodiment 27, wherein the carotenoid comprises lutein, zeaxanthin, or astaxanthin.

[00136] Embodiment 29. The composition of Embodiment 22, wherein the at least one additional ingredient comprises a flavonoid.

[00137] Embodiment 30. The composition of Embodiment 29, wherein the flavonoid comprises anthocyanin.

[00138] Embodiment 31. The composition of Embodiment 22, wherein the at least one additional ingredient comprises an amino acid.

[00139] Embodiment 32. The composition of Embodiment 31, wherein the amino acid comprises taurine.

[00140] Embodiment 33. The composition of any one of Embodiments 1-32, wherein the composition is formulated for an eye of a subject.

[00141] Embodiment 34. The composition of any one of Embodiments 1-33, wherein the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject.

[00142] Embodiment 35. The composition of any one of Embodiments 1-34, wherein the composition modulates gene expression of a retinal pigment epithelial (RPE) cell.

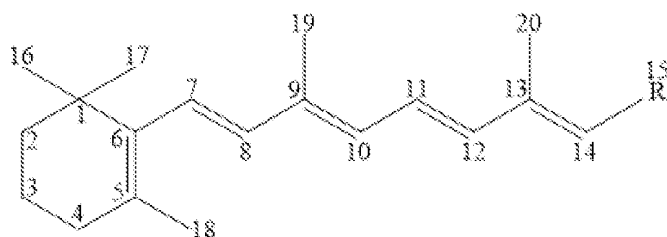
[00143] Embodiment 36. The composition of Embodiment 35, wherein the composition increases the bioavailability of the retinoid delivered to the RPE cell.

[00144] Embodiment 37. The composition of Embodiment 1, wherein the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%.

[00145] Embodiment 38. The composition of Embodiment 37, wherein the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%.

[00146] Embodiment 39. A method for treating an eye disease or condition in a subject, comprising administering a composition comprising: a retinoid; and a lipid excipient, wherein the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient.

[00147] Embodiment 40. The method of Embodiment 39, wherein the retinoid comprises a structure of Formula I:



Formula I,

wherein each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium.

[00148] Embodiment 41. The method of Embodiment 40, wherein the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate).

[00149] Embodiment 42. The method of Embodiment 40, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof.

[00150] Embodiment 43. The method of Embodiment 42, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20.

[00151] Embodiment 44. The method of Embodiment 43, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid).

[00152] Embodiment 45. The method of Embodiment 44, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog.

[00153] Embodiment 46. The method of Embodiment 45, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid ester.

[00154] Embodiment 47. The method of Embodiment 45, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid acetate.

[00155] Embodiment 48. The method of Embodiment 44, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 14 and at the position 20, wherein the position 14 comprises substituting one hydrogen with one deuterium and the position 20 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradutero retinoid).

[00156] Embodiment 49. The method of Embodiment 48, wherein the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid analog.

[00157] Embodiment 50. The method of Embodiment 49, wherein the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid ester.

[00158] Embodiment 51. The method of Embodiment 49, wherein the 14, 20, 20, 20-tetradutero retinoid comprises a 14, 20, 20, 20-tetradutero retinoid acetate.

[00159] Embodiment 52. The method of Embodiment 44, wherein the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 14 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadutero retinoid).

[00160] Embodiment 53. The method of Embodiment 52, wherein the 12, 14, 20, 20, 20-pentadutero retinoid comprises a 12, 14, 20, 20, 20-pentadutero retinoid analog.

[00161] Embodiment 54. The method of Embodiment 53, wherein the 12, 14, 20, 20, 20-pentadutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadutero retinoid ester.

[00162] Embodiment 55. The method of Embodiment 53, wherein the 12, 14, 20, 20, 20-pentadutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadutero retinoid acetate.

[00163] Embodiment 56. The method of Embodiment 39, wherein the composition is formulated as a semi-solid.

[00164] Embodiment 57. The method of any one of Embodiments 39-56, wherein the composition is formulated as a softgel capsule.

[00165] Embodiment 58. The method of any one of Embodiments 39-56, wherein the composition is formulated as a solid dispersion.

[00166] Embodiment 59. The method of any one of Embodiments 39-56, wherein the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.

[00167] Embodiment 60. The method of any one of Embodiments 39-59, wherein the composition comprises at least one additional ingredient.

[00168] Embodiment 61. The method of Embodiment 60, wherein the at least one additional ingredient comprises an antioxidant.

[00169] Embodiment 62. The method of Embodiment 61, wherein the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract.

[00170] Embodiment 63. The method of Embodiment 60, wherein the at least one additional ingredient comprises a fatty acid.

[00171] Embodiment 64. The method of Embodiment 63, wherein the fatty acid comprises omega-3 fatty acid.

[00172] Embodiment 65. The method of Embodiment 60, wherein the at least one additional ingredient comprises a carotenoid.

[00173] Embodiment 66. The method of Embodiment 65, wherein the carotenoid comprises lutein, zeaxanthin, or astaxanthin.

[00174] Embodiment 67. The method of Embodiment 60, wherein the at least one additional ingredient comprises a flavonoid.

[00175] Embodiment 68. The method of Embodiment 67, wherein the flavonoid comprises anthocyanin.

[00176] Embodiment 69. The method of Embodiment 60, wherein the at least one additional ingredient comprises an amino acid.

[00177] Embodiment 70. The method of Embodiment 69, wherein the amino acid comprises taurine.

[00178] Embodiment 71. The method of any one of Embodiments 39-70, wherein the composition is formulated for an eye of a subject.

[00179] Embodiment 72. The method of Embodiment 71, wherein the eye disease or condition is associated with accumulation of N-retinylidene-N-retinylethanolamine (A2E).

[00180] Embodiment 73. The method of Embodiment 72, further comprising decreasing the accumulation of A2E in the subject.

[00181] Embodiment 74. The method of any one of Embodiments 39-73, wherein the eye disease or condition is associated with a retinal pigment epithelial (RPE) cell.

[00182] Embodiment 75. The method of Embodiment 74, further comprising modulating gene expression of the RPE cell.

[00183] Embodiment 76. The method of Embodiment 75, wherein the gene expression comprises expression of ATP-binding cassette, sub-family A (ABC1), member 4 (ABCA4), elongation of very long chain fatty acids protein 4 (ELOVL4), or a combination thereof.

[00184] Embodiment 77. The method of any one of Embodiments 39-76, wherein the eye disease or condition is macular degeneration.

[00185] Embodiment 78. The method of Embodiment 77, wherein the macular degeneration comprises age-related macular degeneration (AMD), bestrophinopathies, bull's eye maculopathy, central serous retinopathy, Charles Bonnet syndrome (CBS), cone dystrophy, Doyne honeycomb dystrophy, diabetic macular oedema (DMO), macular hole, macular oedema, myopic macular degeneration, pattern dystrophy, pseudoxanthoma elasticum (PXE), punctate inner choroidopathy (PIC), retinal vein occlusion (RVO), Sorsby fundus dystrophy, Stargardt disease, geographic atrophy, or a combination thereof.

[00186] Embodiment 79. The method of Embodiment 78, wherein the AMD comprises dry AMD.

[00187] Embodiment 80. The method of Embodiment 78, wherein the AMD comprises early AMD.

[00188] Embodiment 81. The method of Embodiment 78, wherein the AMD comprises wet AMD.

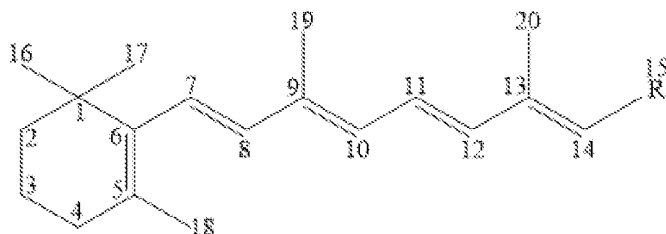
[00189] Embodiment 82. The method of Embodiment 39, wherein the lipid excipient increases the bioavailability of the retinoid in the subject by at least 50% compared to the second bioavailability of the retinoid formulated with the excipient that is different from the lipid excipient.

[00190] Embodiment 83. The method of Embodiment 82, wherein the lipid excipient increases the bioavailability of the retinoid in the subject by 100% compared to the second bioavailability of the retinoid formulated with the excipient that is different from the lipid excipient.

[00191] Embodiment 84. The method of Embodiment 39, wherein the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%.

[00192] Embodiment 85. Use of a composition, comprising contacting a subject with the composition, the composition comprising: a retinoid; and a lipid excipient, wherein the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient, and wherein the use is a non-medical use.

[00193] Embodiment 86. The use of Embodiment 85, wherein the retinoid comprises a structure of Formula I:



Formula I,

wherein each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium.

[00194] Embodiment 87. The use of Embodiment 86, wherein the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), or R₅ (COO-glucuronide).

[00195] Embodiment 88. The use of Embodiment 87, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 10, 12, 14, 19, 20, or a combination thereof.

[00196] Embodiment 89. The use of Embodiment 88, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20.

[00197] Embodiment 90. The use of Embodiment 89, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums.

[00198] Embodiment 91. The use of Embodiment 90, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 20, comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid).

[00199] Embodiment 92. The use of Embodiment 91, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog.

[00200] Embodiment 93. The use of Embodiment 92, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid ester.

[00201] Embodiment 94. The use of Embodiment 92, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid acetate.

[00202] Embodiment 95. The use of Embodiment 90, wherein the position of the carbon for substituting the at least one hydrogen with at least one deuterium is at the position 14 and at the position 20, wherein the position 14 comprises substituting one hydrogen with one deuterium and

the position 20 comprises substituting three hydrogens with three deuteriums (14, 20, 20, 20-tetradеutero retinoid).

[00203] Embodiment 96. The use of Embodiment 95, wherein the 14, 20, 20, 20-tetradеutero retinoid comprises a 14, 20, 20, 20-tetradеutero retinoid analog.

[00204] Embodiment 97. The use of Embodiment 96, wherein the 14, 20, 20, 20-tetradеutero retinoid comprises a 14, 20, 20, 20-tetradеutero retinoid ester.

[00205] Embodiment 98. The use of Embodiment 96, wherein the 14, 20, 20, 20-tetradеutero retinoid comprises a 14, 20, 20, 20-tetradеutero retinoid acetate.

[00206] Embodiment 99. The use of Embodiment 90, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 12, at the position 14, and at the position 20, wherein the position 12 comprises substituting one hydrogen with one deuterium, the position 12 comprises substituting one hydrogen with one deuterium, and the position 20 comprises substituting three hydrogens with three deuteriums (12, 14, 20, 20, 20-pentadeutero retinoid).

[00207] Embodiment 100. The use of Embodiment 99, wherein the 12, 14, 20, 20, 20-pentadeutero retinoid comprises a 12, 14, 20, 20, 20-pentadeutero retinoid analog.

[00208] Embodiment 101. The use of Embodiment 100, wherein the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid ester.

[00209] Embodiment 102. The use of Embodiment 100, wherein the 12, 14, 20, 20, 20-pentadeutero retinoid analog comprises a 12, 14, 20, 20, 20-pentadeutero retinoid acetate.

[00210] Embodiment 103. The use of Embodiment 85, wherein the use is an aesthetic use.

[00211] Embodiment 104. The use of Embodiment 85, wherein the use is a cosmetic use.

[00212] Embodiment 105. The use of Embodiment 85, wherein the use is a supplement use.

[00213] Embodiment 106. The use of any one of Embodiments 85-105, wherein the use does not treat a disease or condition.

[00214] Embodiment 107. The use of any one of Embodiments 85-106, wherein the composition is formulated for transdermal delivery of the retinoid to the subject.

[00215] Embodiment 108. The use of any one of Embodiments 85-107, wherein the composition is formulated as a semi-solid.

[00216] Embodiment 109. The use of any one of Embodiments 85-107, wherein the composition is formulated as a softgel capsule.

[00217] Embodiment 110. The use of any one of Embodiments 85-107, wherein the composition is formulated as a solid dispersion.

[00218] Embodiment 111. The use of any one of Embodiments 85-107, wherein the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.

[00219] Embodiment 112. The use of any one of Embodiments 85-111, wherein the composition comprises at least one additional ingredient.

[00220] Embodiment 113. The use of Embodiment 112, wherein the at least one additional ingredient comprises an antioxidant.

[00221] Embodiment 114. The use of Embodiment 113, wherein the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract.

[00222] Embodiment 115. The use of Embodiment 112, wherein the at least one additional ingredient comprises a fatty acid.

[00223] Embodiment 116. The use of Embodiment 115, wherein the fatty acid comprises omega-3 fatty acid.

[00224] Embodiment 117. The use of Embodiment 112, wherein the at least one additional ingredient comprises a carotenoid.

