degradation by oxidation and hydrolysis. U.S. Patent Publication Nos. 2007/0265341, 2008/0153909 and 2010/0305045, for example, teach certain omega-3 oil containing compositions, but do not address this stability issue. U.S. 2007/0265341 teaches the use of vitamin E as an antioxidant, but vitamin E is not effective in preserving omega-3 oils as described herein. Thus, there is a need for stable ophthalmic compositions containing omega-3 oils.

## SUMMARY

[0005] Provided herein are stabilized ophthalmic compositions containing omega-3 oils and one or more antioxidants. Specifically, the antioxidants are selected from butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), alone or in combination. These compositions may be used, among other things, as artificial tears and as ophthalmic compositions to diagnose, treat, or prevent keratoconjunctivitis or dry eye syndrome in a human or other mammal in need of such diagnosis, treatment, or prevention.

[0005a] In one aspect, there is provided an ophthalmic composition comprising one or more omega-3 oils; one or more antioxidants selected from butylated hydroxytoluene and butylated hydroxyanisole; one or more hydrogels; one or more tonicity agents; one or more surfactants; and an acrylates/C10-30 alkyl acrylate crosspolymer; and wherein the ophthalmic composition does not include an antimicrobial preservative.

[0005b] In one aspect, there is provided an ophthalmic composition comprising 0.1% to 1% w/w flaxseed oil; 0.1% to 1% w/w castor oil; 0.001% to 0.05% w/w butylated hydroxytoluene; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.1% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 0.5% to 3% w/w trehalose; 0.1% to 2% w/w boric acid; 0.1% to 2% w/w polysorbate 80; 0.1% to 2% w/w polyoxyethylene 40 stearate; 0.05% to 1% w/w acrylates/C10-30 alkyl acrylate crosspolymer; and water; and wherein the composition does not include an antimicrobial preservative, or preferably the composition comprises 0.1% to 0.5% w/w flaxseed oil; 0.1% to 0.5% w/w castor oil; 0.005% to 0.02% w/w butylated hydroxytoluene; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to

0.5% w/w carnitine; 0.5% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 1% to 2% w/w trehalose; 0.25% to 1% w/w boric acid; 0.25% to 1% w/w polysorbate 80; 0.1% to 1% w/w polyoxyethylene 40 stearate; and 0.05% to 0.25% w/w acrylates/C10-30 alkyl acrylate crosspolymer or preferably the composition comprises 0.1% to 0.25% w/w flaxseed oil; 0.1% to 0.25% w/w castor oil; 0.02% w/w butylated hydroxytoluene; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.5% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 1% to 2% w/w trehalose; 0.25% to 1% w/w boric acid; 0.25% to 1% w/w polysorbate 80; 0.1% to 1% w/w polyoxyethylene 40 stearate; and 0.05% to 0.25% w/w acrylates/C10-30 alkyl acrylate crosspolymer.

[0005c] In ophthalmic composition comprising 0.1% to 1% w/w flaxseed oil; 0.1% to 1% w/w castor oil; 0.001% to 0.05% w/w butylated hydroxytoluene; 0.001% to 0.05% w/w butylated hydroxyanisole; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.1% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 0.5% to 3% w/w trehalose; 0.1% to 2% w/w boric acid; 0.1% to 2% w/w polysorbate 80; 0.1% to 2% w/w polyoxyethylene 40 stearate; 0.1% to 1% w/w acrylates/C10-30 alkyl acrylate crosspolymer; and water; and wherein the composition does not include an antimicrobial preservative.

[0005d] In one aspect, there is provided a use of an effective amount of an ophthalmic composition as described herein, in the manufacture of a medicament for treating *keratoconjunctivitis sicca* or dry eye syndrome in a human or other mammal.

## BRIEF DESCRIPTION OF THE FIGURES

[0006] **FIG. 1** shows the improved chemical stability of omega-3 oils in emulsions containing BHA and BHT, as compared to emulsions containing omega-3 oil without BHA/BHT.

[0007] **FIG. 2** shows flaxseed oil emulsion formulation stability over time.

[0008] **FIG. 3** shows *in vivo* tolerability results of omega-3 oil emulsions.

What is claimed is:

1. An ophthalmic composition comprising one or more omega-3 oils; one or more antioxidants selected from butylated hydroxytoluene and butylated hydroxyanisole; one or more hydrogels; one or more tonicity agents; one or more surfactants; and an acrylates/C10-30 alkyl acrylate crosspolymer; and wherein the ophthalmic composition does not include an antimicrobial preservative.

2. The ophthalmic composition of claim 1, wherein the composition does not include butylated hydroxyanisole.

3. The ophthalmic composition of claim 1 or 2, wherein the omega-3 oil is selected from the group consisting of flaxseed oil, chia oil, kiwifruit oil, perilla oil, lingonberry oil, camelina oil, purslane oil, black raspberry oil, cod liver oil, salmon oil, anchovy oil and tuna oil.