[00225] Embodiment 118. The use of Embodiment 117, wherein the carotenoid comprises lutein, zeaxanthin, or astaxanthin.

[00226] Embodiment 119. The use of Embodiment 112, wherein the at least one additional ingredient comprises a flavonoid.

[00227] Embodiment 120. The use of Embodiment 119, wherein the flavonoid comprises anthocyanin.

[00228] Embodiment 121. The use of Embodiment 112, wherein the at least one additional ingredient comprises an amino acid.

[00229] Embodiment 122. The use of Embodiment 121, wherein the amino acid comprises taurine.

[00230] Embodiment 123. The use of Embodiment 85, wherein the retinoid is present in the composition at a percentage (w/w) of about 1% to about 50%.

[00231] Embodiment 124. The use of Embodiment 85, wherein the lipid excipient increases the bioavailability of the retinoid in the subject by 100% compared to the second bioavailability of the retinoid formulated with the excipient that is different from the lipid excipient.

[00232] Embodiment 125. The use of any one of Embodiments 85-124, wherein the composition is formulated as a supplement.

EXAMPLES

[00233] The following illustrative examples are representative of embodiments of the stimulation, systems, and methods described herein and are not meant to be limiting in any way.

Example 1. Manufacturing of retinoid composition

[00234] The composition described herein can be formulated as an oil-based capsule, wherein the retinoid can be dissolved in a carrier oil. Non-limiting examples of the carrier oil include soybean oil, sunflower oil, safflower oil, or fish oil. The choice of carrier oil can modulate the stability, bioavailability, or shelf life of the retinoid. The retinoid can be mixed with the carrier oil. This mixture can then be encapsulated within a softgel capsule shell made of gelatin or other suitable materials.

[00235] The composition can further include an additional excipient for increasing water solubility or retinoid bioavailability. For example, hydroxypropyl- β -cyclodextrin (HPBCD) or nanoparticle (e.g., lipid nanoparticle, nanomicelle, nanocapsule, or nanosphere) can be added to the composition. The inclusion of HPBCD can increase water solubility of the retinoid.

[00236] The composition can also be formulated as a polymer or dispersion, wherein the composition includes hydroxypropyl cellulose, hydroxypropyl methylcellulose hypromellose phthalate, polyvinylpyrrolidone-vinyl acetate, hypromellose-acetate-succinate, or a combination of any mixture thereof. The polymer or the dispersion can be further processed by fast evaporation, spray-drying, precipitation, or melt extrusion to obtain an amorphous state of the composition. The composition described herein can also be formulated as a liquid capsule, an oil-in-water emulsion, or a lipid matrix. The composition can be formulated as a solid dispersion. For example, the retinoid can be incorporated into poly(lactic-co-glycolic)(PLGA) millicylindrical implants.

Example 2. Safety study

[00237] A study of a composition described herein can be conducted in twenty (20) healthy human subjects to determine the safety of a composition comprising a retinoid, a lipid excipient, an ingredient, or a combination thereof. The concentration of the retinoid in the composition can be adjusted such that the volume or dose to be administered is convenient. For the dosing range of the study, compositions of various doses of retinoid can be prepared. The composition can be given orally to the subject at a single dose or at escalating doses. The subjects can be examined for adverse events after administration of the composition. Examples of the adverse events can include headache facial flushing, a facial burning sensation, or any symptoms associated with hypervitaminosis.

Example 3. Efficacy study

[00238] A study of a composition described herein can be conducted to determine the efficacy of a composition described herein orally administered to subjects having an eye disease or condition (e.g., macular degeneration). Subjects can receive a once-daily loading dose of the composition orally for one or more days. Subjects can be treated on an outpatient basis. During the study, subjects can be required to limit vigorous physical activity to decrease laboratory variability and avoid excessive vitamin A intake to decrease influence of outside factors on the assessment of safety variables.

[00239] Both eyes of each subject can be evaluated separately. Assessments of visual function can include: best-corrected visual acuity testing using Early Treatment Diabetic Retinopathy Study (ETDRS) testing followed by low contrast or high contrast Smith-Kettlewell Institute Low Luminance (SKILL) charts; visual field testing using Goldmann perimetry; full-field electroretinogram (ERG); or full-field stimulus threshold testing (FST). In vivo retinal microscopy can be performed by optical coherence tomography (OCT) and fundus autofluorescence can be ascertained by Spectralis. Efficacy can be measured by comparing the results of pretreatment objective and subjective visual function testing with results of the same parameters obtained during and after the oral administration of the composition. Baseline ERGs, ETDRS, and SKILL tests can be repeated. During and after treatment, visual function tests can be conducted on one or more days.

Example 4. 20,20,20-trideutero retinoid

[00240] A study of a composition described herein comprising 20,20,20-trideutero retinoid (e.g., Gildeuretinol or C20-D3-retinyl acetate) can be conducted to determine the safety and therapeutic efficacy of the 20,20,20-trideutero retinoid. The 20,20,20-trideutero retinoid can be 20,20,20-trideutero retinoid retinol, 20,20,20-trideutero retinol ester, 20,20,20-trideutero retinol acetate, 20,20,20-trideutero retinal, 20,20,20-trideutero pro-vitamin A carotenoid, or a combination thereof.

[00241] The safety study can include administering the composition comprising the 20,20,20-trideutero retinoid to twenty (20) healthy human subjects to determine the safety of a composition comprising a retinoid, a lipid excipient, an ingredient, or a combination thereof. The concentration of the retinoid in the composition can be adjusted such that the volume or dose to be administered is convenient. For the dosing range of the study, compositions of various doses of retinoid can be prepared. The composition can be given orally to the subject at a single dose or at escalating doses. The subjects can be examined for adverse events after administration of the

composition. Examples of the adverse events can include headache, facial flushing, a facial burning sensation, or any symptoms associated with hypervitaminosis.

[00242] The efficacy study can be conducted by administering the 20,20,20-trideutero retinoid to subjects having an eye disease or condition (e.g., macular degeneration). Subjects can receive a once-daily loading dose of the composition orally for one or more days. Subjects can be treated on an outpatient basis. During the study, subjects can be required to limit vigorous physical activity to decrease laboratory variability and avoid excessive vitamin A intake to decrease influence of outside factors on the assessment of safety variables.

[00243] Both eyes of each subject can be evaluated separately. Assessments of visual function can include: best-corrected visual acuity testing using Early Treatment Diabetic Retinopathy Study (ETDRS) testing followed by low contrast or high contrast Smith-Kettlewell Institute Low Luminance (SKILL) charts; visual field testing using Goldmann perimetry; full-field electroretinogram (ERG); or full-field stimulus threshold testing (FST). In vivo retinal microscopy can be performed by optical coherence tomography (OCT) and fundus autofluorescence can be ascertained by Spectralis. Efficacy can be measured by comparing the results of pretreatment objective and subjective visual function testing with results of the same parameters obtained during and after the oral administration of the composition. Baseline ERGs, ETDRS, and SKILL tests can be repeated. During and after treatment, visual function tests can be conducted on one or more days.

Example 5. Aesthetic, cosmetic, or supplement use

[00244] A retinoid described herein, such as the 20,20,20-trideutero retinoid (e.g., Gildeuretinol or C20-D3-retinyl acetate) can be formulated into a composition or supplement for aesthetic or cosmetic use. The retinoid can be formulated as a topical cream or ointment to be applied to a subject for transdermal administration. The retinoid can be formulated as softgel capsule for oral administration. The retinoid can be used for aesthetic, cosmetic, or supplement purpose, where the subject is not using the retinoid for treating a disease or condition. The retinoid can be used for aesthetic, cosmetic, or supplement purpose, where the retinoid or any other ingredient in the composition comprising the retinoid does not require regulatory approval.

Example 6. Lipid based formulation for retinoid storage and delivery

[00245] Various lipid-based formulations were tested to develop and improve bioavailability of retinoid upon delivery to a subject in need thereof. The lipid formulation tested included 10 milligrams (mg) of lutein, 300 mg of eicosapentaenoic acid (EPA), 110 mg of docosahexaenoic acid (DHA), 2 mg of zeaxanthin, and 50 mg of curcuminoid. **Table 1** illustrates a summary of the test for the lipid-based formulation. As shown in **Table 1**, F21 exhibited the improvement of

bioavailability of retinoid. The composition of F21 was: 2.5 mg of deuterated vitamin A, 10 mg of lutein, 2 mg of zeaxanthin, 50 mg of curcuminoid, 300 mg of EPA, 110 mg of DHA in 0.1 mL Capmul MCM, 0.1 mL of Gelucire 44/14, 0.3 mL of Tween 80, and 0.1 mL of PEG 400. **Table 2** illustrates non-limiting examples of excipients as part of the lipid-based formulation. **Table 3** illustrates an example of an ultra performance liquid chromatography (UPLC) for obtaining the material for formulating the lipid-based formulation described herein.

Table 1. Summary of lipid-based formulation testing

Study content	Items		Results		
Solubility screening	Lutein, EPA, DHA, Zeaxanthin and Curcuminoid		Due to the extremely low solubility of lutein and curcuminoid in organic solvents, an oily suspension was proposed to control the volume that can be filled into a soft capsule.		
LBF screening	Items		Control	F21	F22
	Dilution study		Cannot disperse	Good appearance (blue light microemulsion)	Good particle size distribution (PDI=0.290)
	In-vitro lipolysis study	Solubility in FaSSIF @30min	1.48 µg/mL	Improved 20-fold	Improved 17-fold
		After adding pancreatin @90min	0.43 µg/mL	Improved 25-fold	Improved 16-fold
	Stability study	2-8°C/without light/closed	Not tested	Stable for 7 days	Unstable in 1 day
		25°C/without light/closed	Not tested	Unstable in 1 day	Unstable in 1 day

Table 2. Non-limiting examples of excipients or surfactants

Name	Grade	Manufacturer	Batch No.
Tween 80	EP/USP	Aladdin	G2205383
Kolliphor EL	N/A	Aladdin	A2404306
Vitamin ETPGS	N/A	Healthcare inc.	TPGS20220812
Kolliphor HS15	N/A	BASF	41769336W0
Labrafil® M 2125 CS	EP/USP	GATTEFOSSÉ	184152
Polyethylene glycol 400 (PEG 400)	N/A	BASF	96036424U0
Oleic acid	N/A	energy chemical	0I1ARCDA
Corn oil	N/A	Aladdin	F2214830
Maisine cc	N/A	GATTEFOSSE	191871
Capmul MCM	N/A	ABITEC	231003-6

Name	Grade	Manufacturer	Batch No.
Capryol 90	N/A	GATTEFOSSE	195036
Kolliphor RH40	N/A	BASF	31547356PO
Gelucire 48/16	N/A	GATTEFOSSÉ	18500
Gelucire 44/14	N/A	GATTEFOSSÉ SAS	182873
Labrasol ALF	N/A	Healthcare	TPGS20230211
Labrafil M2125 CS	N/A	GATTEFOSSE	194167
Propylene glycol (PG)	AR	GATTEFOSSE	184152
Ethanol	HPLC	Shanghai Lingfeng Chemical Reagent Co. LTD	AZTXG-QC
Dimethylacetamide (DMA)	HPLC	Shanghai Lingfeng Chemical Reagent Co. LTD	20231228
Transcutol HP	HPLC	GATTEFOSSE	191687
Docosahexaenoic Acid (DHA)	N/A	Shanghai Bide Medicine	FKX838
(5Z,8Z,11Z,14Z,17Z)-Icosa-5,8,11,14,17-pentaenoic acid (EPA)	N/A	Energy Chemical	B0DORRDF
lutein	N/A	Shanghai McLean Biochemical Technology Co., LTD	C16309170
Zeaxanthin	N/A	Aladdin	A2314349
Curcumin	N/A	Shanghai McLean Biochemical Technology Co., LTD	C16551551
(4-bromophenyl)boronic acid	N/A	Shanghai Bide Medicine	DNZ179
Sodium hydroxide	AR	Shanghai Laboratory Reagent Co., LTD	20240902
Pancreatin from porcine pancreas	N/A	SIGMA	SLBZ5739
FaSSIF-V2 powder	N/A	Biorelevant	V2FAS-0823-A

Table 3. UPLC for obtaining material for formulating the lipid-based formulation

Instrument	Agilent 1290 UPLC with UV detector		
Column	XBridge BEH C18 (2.1mm×50mm, 1.7μm)		
Gradient	Time (minutes)	A%: water	B%: methanol
	0.0	40	60
	1.0	40	60

	2.0	2	98
	3.0	2	98
	3.5	40	60
	5.0	40	60
Injection volume	5 μ L		
Flow rate	0.5 mL/min		
Column Temp.	40 $^{\circ}$ C		
Wavelength	325 nm		
Diluent	Methanol		
Concentration	0.1 mg/mL		

[00246] Retinol-d6 was weighed and diluent (e.g., methanol) was added to dissolve as a reference standard. The target concentration was 0.1 mg/mL. The standard solution was prepared in duplicate. One was used as a working standard solution (STD) and another was used as checking a standard solution (STD-check). The working standard solution (STD) was diluted 2,000 times as the sensitivity solution (LOQ). The results of system suitability and the linearity are shown in **Table 4** and **Fig. 1**. As shown in **Table 4** and **Fig. 1**, increased sensitivity, precision, accuracy and linearity were obtained and observed.

Table 4. Results of system suitability test for assay

Sample name	No. of Injection	Criteria	Results
Blank Diluent	1 or more	No significant interference peak (below LOQ*)	Pass
Sensitivity Solution (LOQ)	1	$S/N \geq 10$	18.3
Working Standard Solution (STD-1)	6	$N \geq 2000$	111271
		$0.8 \leq T \leq 2.0$	1.0
		$R_s \geq 1.2$	3.38
		$RSD (\%) \leq 2.0$ (area)	0.55
		$RSD (\%) \leq 2.0$ (retention time)	0.53
checking Standard Solution (STD-2)	1	Recovery: 98.0%-102.0%	99.8%

“N” is theoretical plate count of Retinol-d6.

“T” is the tailing factor of main peak of Retinol-d6.

“Rs” is the resolution factor between the main peak and its adjacent peaks.

*: LOQ is 0.05 μ g/mL for Retinol-d6.

[00247] Different solvents were gradually added into six components (curcuminoid, lutein, zeaxanthin, DHA, EPA and retinol-d6) respectively, then conducted by vortex combined with visual observation to get the approximate solubility. The results are summarized in **Table 5**.

Table 5. Approximate solubility of curcuminoid, lutein, zeaxanthin, DHA, EPA and retinol-d6

Functionality	No.	Ingredients	Solubility (mg/mL)											Retinol-d6, (2.5 mg)
			Curcuminoid (50 mg)			Lutein (10 mg)			Zeaxanthin (2 mg)			DHA (110 mg)	EPA (300 mg)	
			~25°C	~50°C	Note	~25°C	~50°C	Note	~25°C	~50°C	Note	~25°C	~25°C	~25°C
Surfactants	1	Tween 80	8.4-12.6	/	Stirred 1h	<1.7	/	Undissolved	0.62-0.76	/	Stirred 1h	mutually soluble	mutually soluble	/
	2	Kolliphor EL	8.4-12.6	/	Stirred 1h	<1.4	/	Undissolved	0.67-0.82	/	Stirred 1h	mutually soluble	mutually soluble	/
	3	Solutol HS15	/	8.4-12.6	Stirred 1h	/	1.7-1.9	Stirred 1h	/	1.02-1.07	Stirred 1h	mutually soluble	mutually soluble	/
	4	Kolliphor RH40	/	8.5-12.7	Stirred 1h	/	1.6-1.9	Stirred 1h	/	1.18-1.89	Stirred 1h	mutually soluble	mutually soluble	/
	5	Gelucire 44/14	/	35.7-41.7	Stirred 19h	/	>1.5	Stirred 1h	/	>1.13	Stirred 1h	/	/	/
	6	Gelucire 48/16	/	12.3-24.7	Stirred 1h	/	1.5-2.0	Stirred 1h	/	1.13-1.92	Stirred 1h	mutually soluble	mutually soluble	/
			/	41.7-62.5	Stirred 19h									
Co-surfactants	8	Labrasol ALF	8.2-12.4	/	/	1.5-1.8	/	Stirred 1h	0.85-1.13	/	/	mutually soluble	mutually soluble	/
	9	Labrafil M2125 CS	<8.5	/	Undissolved	<1.5	/	Undissolved	<0.61	/	Undissolved	mutually soluble	mutually soluble	/
Co-solvents	10	Propylene glycol (PG)	<8.5	/	Undissolved	<1.4	/	Undissolved	0.67-0.83	/	/	mutually soluble	mutually soluble	/
	11	Ethanol	8.3-12.4	/	/	<1.5	/	Undissolved	1.03-1.25	/	/	mutually soluble	mutually soluble	/
	12	PEG 400	12.2-24.5	/	Stirred 1h	<1.4	/	Undissolved	0.67-0.77	/	/	mutually soluble	mutually soluble	/
			41.7-50.0	/	Stirred 3h									
	13	Glycol	<8.32	/	Undissolved	<1.3	/	Undissolved	<0.54	/	Undissolved	Undissolved	Undissolved	/

Functionality	No.	Ingredients	Solubility (mg/mL)											Retinol-d6, (2.5 mg)
			Curcuminoid (50 mg)			Lutein (10 mg)			Zeaxanthin (2 mg)			DHA (110 mg)	EPA (300 mg)	
			~25°C	~50°C	Note	~25°C	~50°C	Note	~25°C	~50°C	Note	~25°C	~25°C	~25°C
	14	DMA	>247.42	/	/	1.7-1.9	/	Hazy	9.70-16.17	/	/	mutually soluble	mutually soluble	/
	15	Transcutol HP	49.4-83.3	/	/	<1.8	/	Undissolved	1.72-2.58	/	/	mutually soluble	mutually soluble	/
Oil	16	DHA	<11.6	/	Undissolved	<3.5	/	Undissolved	<1.3	/	Undissolved	mutually soluble	mutually soluble	/
	17	EPA	<15.5	/	Undissolved	<3.4	/	Undissolved	<1.3	/	Undissolved	mutually soluble	mutually soluble	≥15
	18	Oleic acid	/	/	/	<1.6	/	Undissolved	/	/	/	/	/	/
	19	Corn oil	/	/	/	<1.6	/	Undissolved	/	/	/	/	/	/
	20	Maisine cc	/	/	/	<1.5	/	Undissolved	/	/	/	/	/	/
	21	Capmul MCM	/	/	/	4.2-5.1	/	Stirred 1h	/	/	/	/	/	/
						4.9-5.3	/	Stirred 19h	/	/	/	/	/	/
	22	Capryol 90	/	/	/	3.6-4.2	/	Stirred 1h	/	/	/	/	/	/

[00248] The excipients with higher solubility and listed in FDA Inactive Ingredients Guidance Database were preferred for lipid formulation development. Curcuminoid and zeaxanthin showed better solubility in Gelucire 44/14, Gelucire 48/16, PEG 400, DMA and Transcutol HP. DHA and EPA showed good mutually solubility with most surfactants and solvents except for glycol. Retinol-d6 showed good solubility in EPA. For lutein, there was no surfactant and co-solvent with suitable solubility. However, lutein showed higher solubility in DMA, Capmul MCM and Capryol 90. DMA and Capryol 90, which have higher toxicity, were not used in the formulation development. Gelucire 44/14, Gelucire 48/16, PEG 400, Transcutol HP and Capmul MCM were selected to improve solubility in the formulation.

Appearance of lipid formulation

[00249] The lipid formulation was developed based on the preliminary formula-01 without Retinol-d6. Oil, surfactant and co-solvent were added to dissolve all ingredients in the preliminary formula-01. The vehicles, without preliminary formula ingredients, were prepared to

observe whether the formulation would solidify or precipitate. Since solids ingredients may not be dissolved by stirring at room temperature (20°C -25°C) within 20 hours, all formulations were prepared at 40°C to speed up the preparation time. The compositions added to the preliminary formula-01 and the appearance of first round formulations were recorded in **Table 6**. The appearance of the formulations and corresponding vehicles are illustrated in **Fig. 2**. All lipid formulations were clear at 40°C, but F02-F10 changed to solid state quickly at room temperature (20-25°C) in less than 2 hours. F11-F17 kept a liquid state for a longer time at room temperature and were further run in dilution study.

Table 6. Lipid formulations compositions and appearance in first round screening

Sample	Oil	Surfactant	Co-solvent	Appearance of formulation
F01	3 mL Capmul MCM	/	/	Undissolved @50C
F02	1.6 mL Capmul MCM	1.6 mL Gelucire 48/16	/	Clear at 40C, then precipitate/solid @RT after 0.5h
F03	1.6 mL Capmul MCM	1.6 mL Gelucire 48/16	0.5mL PEG 400	Clear at 40C, then precipitate/solid @RT after 1.5h
F04	1.6 mL Capmul MCM	1.6 mL Gelucire 48/16	0.5mL Transcutol HP	Clear at 40C, then precipitate/solid @RT after 0.5h
F05	1.6 mL Capmul MCM	2 mL Gelucire 48/16	/	Clear at 40C, solid@RT after 1.5h
F06	1.6 mL Capmul MCM	2 mL TPGS	/	Clear at 40C, solid@RT after 1.5h
F07	1.6 mL Capmul MCM	2 mL Gelucire 48/16	0.5mL PEG 400	Clear at 40C, Semi-solid @RT
F08	1.5 mL Capmul MCM	1.5 mL Gelucire 48/16	0.7mL PEG 400	Clear at 40C, Semi-solid @RT 0.5h
F09	1.5 mL Capmul MCM	1.2 mL Gelucire 48/16+0.4 mL TW80	0.7mL PEG 400	Clear at 40C, Semi-solid @RT 1.5h
F10	1.5 mL Capmul MCM	1.8 mL TPGS	0.7mL PEG 400	Clear at 40C, Semi-solid @RT

Sample	Oil	Surfactant	Co-solvent	Appearance of formulation
F11	1.5 mL Capmul MCM	1.2 mL Gelucire 44/14+0.4 mL TW80	0.7mL PEG 400	Clear @RT 6h, partially solidified @RT 1d
F12	1.8 mL Capmul MCM	0.6 mL Gelucire 48/16+1 mL TW80	0.4mL PEG 400	Clear @RT 6h, solid @RT 1d
F13	1.6 mL Capmul MCM	1.6 mL Gelucire 44/14	/	Clear @RT 6h, partially solidified @RT 1d
F14	1.6 mL Capmul MCM	1.5 mL Gelucire 44/14	0.5mL PEG 400	Clear @RT 6h, partially solidified @RT 1d
F15	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14+1.5 mL TW80	0.4mL PEG 400	Clear @RT 3h, partially solidified @RT 1d
F16	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14+1.5 mL Kolliphor EL	0.4mL PEG 400	Clear @RT 5h, hazy @RT 1d, vehicle became white liquid @1d
F17	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14+1.5 mL Kolliphor EL	0.4mL Transcutol HP	Clear @RT 5h, hazy @RT 2d, vehicle became white liquid @1d

Note: Gelucire 48/16 and Gelucire 44/14 were pre-heated at 50°C before adding

Dilution test for formulation without retinol-d6

[00250] Formulations prepared previously were used directly for the dilution test. All lipid formulations were diluted by SGF with 1:9 (v/v) while stirred at 300 rpm and 37°C for 0.5 hours, and then diluted by FaSSIF with 1:3 (v/v) at the same condition for 1 hour. Appearance, power spectral density (PSD) and pH were recorded. The results are shown in **Table 7** and **Fig. 3**. F12 showed good particle size distribution (PDI=0.299) while F15 showed better appearance (nearly clear solution) in a dilution study.

Table 7. Dilution study of first round of lipid formulations without Retinol-d6

No.	Compositions (v/v)			Diluted with SGF (1:9, v/v) for 0.5 h	pH	Further diluted with FaSSIF (1:3, v/v) for 2h	pH	PSD (nm)	Appearance of diluted solution after 5min @RT
	Oil	Surfactant	Co- solvent						
F11		1.2 mL Gelucire	0.7mL PEG 400	Yellow emulsion,	1.42	Yellow emulsion	5.44	D10:82 D50: 299	Yellow emulsion

	1.5mL Capmul MCM	44/14 +0.4 mL Tween80		1 min dispersed				D90: 513 PDI: 0.320	with little orange droplets
F12	1.8 mL Capmul MCM	0.6 mL Gelucire 48/16 +1 mL Tween80	0.4mL PEG 400	Yellow emulsion, 1 min dispersed	1.45	Yellow emulsion	5.53	D10: 71.1 D50: 284 D90: 568 PDI: 0.299	N/A
F13	1.6 mL Capmul MCM	1.6 mL Gelucire 44/14	/	Yellow emulsion, 1 min dispersed	1.45	Yellow emulsion	4.49	D10:82.5 D50:392 D90: 787 PDI: 0.469	Yellow emulsion with little orange droplets
F14	1.5 mL Capmul MCM	1.5 mL Gelucire 44/14	0.5mL PEG 400	Yellow emulsion, 1 min dispersed	1.53	Yellow emulsion	5.47	D10: 98.5 D50: 320 D90: 772 PDI: 0.417	Yellow emulsion with little orange droplets
F15	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5 mL Tween80	0.4mL PEG 400	Yellow emulsion, 1 min dispersed	1.51	Nearly clear yellow solution	5.58	Cannot get accurate value	N/A
F16	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5 mL Kolliphor EL	0.4mL PEG 400	Yellow emulsion, 1 min dispersed	1.5	Yellow emulsion	5.58	D10: 107 D50: 399 D90: 721 PDI: 0.327	Yellow emulsion with little orange droplets
F17	1.8 mL Capmul MCM	0.6 mL Gelucire 44/16 +1.5 mL Kolliphor EL	0.4mL transcutol HP	Yellow emulsion, 1 min dispersed	1.57	Yellow emulsion	5.55	D10: 210 D50: 426 D90: 1010 PDI: 0.328	N/A

Dilution test for formulations with retinol-d6

[00251] Each formulation prepared previously was mixed well with 2.5 mg of Retinol-d6 for a dilution test. The amount of Retinol-d6 added was adjusted according to the formulation volume. A control was prepared by adding 2.5 mg of Retinol-d6 into 3.6 mL of corn oil and mixing well.

All lipid formulations with retinol-d6 were diluted by SGF and FaSSIF. The results are shown in **Table 8** and **Fig. 4**. F12, F14 and F17 showed good particle size distribution and their Polydispersity Index (PDI) were 0.299, 0.268 and 0.263, respectively.

Table 8 Dilution study of first round lipid formulations with retinol-d6

No.	Compositions (v/v)			Diluted with SGF (1:9, v/v) for 0.5 hours	pH	Further diluted with FaSSIF (1:3, v/v) for 2 hours	pH	PSD (nm)	Appearance after 5 minutes
	Oil	Surfactant	Co-solvent						
Control	3.6 mL Corn oil	/	/	Layered	1.49	Layered	5.33	N/A	N/A
F11	1.5mL Capmul MCM	1.2 mL Gelucire 44/14 +0.4 mL Tween80	0.7mL PEG 400	Yellow emulsion, 1 min dispersed	1.48	Yellow emulsion	5.46	D10:46.9	Yellow emulsion with little orange droplets
								D50: 152	
								D90: 284	
								PDI: 0.376	
F12	1.8 mL Capmul MCM	0.6 mL Gelucire 48/16 +1 mL Tween80	0.4mL PEG 400	Yellow emulsion, 1 min dispersed	1.47	Yellow emulsion	5.51	D10: 108	N/A
								D50: 136;	
								D90: 175	
								PDI: 0.299	
F13	1.6 mL Capmul MCM	1.6 mL Gelucire 44/14	/	Yellow emulsion, 1 min dispersed	1.45	Yellow emulsion	5.44	D10:92.1	Yellow emulsion with little orange droplets
								D50:130	
								D90: 188	
								PDI: 0.415	
F14	1.5 mL Capmul MCM	1.5 mL Gelucire 44/14	0.5mL PEG 400	Yellow emulsion, 1 min dispersed	1.48	Yellow emulsion	5.47	D10: 61	Yellow emulsion with little orange droplets
								D50: 97.7	
								D90: 132	
								PDI: 0.268	
F15	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5 mL Tween80	0.4mL PEG 400	Yellow emulsion, 1 min dispersed	1.47	Yellow emulsion	5.55	D10: 89.3	N/A
								D50: 229	
								D90: 473	
								PDI: 0.345	
F16	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5 mL Kolliphor EL	0.4mL PEG 400	Yellow emulsion, 1 min dispersed	1.47	Yellow emulsion	5.33	D10: 73.7	Yellow emulsion with little orange droplets
								D50: 131	
								D90: 253	
								PDI: 0.319	
F17	1.8 mL Capmul MCM	0.6 mL Gelucire 44/16 +1.5 mL	0.4mL transcuto HP	Yellow emulsion, 1 min dispersed	1.48	Yellow emulsion	5.29	D10: 56.1	N/A
								D50: 132	
								D90: 276	

No.	Compositions (v/v)			Diluted with SGF (1:9, v/v) for 0.5 hours	pH	Further diluted with FaSSIF (1:3, v/v) for 2 hours	pH	PSD (nm)	Appearance after 5 minutes
	Oil	Surfactant	Co-solvent						
		Kolliphor EL						PDI: 0.263	

Second round of formulations screening

[00252] In order to decrease the total volume of the formulation to less than 1.3 mL, which may be contained in a single soft gel, a second round of lipid formulations in a suspension state were developed. Meanwhile, the proportion of Gelucire was reduced to maintain the liquid state of the formulations, as Gelucire solidifies at room temperature. The preliminary formula-02 to be tested included 2.5 mg of retinol-d6, 10 mg of lutein, 2 mg of zeaxanthin, and 50 mg of curcuminoid.

Appearance of lipid formulations

[00253] A lipid formulation was developed based on the preliminary formula-02 without retinol-d6. 300 mg of EPA and 110 mg of DHA were added as oil components into the formulation. Other oils, surfactants and co-solvents were added to the formulation to help dissolve the solid ingredients. The vehicles, without preliminary formula-02 components, were prepared to help observe whether the formulation would solidify.

[00254] The compositions added to the preliminary formula-02 and appearance of second round formulations are recorded in **Table 9**. The appearance of the formulations and corresponding vehicles are shown in **Fig. 5**. All lipid formulations kept red brown suspension state at RT (20-25°C) for 4 days (4d). But vehicle of 18 showed tendency of solid state.

Table 9. Lipid formulations compositions and appearance in second round screening

Sample	Oil	Surfactant	Co-solvent	Appearance of formulation
F18	300 mg EPA+110 mg DHA	0.1 mL Gelucire 44/14+ 0.3 mL Labrasol ALF	/	Red brown suspension, RT 4d
F19	300 mg EPA+110 mg DHA	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.2mL PEG 400	Red brown suspension, RT 4d

Sample	Oil	Surfactant	Co-solvent	Appearance of formulation
F20	300 mg EPA+110 mg DHA+0.2 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	/	Red brown suspension, RT 4d
F21	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.1mL PEG 400	Red brown suspension, RT 4d
F22	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Kolliphor EL	0.1mL Transcutol HP	Red brown suspension, RT 4d

Gelucire 48/16 and Gelucire 44/14 were pre-heated at 50°C before adding

Dilution test for formulations without retinol-d6

[00255] Formulations prepared previously were used directly for the dilution test. All lipid formulations were diluted by SGF with 1:9 (v/v) while stirred at 300 rpm at a temperature of 37°C for 0.5 hours, and then diluted by FaSSIF with 1:3 (v/v) at same condition for 1 hour. Appearance, PSD and pH were recorded. All results are shown in **Table 10** and **Fig. 6**. In the dilution study without retinol-d6 but with lutein, zeaxanthin and curcuminoid, F22 showed good PDI. F18-F22 showed suspension with coarse particle state after diluted with SGF and FaSSIF. The PSD results were significantly impacted by the presence of insoluble substances, resulting in multiple peaks and poor data quality. Consequently, in following the dilution study involving retinol-d6, lutein, zeaxanthin, and curcuminoid were excluded to avoid their influence.

[00256] F22 showed good particle size distribution (PDI=0.275) in the dilution study. However, F18-F22 showed suspension with coarse particle state after diluted with SGF and FaSSiF. The PSD results were significantly impacted by the presence of insoluble substances, resulting in multiple peaks and poor data quality. Consequently, in following the dilution study involving retinol-d6, lutein, zeaxanthin, and curcuminoid were excluded to avoid their influence.

Table 10. Dilution study of second round lipid formulations without retinol-d6

No.	Compositions (v/v)			Diluted with SGF (1:9, v/v)	pH	Further diluted with FaSSiF	pH	PSD (nm)	Appearance of diluted solution after 5
	Oil	Surfactant	Co-solvent						

				for 0.5 hours		(1:3, v/v) for 2 hours			minutes @RT
F18	300 mg EPA+110 mg DHA	0.1 mL Gelucire 44/14+ 0.3 mL Labrasol ALF	/	Orange suspension with coarse particle	1.47	Orange suspension with coarse particle	5.24	Cannot get accurate value	Orange suspension with little droplets
F19	300 mg EPA+110 mg DHA	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.2mL PEG 400	Orange suspension with coarse particle	1.45	Orange suspension with coarse particle	5.22	Cannot get accurate value	Orange suspension with little droplets
F20	300 mg EPA+110 mg DHA+0.2 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	/	Orange suspension with coarse particle	1.45	Orange suspension with coarse particle	5.21	Cannot get accurate value	Orange suspension with little droplets
F21	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.1mL PEG 400	Orange suspension with coarse particle	1.49	Orange suspension with coarse particle	5.24	Cannot get accurate value	Orange suspension with little droplets
F22	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Kolliphor EL	0.1mL Transcutol HP	Yellow suspension	1.48	Yellow suspension	5.27	D10: 102 D50: 209 D90: 392 PDI: 0.275	N/A

Gelucire 48/16 and Gelucire 44/14 were pre-heated at 50°C before adding

Dilution test for formulations with retinol-d6

[00257] Each vehicle prepared previously was mixed well with 2.5 mg of Retinol-d6 for dilution test. Since F18 had a tendency to solidify, F18 was deleted and F23 was added in dilution study with retinol-d6. The results of appearance, PSD and pH are shown in **Table 11** and **Fig. 7**. F23 kept liquid state without solidification tendency at RT (20-25°C) for 2 days. F21 showed better appearance (blue light microemulsion) and F22 showed good particle size distribution (PDI=0.290) after diluted with SGF and FaSSIF. Thus F21 and F22 were proceeded for digestion and stability studies.

Table 11. Dilution study of second round lipid formulations with retinol-d6

No.	Compositions (v/v)			Diluted with SGF (1:9, v/v) for 0.5 h	pH	Further diluted with FaSSIF (1:3, v/v) for 2h	pH	PSD (nm)	Appearance of diluted solution after 5min @RT
	Oil	Surfactant	Co-solvent						
Control	3.6 mL Corn oil	/	/	Layered	1.49	Layered	5.33	N/A	N/A
F19	300 mg EPA+110 mg DHA	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.2mL PEG 400	White emulsion, 1min dispersed	1.49	White emulsion	5.37	Cannot get accurate value	White emulsion with little oil droplets
F20	300 mg EPA+110 mg DHA+0.2 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	/	White emulsion, 1min dispersed	1.52	White emulsion	5.41	Cannot get accurate value	White emulsion with little oil droplets
F21	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.1mL PEG 400	White emulsion, 1min dispersed	1.52	Blue light microemulsion	5.43	D10: 48.1	N/A
								D50: 152	
								D90: 293	
								PDI: 0.377	
F22	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Kolliphor EL	0.1mL Transcutol HP	White emulsion, 1min dispersed	1.50	White emulsion	5.47	D10: 91.2	N/A
								D50: 227	
								D90: 455	
								PDI: 0.290	
F23	300 mg EPA+110 mg	0.1 mL Gelucire 44/14 +	0.1mL PEG 400	White emulsion	1.50	White emulsion	5.47	Cannot get	White emulsion

	DHA+0.1 mL Capmul MCM	0.3 mL Labrasol ALF		, 1min dispersed				accurate value	with little oil droplets
--	-----------------------------	---------------------------	--	---------------------	--	--	--	----------------	-----------------------------

Gelucire 48/16 and Gelucire 48/16 were pre-heated at 50°C before adding

Lipolysis test of F21 and F22

[00258] Formulation of F21 included 2.5 mg of retinol-d6, 10 mg of lutein, 2 mg of zeaxanthin, 50 mg of curcuminoid, 300 mg of EPA, 110 mg of DHA, 0.1 mL of Capmul MCM, 0.1 mL of Gelucire 44/14, 0.3 mL of Tween 80 and 0.1 mL of PEG 400. Formulation of F22 included 2.5 mg of retinol-d6, 10 mg of lutein, 2 mg of zeaxanthin, 50 mg of curcuminoid, 300 mg of EPA, 110 mg of DHA, 0.1 mL of Capmul MCM, 0.1 mL of Gelucire 44/14, 0.3 mL of Kolliphor EL and 0.1 mL of Transcutol HP. F21 and F22 with good dilution effects were tested for lipolysis. 2.5 mg of Retinol-d6 was added into 1 mL of corn oil and mixed well as control for lipolysis test. Lipid formulations were dispersed in FaSSIF at 37°C, and then pancreatin extract solution was added after 30 minutes. At each time point of 15 minutes and 30 minutes in FaSSIF and 5 minutes, 15 minutes, 30 minutes and 60 minutes in pancreatin extract solution, a 0.5 mL suspension was added into 5 µL 1 M 4-bromophenylboronic acid solution to inhibit lipolysis and the assay of supernatant was tested. The phenomenon at 30 minutes and final pH were recorded. The results are summarized in **Table 12**. F21 and F22 exhibited significant effects with about 20-fold and 17-fold improvement respectively in solubility in FaSSIF at 30 minutes. After adding pancreatin extract solution, F21 and F22 kept higher concentration at 11.2 and 7.6 µg/mL at 90 minutes while retinol-d6 in corn oil was 0.43 µg/mL. F21 and F22 exhibited significant effects with about 20-fold and 17-fold improvement in solubility of FaSSIF at 30 minutes respectively. After adding pancreatin extract solution, F21 and F22 kept higher concentration at 11.2 and 7.6 µg/mL for 60 minutes while retinol-d6 in corn oil was 0.43 µg/mL.

Table 12. Lipolysis results for lipid based formulations

No.	Compositions (v/v)			Concentration (µg/mL)								Final pH
				Lipid in FaSSIF at 37°C (target concentration of 66 µg/mL)			+ pancreatin extract solution at 37°C (target concentration of 62 µg/mL)					
	Oil	Surfactant	Co-solvent	15 min	30 min	Phenomenon	35 min	45 min	60 min	90 min		
Control	1 mL Corn oil	/	/	0.84	1.48	Irregular oil droplets dispersed in	0.45	0.44	0.48	0.43	6.53	

						the solution, layered easily					
F21	300 mg EPA+110 mg DHA+0. 1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.1mL PEG 400	20. 0	29. 9	Orange suspension with coarse particle	16. 1	14. 9	13. 1	11.2	6.58
F22	300 mg EPA+110 mg DHA+0. 1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Kolliphor EL	0.1mL Transcuto 1 HP	26. 2	25. 1	Yellow suspension	10. 1	7.9	7.6	7.3	6.47

Stability test of F21 and F22

[00259] F21 and F22 were tested at 1 week stability at 2-8°C and RT (20-25°C) separately. For purity method development (*see Fig. 8*): Placebo (without retinol-d6) contain a lot of UPLC peaks in method-01 and affect the evaluation of related substance of retinol-d6. After optimizing the method to separated retinol-d6 from the placebo, the main peak of retinol-d6 was separated out using method-02, but more impurity peaks appeared. These impurity peaks were still affected by the placebo peaks, making it difficult to test the purity of retinol-d6 in the formulation. Since it was difficult to evaluate the stability of the formulations by purity, the concentration of effective retinol-d6 in the formulations was tested at different time point to assess the stability of the formulation. The results are shown in **Tables 13-15**. At 2-8°C/without light/closed condition, concentration of retinol-d6 showed no obvious change in F21 for 7 days but decreased by 18.2% in F22 form 1 day. At 25°C/without light/closed condition, concentration of retinol-d6 decreased by 7.6% and 25.3% respectively in F21 and F22 form 1 day. Thus, F21 was stable at 2-8°C/without light/closed and unstable at 25°C/without light/closed. F22 was unstable under neither 2-8°C/avoid light/closed nor 25°C/avoid light/closed conditions. F21 with good stability was suggested for PK study. At 2-8°C/avoid light/closed condition, concentration of retinol-d6 showed no obvious change in F21 for 7 days but changed 18.2% in F22 form 1 day. At 25°C/avoid light/closed condition, concentration of retinol-d6 changed by 7.6% and 25.3% in F21 and F22, respectively, form 1 day. Thus, F21 was stable at 2-8°C/avoid light/closed and unstable at 25°C/avoid light/closed. F22 was unstable under both 2-8°C/avoid light/closed and 25°C/avoid light/closed conditions.

Table 13. Stability test of F21 and F22

Sample s	Formulation	Condition	Time point	Conc. (mg/mL)	Compar e with initial (%)	Appearance
F21	Compound: 2.5 mg retinol-d6 Ingredients: 10 mg lutein, 2 mg zeaxanthin and 50 mg curcuminoid Oils: 300 mg EPA, 110 mg DHA, 0.1 mL Capmul MCM Surfactant: 0.1 mL Gelucire 44/14 + 0.3 mL Tween 80 Co-solvent: 0.1mL PEG 400	Initial		1.92	100.0	Red brown suspension
		2-8°C/avoid light/closed	1d	1.94	101.0	Red brown solid, suspension after 10 minutes at 25°C
			4d	2.02	105.2	Red brown solid, suspension after 10 minutes at 25°C
			6d	2.01	104.7	Red brown solid, suspension after 10 minutes at 25°C
			7d	1.90	99.0	Red brown solid, suspension after 10 minutes at 25°C
		25°C/avoid light/closed	1d	1.57	81.8	Red brown suspension
			4d	1.23	64.1	Red brown suspension with sedimentation solid at bottle
			6d	1.10	57.3	Red brown suspension with sedimentation solid at bottle
			7d	1.17	60.9	Red brown suspension with sedimentation solid at bottle
F22	Compound: 2.5 mg retinol-d6 Ingredients: 10 mg lutein, 2 mg zeaxanthin and 50 mg curcuminoid Oils: 300 mg EPA, 110 mg DHA, 0.1 mL Capmul MCM Surfactant: 0.1 mL Gelucire 44/14 and 0.3 mL Kolliphor EL Co-solvent: 0.1mL Transcutol	Initial		1.98	100.0	Red brown suspension
		2-8°C/avoid light/closed	1d	1.83	92.4	Red brown solid, suspension after 10 minutes at 25°C
			4d	1.86	93.9	Red brown solid, suspension after 10 minutes at 25°C
			6d	1.83	92.4	Red brown solid, suspension after 10 minutes at 25°C
			7d	1.73	87.4	Red brown solid, suspension after 10 minutes at 25°C
		25°C/avoid light/closed	1d	1.48	74.7	Red brown suspension
			4d	1.26	63.6	Red brown suspension with sedimentation solid at bottle
			6d	0.96	48.5	Red brown suspension with sedimentation solid at bottle
			7d	0.76	38.4	Red brown suspension with sedimentation solid at bottle

Sample s	Formulation	Condition	Time point	Conc. (mg/mL)	Compar e with initial (%)	Appearance
	HP					

Table 14. Stability test of F21 and F22

Instrument	Agilent 1290 UPLC with UV detector		
Column	XBridge BEH C18 (2.1mm×150mm, 1.7µm)		
Gradient	Time (minutes)	A%: water	B%: methanol
	0	90	10
	1	40	60
	5	15	85
	16	15	85
	16.1	90	10
	18	90	10
Injection volume	3 µL		
Flow rate	0.4 mL/min		
Column Temp.	40 °C		
Wavelength	325 nm		
Diluent	Methanol		
Concentration	0.1 mg/mL		

Table 15. Stability test of F21 and F22

Sample name	No. of injection	Criteria	Results
Blank (Diluent)	1 or more	No significant interference peak (below LOQ)	Pass
Sensitivity Solution (LOQ) 0.05 µg/mL	1	S/N $\geq$ 10	12.5
Working Standard Solution (STD) 0.1 mg/mL	5	N $\geq$ 2000	147420
		0.8 $\leq$ T $\leq$ 2.0	1.1
		Rs $\geq$ 1.2	10.9
		RSD (%) $\leq$ 2.0 (area)	0.1
		RSD (%) $\leq$ 2.0 (retention time)	0.02
Checking Standard Solution (STD-check)	1	Recovery: 98.0%-102.0%	101.2

[00260] **Table 16** illustrates solubility screening for the lipid-based formulation or emulsion in Example 6, where lutein showed better solubility in Capmul MCM and Capryol 90. **Table 17**

illustrates formulations 1-17 (F1-F17). All lipid formulations were prepared at 40°C, but F02-F10 changed to solid quickly (<2 hours). Formulations F11- F17 may be kept at a longer liquid state at room temperature (20-25°C) and was continued to dilution study. **Table 18** illustrates lipid based emulsion formulation study with retinol-d6. **Table 19** illustrates lipid based emulsion formulation study without retinol-d6. **Tables 20-22** illustrate second round of formulation screening. All lipid formulation kept red brown suspension state at room temperature (RT)(20-25°C) for 4 days, but vehicle of 18 showed tendency of solid state. **Table 23** illustrates a non-limiting example of formulation for delivering retinoid to human.

Table 16. Solubility screening

Functionality	No.	Ingredients	Solubility (mg/mL)	
			Lutein (10 mg)	
			~25°C	Note
oil	17	Oleic acid	<1.6	Undissolved
	18	Corn oil	<1.6	Undissolved
	19	Maisine cc	<1.5	Undissolved
	20	Capmul MCM	4.2-5.1	Stirred 1h
			4.9-5.3	Stirred 19h
	21	Capryol 90	3.6-4.2	Stirred 1h

Table 17. Lipid based emulsion formulation study

	Oil	Surfactant	Co-solvent	Appearance of formulation
Formulation 01	3 mL Capmul MCM	/	/	Undissolved @50°C
Formulation 02	1.6 mL Capmul MCM	1.6 mL Gelucire 48/16	/	Clear at 40°C, then precipitate/solid @RT after 0.5 hours
Formulation 03	1.6 mL Capmul MCM	1.6 mL Gelucire 48/16	0.5 mL PEG 400	Clear at 40°C, then precipitate/solid @RT after 1.5 hours
Formulation 04	1.6 mL Capmul MCM	1.6 mL Gelucire 48/16	0.5mL Transcutol HP	Clear at 40°C, then precipitate/solid @RT after 0.5 hours

	Oil	Surfactant	Co-solvent	Appearance of formulation
Formulation 05	1.6 mL Capmul MCM	2 mL Gelucire 48/16	/	Clear at 40°C, solid@RT after 1.5 hours
Formulation 06	1.6 mL Capmul MCM	2 mL TPGS	/	Clear at 40°C, solid@RT after 1.5 hours
Formulation 07	1.6 mL Capmul MCM	2 mL Gelucire 48/16	0.5 mL PEG 400	Clear at 40°C, Semi-solid @RT
Formulation 08	1.5 mL Capmul MCM	1.5 mL Gelucire 48/16	0.7 mL PEG 400	Clear at 40°C, Semi-solid @RT 0.5 hours
Formulation 09	1.5 mL Capmul MCM	1.2 mL Gelucire 48/16+0.4 mL TW80	0.7 mL PEG 400	Clear at 40°C, Semi-solid @RT 1.5 hours
Formulation 10	1.5 mL Capmul MCM	1.8 mL TPGS	0.7 mL PEG 400	Clear at 40°C, Semi-solid @RT
Formulation 11	1.5 mL Capmul MCM	1.2 mL Gelucire 44/14+0.4 mL TW80	0.7 mL PEG 400	Clear @RT 6 hours, partially solidified @RT 1 day
Formulation 12	1.8 mL Capmul MCM	0.6 mL Gelucire 48/16+1 mL TW80	0.4 mL PEG 400	Clear @RT 6 hours, solid @RT 1 day
Formulation 13	1.6 mL Capmul MCM	1.6 mL Gelucire 44/14	/	Clear @RT 6 hours, partially solidified @RT 1 day
Formulation 14	1.6 mL Capmul MCM	1.5 mL Gelucire 44/14	0.5 mL PEG 400	Clear @RT 6 hours, partially solidified @RT 1 day
Formulation 15	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14+1.5 mL TW80	0.4 mL PEG 400	Clear @RT 3 hours, partially solidified @RT 1 day
Formulation 16	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14+1.5 mL Kolliphor EL	0.4 mL PEG 400	Clear @RT 5 hours, hazy @RT 1 day, vehicle became white liquid @1 day
Formulation 17	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14+1.5 mL Kolliphor EL	0.4 mL Transcutol HP	Clear @RT 5 hours, hazy @RT 2 days, vehicle became white liquid @1 day

Table 18. Lipid based emulsion formulation study with retinol-d6

No.	Compositions (v/v)			Diluted with SGF (1:9, v/v) for 0.5 hours	pH	Further diluted with FaSSIF (1:3, v/v) for 2 hours	pH	PSD (nm)	Appearance after 5 minutes
	Oil	Surfactant	Co-solvent						
Control	3.6 mL Corn oil	/	/	Layered	1.49	Layered	5.33	N/A	N/A
F11	1.5 mL Capmul MCM	1.2 mL Gelucire 44/14 +0.4 mL Tween80	0.7 mL PEG 400	Yellow emulsion, 1 min dispersed	1.48	Yellow emulsion	5.46	D10:46.9	Yellow emulsion with little orange droplets
								D50: 152	
								D90: 284	
								PDI: 0.376	
F12	1.8 mL Capmul MCM	0.6 mL Gelucire 48/16 +1 mL Tween80	0.4 mL PEG 400	Yellow emulsion, 1 min dispersed	1.47	Yellow emulsion	5.51	D10: 108	N/A
								D50: 136;	
								D90: 175	
								PDI: 0.299	
F13	1.6 mL Capmul MCM	1.6 mL Gelucire 44/14	/	Yellow emulsion, 1 min dispersed	1.45	Yellow emulsion	5.44	D10:92.1	Yellow emulsion with little orange droplets
								D50:130	
								D90: 188	
								PDI: 0.415	
F14	1.5 mL Capmul MCM	1.5 mL Gelucire 44/14	0.5 mL PEG 400	Yellow emulsion, 1 min dispersed	1.48	Yellow emulsion	5.47	D10: 61	Yellow emulsion with little orange droplets
								D50: 97.7	
								D90: 132	
								PDI: 0.268	
F15	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5 mL Tween80	0.4 mL PEG 400	Yellow emulsion, 1 min dispersed	1.47	Yellow emulsion	5.55	D10: 89.3	N/A
								D50: 229	
								D90: 473	
								PDI: 0.345	
F16	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5 mL Kolliphor EL	0.4 mL PEG 400	Yellow emulsion, 1 min dispersed	1.47	Yellow emulsion	5.33	D10: 73.7	Yellow emulsion with little orange droplets
								D50: 131	
								D90: 253	
								PDI: 0.319	
F17		0.6 mL Gelucire		Yellow emulsion,	1.48	Yellow emulsion	5.29	D10: 56.1	N/A

	1.8 mL Capmul MCM	44/16 +1.5 mL Kolliphor EL	0.4mL transcutol HP	1 min dispersed				D50: 132	
								D90: 276	
								PDI: 0.263	

Table 19. lipid based emulsion formulation study without retinol-d6

No.	Compositions (v/v)			Diluted with SGF (1:9, v/v) for 0.5 hours	pH	Further diluted with FaSSIF (1:3, v/v) for 2h	pH	PSD (nm)	Appearance of diluted solution after 5 minutes @RT
	Oil	Surfactant	Co- solvent						
Control	3.6 mL Corn oil	/	/	Layered	1.49	Layered	5.33	N/A	N/A
F11	1.5 mL Capmul MCM	1.2 mL Gelucire 44/14 +0.4 mL Tween80	0.7 mL PEG 400	Yellow emulsion, 1 min dispersed	1.42	Yellow emulsion	5.44	D10:82	Yellow emulsion with little orange droplets
								D50: 299	
								D90: 513	
								PDI: 0.320	
F12	1.8 mL Capmul MCM	0.6 mL Gelucire 48/16 +1 mL Tween80	0.4 mL PEG 400	Yellow emulsion, 1 min dispersed	1.45	Yellow emulsion	5.53	D10 : 71.1	N/A
								D50: 284	
								D90: 568	
								PDI: 0.299	
F13	1.6 mL Capmul MCM	1.6 mL Gelucire 44/14	/	Yellow emulsion, 1 min dispersed	1.45	Yellow emulsion	4.49	D10:82.5	Yellow emulsion with little orange droplets
								D50:392	
								D90: 787	
								PDI: 0.469	
F14	1.5 mL Capmul MCM	1.5 mL Gelucire 44/14	0.5 mL PEG 400	Yellow emulsion, 1 min dispersed	1.53	Yellow emulsion	5.47	D10: 98.5	Yellow emulsion with little orange droplets
								D50: 320	
								D90: 772	
								PDI: 0.417	
F15	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5 mL Tween80	0.4 mL PEG 400	Yellow emulsion, 1 min dispersed	1.51	Nearly clear yellow solution	5.58	Cannot get accurate value	N/A
F16	1.8 mL Capmul MCM	0.6 mL Gelucire 44/14 +1.5	0.4 mL PEG 400	Yellow emulsion,	1.5	Yellow emulsion	5.58	D10: 107	Yellow emulsion with little
								D50: 399	

		mL Kolliphor EL		1 min dispersed				D90: 721 PDI: 0.327	orange droplets
F17	1.8 mL Capmul MCM	0.6 mL Gelucire 44/16 +1.5 mL Kolliphor EL	0.4 mL transcutol HP	Yellow emulsion, 1 min dispersed	1.57	Yellow emulsion	5.55	D10: 210	N/A
								D50: 426	
								D90: 1010	
								PDI: 0.328	

Table 20. Second round of formulation screening

	Oil	Surfactant	Co-solvent	Appearance of formulation
Formulation 18	300 mg EPA+110 mg DHA	0.1 mL Gelucire 44/14+ 0.3 mL Labrasol ALF	/	Red brown suspension, RT 4 days
Formulation 19	300 mg EPA+110 mg DHA	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.2 mL PEG 400	Red brown suspension, RT 4 days
Formulation 20	300 mg EPA+110 mg DHA+0.2 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	/	Red brown suspension, RT 4 days
Formulation 21	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	0.1 mL PEG 400	Red brown suspension, RT 4 days

Formulation 22	300 mg EPA+110 mg DHA+0.1 mL Capmul MCM	0.1 mL Gelucire 44/14 + 0.3 mL Kolliphor EL	0.1 mL Transcutol HP	Red brown suspension, RT 4 days
-------------------	---	--	----------------------------	---------------------------------------

Table 21. Second round of formulation screening

Function	Name	Maximum Daily Exposure form IIG (mg)
		Oral
Oil	Capmul MCM	400
Surfactant	Gelucire 44/14	7200
	Labrasol ALF	13770
	Tween 80	418.37
	Kolliphor EL	1170
Solvent	PEG 400	24000
	Transcutol	No commercial drug product

Table 22. Second round of formulation screening

Softgel	
Size	Volume (mL)
5	0.246-0.308
6	0.308-0.370
8	0.400-0.493
9.5	0.462-0.585
11	0.524-0.678
14	0.777-0.862
16	0.862-0.986
20	0.986-1.232
22	1.109-1.355

Table 23. Formulation for retinoid delivery for human

	Product A	Product B (no need for PK, for lower cost product)	Product C PK comparison arm (in corn oil)	Solubility	Stability
Deuterated Vitamin A	2.5 mg	X	2.5 mg	Soluble in EtOH, MeOH	Light sensitive, -20°C@2Y
Vitamin E	400 IU	400 IU			
Vitamin C	500 mg	500 mg			
Lutein	10 mg	10 mg		Insoluble in water, soluble in EtOH	Light sensitive, 2-8°C
Zinc	80 mg	80 mg			
EPA	300 mg	300 mg		Ethanol: ≥ 100 mg/mL, DMSO: ≥ 30 mg/mL, Insoluble in water	-20°C @3 years
DHA	110 mg	110 mg		Insoluble in water, soluble in EtOH	Hygroscopic, decomposition

Zeaxanthin	2 mg	2 mg		Insoluble in water, Soluble in ether, acetone	−20°C
Curcuminoid	50 mg	50 mg		Insoluble in water, soluble in EtOH, acetone, DMSO, Alkaline solution	2-8°C, 1 month
Black pepper	0.5 mg	0.5 mg			

[00261] **Table 24** illustrates a summary of the screening as described in Example 6. **Table 25** illustrates solubility screening with various oil. Lutein showed increased solubility in Capmul MCM and Capryol 90.

Table 24. Lipid formulation screening summary

Work content	Activity	Result
Lipid formulation screening	Solubility screening	Curcuminoid, zeaxanthin, DHA and EPA showed better solubility in Gelucire 44/14, Gelucire 48/16, PEG 400 and Transcutol HP. Lutein showed better solubility in Capmul MCM and Capryol 90. Retinol-d6 showed good mutually solubility with EPA.
	Formulation screening	In first round lipid formulation screening, F11-F17 showed better formulation appearance. F15 showed better appearance in dilution study and F12, F14, F15 and F17 showed small PDI. In 2nd round lipid formulation screening, F19-23 showed good formulation appearance. In

Work content	Activity	Result
		dilution study, F21 showed better appearance and F22 showed better PDI. Digestion study: F21 and F22 improved solubility significantly. After adding pancreatin extract solution, F21 and F22 kept higher concentration at 11.2 and 7.6 $\mu\text{g/mL}$ for 60 minutes while retinol-d6 in corn oil was 0.43 $\mu\text{g/mL}$.
	Stability study	Method development: It is difficult to evaluate the stability of the formulations by purity, and it is suggested to assess the stability of the formulation by testing the concentration of effective retinol-d6 in the formulation. (slide 20-21) Stability evaluation: F21 was stable at 2-8°C/avoid light/closed and unstable at 25°C/avoid light/closed. F22 was unstable under both 2-8°C/avoid light/closed and 25°C/avoid light/closed conditions.

Table 25. Lipid based emulsion formulation study

Functionality	No.	Ingredients	Solubility (mg/mL)	
			Lutein (10 mg)	
			~25°C	Note
oil	17	Oleic acid	<1.6	Undissolved
	18	Corn oil	<1.6	Undissolved
	19	Maisine cc	<1.5	Undissolved
	20	Capmul MCM	4.2-5.1	Stirred 1h
			4.9-5.3	Stirred 19h

	21	Capryol 90	3.6-4.2	Stirred 1h
--	----	------------	---------	------------

[00262] Table 26 illustrates a non-limiting example of an *in vivo* pharmacokinetics (PK) study, where rats were administered Product A, Product B, or Product C by oral gavage. Following the administration, blood samples were collected to measure retinol-d3 (Vitamin A-d3) levels in circulation. Fig. 9 illustrates time-course measurements of the plasma concentration of retinol-d3 for a 24-hour duration. As shown in Fig. 9, administration of retinol-d3 by Product A did not result in a decrease of the bioavailability of the retinol-d3 *in vivo*.

Table 26. Formulation for *in vivo* pharmacokinetics (PK) study

Product A	Product B	Product C
(Study Group: PO1)	(Study Group: PO2)	(Study Group: PO3)
Compound: 2.5 mg retinol-d3	Compound: 2.5 mg retinol-d3	Compound: 2.58 mg retinol-d3
Ingredients: 10 mg lutein, 2 mg Zeaxanthin and 50 mg Curcuminoid	Oils: 300 mg EPA, 0.1 mL Capmul MCM	Vehicle: 1mL corn oil
Oils: 300 mg EPA, 110 mg DHA, 0.1 mL Capmul MCM	Surfactant: 0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	
Surfactant: 0.1 mL Gelucire 44/14 + 0.3 mL Tween 80	Co-solvent: 0.1mL PEG 400	

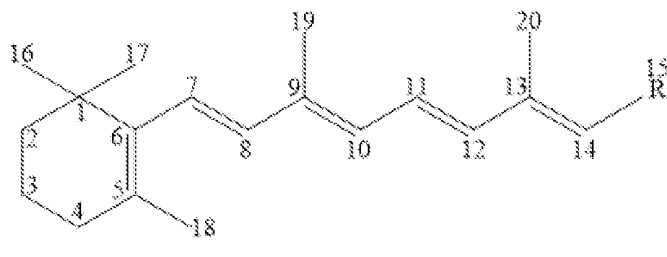
[00263] While the foregoing disclosure has been described in some detail for purposes of clarity and understanding, it will be clear to one skilled in the art from a reading of this disclosure that various changes in form and detail can be made without departing from the true scope of the disclosure. For example, all the techniques and apparatus described above can be used in various combinations. All publications, patents, patent applications, and/or other documents cited in this application are incorporated by reference in their entirety for all purposes to the same extent as if each individual publication, patent, patent application, and/or other document were individually and separately indicated to be incorporated by reference for all purposes.

CLAIMS

WHAT IS CLAIMED IS:

1. A composition comprising:

(a) a retinoid comprising a structure of Formula I:

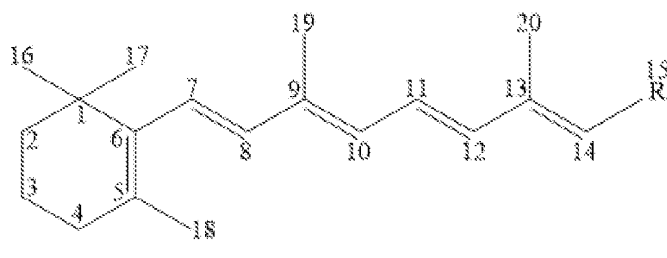


(b) a lipid excipient; and

(c) a surfactant,

wherein the retinoid is present in the composition at a percentage (w/w) of about 0.1% to about 90%.

2. The composition of claim 1, wherein the retinoid comprises a structure of Formula I:



wherein each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium.

3. The composition of claim 2, wherein the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), R₅ (COO-glucuronide), or R₆ (CH₂OCHOCH₃ or retinyl acetate).

4. The composition of claim 2, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at position 10, 12, 14, 19, 20, or a combination thereof.

5. The composition of claim 4, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 or at the position 20.

6. The composition of claim 5, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three

- hydrogens with three deuteriums (19, 19, 19-trideutero retinoid) or is at the position 20 comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid).
7. The composition of claim 6, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums and at the position 20 comprising substituting three hydrogens with three deuteriums.
8. The composition of claim 6 or 7, wherein the 19, 19, 19-trideutero retinoid comprises a 19, 19, 19-trideutero retinoid analog.
9. The composition of claim 8, wherein the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid ester.
10. The composition of claim 8, wherein the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid acetate.
11. The composition of claim 6 or 7, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog.
12. The composition of claim 11, wherein the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid ester.
13. The composition of claim 11, wherein the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid acetate.
14. The composition of claim 7, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 and at the position 20, wherein the position 19 comprises substituting three hydrogens with three deuteriums and the position 20 comprises substituting three hydrogens with three deuteriums (19, 19, 19, 20, 20, 20-hexadeutero retinoid).
15. The composition of claim 14, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog.
16. The composition of claim 15, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid ester.
17. The composition of claim 15, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid acetate.
18. The composition of any one of claims 1-17, wherein the composition comprises from about 1.0 mg to about 5.0 mg of the retinoid.
19. The composition of claim 18, wherein the composition comprises from about 2.0 mg to about 3.0 mg of the retinoid.

20. The composition of claim 19, wherein the composition comprises about 2.5 mg of the retinoid.
21. The composition of claim 1, wherein the lipid excipient comprises an omega-3 fatty acid.
22. The composition of claim 21, wherein the omega-3 fatty acid comprises eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA).
23. The composition of claim 21, wherein the omega-3 fatty acid comprises EPA and DHA.
24. The composition of claim 22 or 23, wherein the composition comprises from about 100 mg to about 500 mg of the EPA.
25. The composition of claim 24, wherein the composition comprises from about 200 mg to about 400 mg of the EPA.
26. The composition of claim 25, wherein the composition comprises about 300 mg of the EPA.
27. The composition of any one of claims 22-26, wherein the composition comprises from about 50 mg to about 200 mg of the DHA.
28. The composition of claim 27, wherein the composition comprises from about 100 mg to about 150 mg of the DHA.
29. The composition of claim 28, wherein the composition comprises about 110 mg of the DHA.
30. The composition of any one of claims 1-29, wherein the composition comprises at least one additional ingredient.
31. The composition of claim 30, wherein the at least one additional ingredient comprises an antioxidant.
32. The composition of claim 31, wherein the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract.
33. The composition of claim 31, wherein the at least one additional ingredient comprises a turmeric compound.
34. The composition of claim 33, wherein the at least one additional ingredient comprises a curcuminoid.
35. The composition of claim 34, wherein the composition comprises from about 20 mg to about 100 mg of the curcuminoid.
36. The composition of claim 35, wherein the composition comprises about 50 mg of the curcuminoid.
37. The composition of claim 30, wherein the at least one additional ingredient comprises a carotenoid.
38. The composition of claim 37, wherein the carotenoid comprises lutein, zeaxanthin, or astaxanthin.

39. The composition of claim 38, wherein the carotenoid comprises lutein and zeaxanthin.
40. The composition of claim 38, wherein the composition comprises from about 1 mg to about 100 mg of the lutein.
41. The composition of claim 38, wherein the composition comprises about 10 mg of the lutein.
42. The composition of claim 38, wherein the composition comprises from about 1 mg to about 10 mg of the zeaxanthin.
43. The composition of claim 42, wherein the composition comprises about 2 mg of the zeaxanthin.
44. The composition of claim 30, wherein the at least one additional ingredient comprises a flavonoid.
45. The composition of claim 44, wherein the flavonoid comprises anthocyanin.
46. The composition of claim 30, wherein the at least one additional ingredient comprises an amino acid.
47. The composition of claim 46, wherein the amino acid comprises taurine.
48. The composition of claim 30, wherein the at least one additional ingredient comprises an emulsifier.
49. The composition of any one of claims 1-48, wherein the surfactant comprises Tween, Kolliphor, Labrasol, Gelucire, Capmul, polyethylene glycol (PEG), Transcutol, Capryol, or a combination thereof.
50. The composition of claim 49, wherein the surfactant consists of the Gelucire, the Capmul, the Tween, and the PEG.
51. The composition of claim 49 or 50, wherein the Gelucire comprises Gelucire 44/14.
52. The composition of any one of claims 49-51, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Gelucire.
53. The composition of claim 52, wherein the composition comprises about 0.1 mL of the Gelucire.
54. The composition of claim 49 or 50, wherein the Capmul comprises Capmul MCM.
55. The composition of any one of claims 49, 50, or 54, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Capmul.
56. The composition of claim 55, wherein the composition comprises about 0.1 mL of the Capmul.
57. The composition of claim 49 or 50, wherein the Tween comprises Tween 80.
58. The composition of any one of claims 49, 50, or 57, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Tween.

59. The composition of claim 58, wherein the composition comprises about 0.3 mL of the Tween.
60. The composition of claim 49 or 50, wherein the PEG comprises PEG 400.
61. The composition of any one of claims 49, 50, or 60, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the PEG.
62. The composition of claim 61, wherein the composition comprises about 0.1 mL of the PEG.
63. The composition of claim 49, wherein the Kolliphor comprises Kolliphor EL.
64. The composition of claim 49 or 63, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Kolliphor.
65. The composition of claim 64, wherein the composition comprises about 0.3 mL of the Kolliphor.
66. The composition of claim 49, wherein the Transcutol comprises Transcutol HP.
67. The composition of claim 49 or 66, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Transcutol.
68. The composition of claim 67, wherein the composition comprises about 0.1 mL of the Transcutol.
69. The composition of any one of claims 1-68, wherein the composition is formulated as a semi-solid.
70. The composition of any one of claims 1-68, wherein the composition is formulated as a softgel capsule.
71. The composition of any one of claims 1-68, wherein the composition is formulated as a solid dispersion.
72. The composition of any one of claims 1-68, wherein the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.
73. The composition of any one of claims 1-72, wherein the composition is formulated for an eye administration of a subject.
74. The composition of claim 73, wherein the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject.
75. The composition of any one of claims 1-74, wherein the composition modulates gene expression of a retinal pigment epithelial (RPE) cell.
76. The composition of claim 75, wherein the composition increases a bioavailability of the retinoid delivered to the RPE cell.

77. The composition of claim 76, wherein the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant.

78. The composition of any one of claims 1-77, wherein the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject.

79. The composition of claim 78, wherein the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject.

80. The composition of any one of claims 1-75, wherein the composition does not decrease a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject.

81. The composition of claim 80, wherein the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject.

82. The composition of any one of claims 1-81, wherein the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant.

83. The composition of claim 82, wherein the stability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant.

84. The composition of any one of claims 1-83, wherein the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant.

85. The composition of claim 84, wherein the solubility is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant.

86. The composition of any one of claims 1-85, wherein the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%.

87. The composition of claim 86, wherein the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%.

88. The composition of any one of claims 1-87, further comprising an oil.

89. The composition of claim 84, wherein the oil comprises corn oil, oleic acid, Maisine cc, or a combination thereof.

90. A method for treating an eye disease or condition in a subject, the method comprising administering a composition comprising:

98. The method of claim 97, wherein the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid ester.
99. The method of claim 97, wherein the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid acetate.
100. The method of claim 95 or 96, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog.
101. The method of claim 100, wherein the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid ester.
102. The method of claim 100, wherein the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid acetate.
103. The method of claim 96, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 and at the position 20, wherein the position 19 comprises substituting three hydrogens with three deuteriums and the position 20 comprises substituting three hydrogens with three deuteriums (19, 19, 19, 20, 20, 20-hexadeutero retinoid).
104. The method of claim 103, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog.
105. The method of claim 104, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid ester.
106. The method of claim 104, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid acetate.
107. The method of any one of claims 90-106, wherein the composition comprises from about 1.0 mg to about 5.0 mg of the retinoid.
108. The method of claim 107, wherein the composition comprises from about 2.0 mg to about 3.0 mg of the retinoid.
109. The method of claim 108, wherein the composition comprises about 2.5 mg of the retinoid.
110. The method of claim 90, wherein the lipid excipient comprises an omega-3 fatty acid.
111. The method of claim 110, wherein the omega-3 fatty acid comprises eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA).
112. The method of claim 110, wherein the omega-3 fatty acid comprises EPA and DHA.
113. The method of claim 111 or 112, wherein the composition comprises from about 100 mg to about 500 mg of the EPA.
114. The method of claim 113, wherein the composition comprises from about 200 mg to about 400 mg of the EPA.

115. The method of claim 114, wherein the composition comprises about 300 mg of the EPA.
116. The method of any one of claims 111-115, wherein the composition comprises from about 50 mg to about 200 mg of the DHA.
117. The method of claim 116, wherein the composition comprises from about 100 mg to about 150 mg of the DHA.
118. The method of claim 117, wherein the composition comprises about 110 mg of the DHA.
119. The method of any one of claims 90-118, wherein the composition comprises at least one additional ingredient.
120. The method of claim 119, wherein the at least one additional ingredient comprises an antioxidant.
121. The method of claim 120, wherein the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract.
122. The method of claim 119, wherein the at least one additional ingredient comprises a turmeric compound.
123. The method of claim 120, wherein the at least one additional ingredient comprises a curcuminoid.
124. The method of claim 123, wherein the composition comprises from about 20 mg to about 100 mg of the curcuminoid.
125. The method of claim 124, wherein the composition comprises about 50 mg of the curcuminoid.
126. The method of claim 119, wherein the at least one additional ingredient comprises a carotenoid.
127. The method of claim 126, wherein the carotenoid comprises lutein, zeaxanthin, or astaxanthin.
128. The method of claim 127, wherein the carotenoid comprises lutein and zeaxanthin.
129. The method of claim 127, wherein the composition comprises from about 1 mg to about 100 mg of the lutein.
130. The method of claim 127, wherein the composition comprises about 10 mg of the lutein.
131. The method of claim 127, wherein the composition comprises from about 1 mg to about 10 mg of the zeaxanthin.
132. The method of claim 131, wherein the composition comprises about 2 mg of the zeaxanthin.
133. The method of claim 119, wherein the at least one additional ingredient comprises a flavonoid.
134. The method of claim 133, wherein the flavonoid comprises anthocyanin.

135. The method of claim 119, wherein the at least one additional ingredient comprises an amino acid.
136. The method of claim 135, wherein the amino acid comprises taurine.
137. The method of claim 119, wherein the at least one additional ingredient comprises an emulsifier.
138. The method of any one of claims 90-137, wherein the surfactant comprises Tween, Kolliphor, Labrasol, Gelucire, Capmul, polyethylene glycol (PEG), Transcutol, Capryol, or a combination thereof.
139. The method of claim 138, wherein the surfactant consists of the Gelucire, the Capmul, the Tween, and the PEG.
140. The method of claim 138 or 139, wherein the Gelucire comprises Gelucire 44/14.
141. The method of any one of claims 138-140, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Gelucire.
142. The method of claim 114, wherein the composition comprises about 0.1 mL of the Gelucire.
143. The method of claim 138 or 139, wherein the Capmul comprises Capmul MCM.
144. The method of any one of claims 138, 139, or 143, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Capmul.
145. The method of claim 144, wherein the composition comprises about 0.1 mL of the Capmul.
146. The method of claim 138 or 139, wherein the Tween comprises Tween 80.
147. The method of any one of claims 138, 139, or 146, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Tween.
148. The method of claim 147, wherein the composition comprises about 0.3 mL of the Tween.
149. The method of claim 142 or 143, wherein the PEG comprises PEG 400.
150. The method of any one of claims 138, 139, or 149, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the PEG.
151. The method of claim 150, wherein the composition comprises about 0.1 mL of the PEG.
152. The method of claim 138, wherein the Kolliphor comprises Kolliphor EL.
153. The method of any one of claims 138 or 152, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Kolliphor.
154. The method of claim 153, wherein the composition comprises about 0.3 mL of the Kolliphor.
155. The method of claim 138, wherein the Transcutol comprises Transcutol HP.
156. The method of claim 138 or 155, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Transcutol.

157. The method of claim 156, wherein the composition comprises about 0.1 mL of the Transcutol.
158. The method of any one of claims 90-157, wherein the composition is formulated as a semi-solid.
159. The method of any one of claims 90-157, wherein the composition is formulated as a softgel capsule.
160. The method of any one of claims 90-157, wherein the composition is formulated as a solid dispersion.
161. The method of any one of claims 90-157, wherein the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.
162. The method of any one of claims 90-161, wherein the composition is formulated for an eye administration of a subject.
163. The method of claim 162, wherein the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject.
164. The method of any one of claims 90-163, wherein the composition modulates gene expression of a retinal pigment epithelial (RPE) cell.
165. The method of claim 164, wherein the composition increases a bioavailability of the retinoid delivered to the RPE cell.
166. The method of claim 165, wherein the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant.
167. The method of any one of claims 90-166, wherein the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject.
168. The method of claim 167, wherein the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject.
169. The method of any one of claims 90-165, wherein the composition does not decrease a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject.
170. The method of claim 169, wherein the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject.
171. The method of any one of claims 90-170, wherein the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant.

172. The method of claim 171, wherein the stability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant.

173. The method of any one of claims 90-172, wherein the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant.

174. The method of claim 173, wherein the solubility is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant.

175. The method of any one of claims 90-174, wherein the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%.

176. The method of claim 175, wherein the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%.

177. The method of any one of claims 90-176, wherein the composition further comprises an oil.

178. The method of claim 177, wherein the oil comprises corn oil, oleic acid, Maisine cc, or a combination thereof.

179. The method of any one of claims claim 90-178, wherein the eye disease or condition is associated with accumulation of N-retinylidene-N-retinylethanolamine (A2E).

180. The method of claim 161, further comprising decreasing the accumulation of A2E in the subject.

181. The method of any one of claims 90-180, wherein the eye disease or condition is associated with a retinal pigment epithelial (RPE) cell.

182. The method of claim 181, further comprising modulating gene expression of the RPE cell.

183. The method of claim 182, wherein the gene expression comprises expression of ATP-binding cassette, sub-family A (ABC1), member 4 (ABCA4), elongation of very long chain fatty acids protein 4 (ELOVL4), or a combination thereof.

184. The method of any one of claims 90-183, wherein the eye disease or condition is macular degeneration.

185. The method of claim 184, wherein the macular degeneration comprises age-related macular degeneration (AMD), bestrophinopathies, bull's eye maculopathy, central serous retinopathy, Charles Bonnet syndrome (CBS), cone dystrophy, Doyne honeycomb dystrophy, diabetic macular oedema (DMO), macular hole, macular oedema, myopic macular degeneration, pattern dystrophy, pseudoxanthoma elasticum (PXE), punctate inner choroidopathy (PIC), retinal vein

occlusion (RVO), Sorsby fundus dystrophy, Stargardt disease, geographic atrophy, or a combination thereof.

186. The method of claim 185, wherein the AMD comprises dry AMD.

187. The method of claim 185, wherein the AMD comprises early AMD.

188. The method of claim 185, wherein the AMD comprises wet AMD.

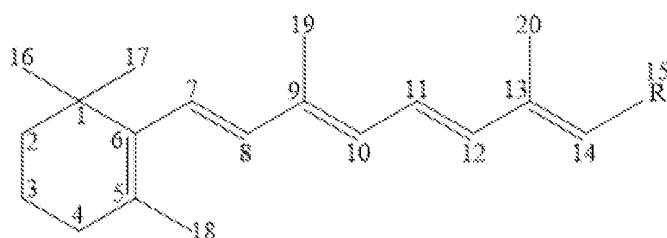
189. Use of a composition, comprising contacting a subject with the composition, the composition comprising:

- (a) a retinoid;
- (b) a lipid excipient; and
- (c) a surfactant,

wherein the lipid excipient increases a bioavailability of the retinoid in the subject by at least 10% compared to a second bioavailability of the retinoid formulated with an excipient that is different from the lipid excipient, and

wherein the use is a non-medical use.

190. The use of claim 189, wherein the retinoid comprises a structure of Formula I:



wherein each of numbers 1 through 20 denotes a position of a carbon covalently linked to at least one hydrogen, wherein at least one hydrogen is substituted with at least one deuterium.

191. The use of claim 190, wherein the R comprises R₁ (CH₂OH or retinol), R₂ (CH₂O-fatty acid or retinyl ester), R₃ (CHO or retinal), R₄ (COOH or retinoic acid), or R₅ (COO-glucuronide).

192. The use of claim 191, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 10, 12, 14, 19, 20, or a combination thereof.

193. The use of claim 192, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 or at the position 20.

194. The use of claim 193, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums (19, 19, 19-trideutero retinoid) or is at the position 20 comprising substituting three hydrogens with three deuteriums (20, 20, 20-trideutero retinoid).

195. The use of claim 194, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 comprising substituting three hydrogens with three deuteriums; and at the position 20 comprising substituting three hydrogens with three deuteriums.
196. The use of claim 194 or 195, wherein the 19, 19, 19-trideutero retinoid comprises a 19, 19, 19-trideutero retinoid analog.
197. The use of claim 196, wherein the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid ester.
198. The use of claim 196, wherein the 19, 19, 19-trideutero retinoid analog comprises a 19, 19, 19-trideutero retinoid acetate.
199. The use of claim 194 or 195, wherein the 20, 20, 20-trideutero retinoid comprises a 20, 20, 20-trideutero retinoid analog.
200. The use of claim 199, wherein the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid ester.
201. The use of claim 199, wherein the 20, 20, 20-trideutero retinoid analog comprises a 20, 20, 20-trideutero retinoid acetate.
202. The use of claim 195, wherein the position of the carbon for substituting the at least one hydrogen with the at least one deuterium is at the position 19 and at the position 20, wherein the position 19 comprises substituting three hydrogens with three deuteriums and the position 20 comprises substituting three hydrogens with three deuteriums (19, 19, 19, 20, 20, 20-hexadeutero retinoid).
203. The use of claim 202, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog.
204. The use of claim 203, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid ester.
205. The use of claim 203, wherein the 19, 19, 19, 20, 20, 20-hexadeutero retinoid analog comprises a 19, 19, 19, 20, 20, 20-hexadeutero retinoid acetate.
206. The use of any one of claims 189-205, wherein the composition comprises from about 1.0 mg to about 5.0 mg of the retinoid.
207. The use of claim 206, wherein the composition comprises from about 2.0 mg to about 3.0 mg of the retinoid.
208. The use of claim 207, wherein the composition comprises about 2.5 mg of the retinoid.
209. The use of claim 189, wherein the lipid excipient comprises an omega-3 fatty acid.
210. The use of claim 209, wherein the omega-3 fatty acid comprises EPA or DHA.

211. The use of claim 210, wherein the omega-3 fatty acid comprises EPA and DHA.
212. The use of claim 209 or 210, wherein the composition comprises from about 100 mg to about 500 mg of the EPA.
213. The use of claim 212, wherein the composition comprises from about 200 mg to about 400 mg of the EPA.
214. The use of claim 213, wherein the composition comprises about 300 mg of the EPA.
215. The use of any one of claims 210-214, wherein the composition comprises from about 50 mg to about 200 mg of the DHA.
216. The use of claim 215, wherein the composition comprises from about 100 mg to about 150 mg of the DHA.
217. The use of claim 216, wherein the composition comprises about 110 mg of the DHA.
218. The use of any one of claims 189-217, wherein the composition comprises at least one additional ingredient.
219. The use of claim 218, wherein the at least one additional ingredient comprises an antioxidant.
220. The use of claim 219, wherein the antioxidant comprises vitamin C, vitamin E, zinc, or grape seed extract.
221. The use of claim 218, wherein the at least one additional ingredient comprises a turmeric compound.
222. The use of claim 218, wherein the at least one additional ingredient comprises a curcuminoid.
223. The use of claim 222, wherein the composition comprises from about 20 mg to about 100 mg of the curcuminoid.
224. The use of claim 223, wherein the composition comprises about 50 mg of the curcuminoid.
225. The use of claim 218, wherein the at least one additional ingredient comprises a carotenoid.
226. The use of claim 225, wherein the carotenoid comprises lutein, zeaxanthin, or astaxanthin.
227. The use of claim 226, wherein the composition comprises from about 1 mg to about 100 mg of the lutein.
228. The use of claim 227, wherein the composition comprises about 10 mg of the lutein.
229. The use of claim 226, wherein the composition comprises from about 1 mg to about 10 mg of the zeaxanthin.
230. The use of claim 229, wherein the composition comprises about 2 mg of the zeaxanthin.
231. The use of claim 218, wherein the at least one additional ingredient comprises a flavonoid.
232. The use of claim 231, wherein the flavonoid comprises anthocyanin.

233. The use of claim 218, wherein the at least one additional ingredient comprises an amino acid.
234. The use of claim 233, wherein the amino acid comprises taurine.
235. The use of claim 218, wherein the at least one additional ingredient comprises an emulsifier.
236. The use of any one of claims 189-235, wherein the surfactant comprises Tween, Kolliphor, Labrasol, Gelucire, Capmul, PEG, Transcutol, Capryol, or a combination thereof.
237. The use of claim 236, wherein the surfactant consists of the Gelucire, the Capmul, the Tween, and the PEG.
238. The use of claim 236 or 237, wherein the Gelucire comprises Gelucire 44/14.
239. The use of any one of claims 236-238, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Gelucire.
240. The use of claim 239, wherein the composition comprises about 0.1 mL of the Gelucire.
241. The use of claim 236 or 237, wherein the Capmul comprises Capmul MCM.
242. The use of any one of claims 236, 237, or 241, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Capmul.
243. The use of claim 242, wherein the composition comprises about 0.1 mL of the Capmul.
244. The use of claim 236 or 237, wherein the Tween comprises Tween 80.
245. The use of any one of claims 236, 237, or 244, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Tween.
246. The use of claim 245, wherein the composition comprises about 0.3 mL of the Tween.
247. The use of claim 236 or 237, wherein the PEG comprises PEG 400.
248. The use of any one of claims 236, 237, or 247, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the PEG.
249. The use of claim 248, wherein the composition comprises about 0.1 mL of the PEG.
250. The use of claim 236, wherein the Kolliphor comprises Kolliphor EL.
251. The use of claim 236 or 250, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Kolliphor.
252. The use of claim 251, wherein the composition comprises about 0.3 mL of the Kolliphor.
253. The use of claim 236, wherein the Transcutol comprises Transcutol HP.
254. The use of claim 236 or 253, wherein the composition comprises from about 0.05 mL to about 0.5 mL of the Transcutol.
255. The use of claim 254, wherein the composition comprises about 0.1 mL of the Transcutol.
256. The use of any one of claims 189-255, wherein the composition is formulated as a semi-solid.

257. The use of any one of claims 189-255, wherein the composition is formulated as a softgel capsule.
258. The use of any one of claims 189-255, wherein the composition is formulated as a solid dispersion.
259. The use of any one of claims 189-255, wherein the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.
260. The use of any one of claims 189-259, wherein the composition is formulated for an eye administration of a subject.
261. The use of claim 260, wherein the composition decreases accumulation of N-retinylidene-N-retinylethanolamine (A2E) in the subject.
262. The use of any one of claims 189-261, wherein the composition modulates gene expression of a retinal pigment epithelial (RPE) cell.
263. The use of claim 262, wherein the composition increases a bioavailability of the retinoid delivered to the RPE cell.
264. The use of claim 263, wherein the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second bioavailability of delivering the retinoid to the RPE cell without the lipid excipient or the surfactant.
265. The use of any one of claims 189-264, wherein the composition increases a stability of the retinoid compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant.
266. The use of claim 265, wherein the stability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second stability of the retinoid in a comparable composition without the lipid excipient or the surfactant.
267. The use of any one of claims 189-266, wherein the composition increases a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject.
268. The use of claim 267, wherein the bioavailability is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to the second bioavailability in the subject.
269. The use of any one of claims 189-265, wherein the composition does not decrease a bioavailability of the retinoid in a subject compared to a second bioavailability of the retinoid in a comparable composition without the lipid excipient or the surfactant in the subject.
270. The use of claim 269, wherein the bioavailability and the second bioavailability are determined by plasma concentration of the retinoid obtained from the subject.

271. The use of any one of claims 189-270, wherein the composition increases a solubility of the retinoid compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant.
272. The use of claim 271, wherein the solubility is increased by at least 10%, at least 50%, at least 100%, or at least 500% compared to a second solubility of the retinoid in a comparable composition without the lipid excipient or the surfactant.
273. The use of any one of claims 189-272, wherein the retinoid is present in the composition at the percentage (w/w) of about 0.5% to about 90%.
274. The use of claim 273, wherein the retinoid is present in the composition at the percentage (w/w) of about 1% to about 50%.
275. The use of any one of claims 189-274, wherein the composition comprises an oil.
276. The use of claim 275, wherein the oil comprises corn oil, oleic acid, Maisine cc, or a combination thereof.
277. The use of any one of claims 189-276, wherein the use is an aesthetic use.
278. The use of any one of claims 189-276, wherein the use is a cosmetic use.
279. The use of any one of claims 189-276, wherein the use is a supplement use.
280. The use of any one of claims 189-276, wherein the use does not treat a disease or condition.
281. The use of any one of claims 189-276, wherein the composition is formulated for transdermal delivery of the retinoid to the subject.
282. The use of any one of claims 189-281, wherein the composition is formulated as a semi-solid.
283. The use of any one of claims 189-281, wherein the composition is formulated as a softgel capsule.
284. The use of any one of claims 189-281, wherein the composition is formulated as a solid dispersion.
285. The use of any one of claims 189-284, wherein the composition is formulated as a lipid nanoparticle, an amorphous solid dispersion, a lipid polymer, or a combination thereof.
286. The use of any one of claims 189-285, wherein the composition is formulated as a supplement.