4. The ophthalmic composition of claim 1 or 2, wherein the omega-3 oil is flaxseed oil, whereby the flaxseed oil is preferably present at a concentration of 0.1% or 1% w/w.

5. The ophthalmic composition of any one of claims 1-4, wherein the composition further comprises castor oil, which is preferably present at a concentration of 0.1% or 1% w/w.

6. The ophthalmic composition of any one of claims 1-5, wherein the hydrogel is carboxymethyl cellulose or a salt thereof.

7. The ophthalmic composition of any one of claims 1-6, wherein the one or more tonicity agents are selected from carnitine, glycerin, erythritol and trehalose.

8. The ophthalmic composition of any one of claims 1-7, wherein the one or more surfactants are selected from polysorbate 80, polyoxyethylene 40 stearate, and polyethylene glycol (15)-hydroxystearate.

9. The ophthalmic composition of claim 8, wherein the surfactant is polysorbate 80 and/or polyoxyethylene 40 stearate.

10. The ophthalmic composition of claim 8, wherein the surfactants are polyethylene glycol (15)-hydroxystearate and polyoxyethylene 40 stearate.

11. The ophthalmic composition of any one of claims 1-10, wherein the ophthalmic composition further comprises a buffer such as boric acid.

12. An ophthalmic composition comprising 0.1% to 1% w/w flaxseed oil; 0.1% to 1% w/w castor oil; 0.001% to 0.05% w/w butylated hydroxytoluene; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.1% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 0.5% to 3% w/w trehalose; 0.1% to 2% w/w boric acid; 0.1% to 2% w/w polysorbate 80; 0.1% to 2% w/w polyoxyethylene 40 stearate; 0.05% to 1% w/w acrylates/C10-30 alkyl acrylate crosspolymer; and water; and wherein the composition does not include an antimicrobial preservative, or preferably the composition comprises 0.1% to 0.5% w/w flaxseed oil; 0.1% to 0.5% w/w castor oil; 0.005% to 0.02% w/w butylated hydroxytoluene; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.5% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 1% to 2% w/w trehalose; 0.25% to 1% w/w boric acid; 0.25% to 1% w/w polysorbate 80; 0.1% to 1% w/w polyoxyethylene 40 stearate; and 0.05% to 0.25% w/w acrylates/C10-30 alkyl acrylate crosspolymer or preferably the composition comprises 0.1% to 0.25% w/w flaxseed oil; 0.1% to 0.25% w/w castor oil; 0.02% w/w butylated hydroxytoluene; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.5% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 1% to 2% w/w trehalose; 0.25% to 1% w/w boric acid; 0.25% to 1% w/w polysorbate 80; 0.1% to 1% w/w polyoxyethylene 40 stearate; and 0.05% to 0.25% w/w acrylates/C10-30 alkyl acrylate crosspolymer.

13. An ophthalmic composition comprising 0.1% to 1% w/w flaxseed oil; 0.1% to 1% w/w castor oil; 0.001% to 0.05% w/w butylated hydroxytoluene; 0.001% to 0.05% w/w butylated hydroxyanisole; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.1% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 0.5% to 3% w/w trehalose; 0.1% to 2% w/w boric acid; 0.1% to 2% w/w polysorbate 80; 0.1% to 2% w/w polyoxyethylene 40 stearate; 0.1% to 1% w/w acrylates/C10-30 alkyl acrylate

crosspolymer; and water; and wherein the composition does not include an antimicrobial preservative.

14. The ophthalmic composition of claim 11, wherein the composition comprises 0.1% to 0.5% w/w flaxseed oil; 0.1% to 0.5% w/w castor oil; 0.005% to 0.02% w/w butylated hydroxytoluene; 0.005% to 0.02% w/w butylated hydroxyanisole; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.5% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 1% to 2% w/w trehalose; 0.25% to 1% w/w boric acid; 0.25% to 1% w/w polysorbate 80; 0.1% to 1% w/w polyoxyethylene 40 stearate; and 0.05% to 0.25% w/w acrylates/C10-30 alkyl acrylate crosspolymer.

15. The ophthalmic composition of claim 11, wherein the composition comprises 0.1% to 0.25% w/w flaxseed oil; 0.1% to 0.25% w/w castor oil; 0.005% to 0.02% w/w butylated hydroxytoluene; 0.005% to 0.02% w/w butylated hydroxyanisole; 0.25% to 1% w/w sodium carboxymethyl cellulose; 0.1% to 0.5% w/w carnitine; 0.5% to 2% w/w glycerin; 0.1% to 0.5% w/w erythritol; 1% to 2% w/w trehalose; 0.25% to 1% w/w boric acid; 0.25% to 1% w/w polysorbate 80; 0.1% to 1% w/w polyoxyethylene 40 stearate; and 0.05% to 0.25% w/w acrylates/C10-30 alkyl acrylate crosspolymer.

16. Use of an ophthalmic composition according to any one of claims 1-15 in the manufacture of a medicament for *keratoconjunctivitis sicca* or dry eye syndrome in a human or other mammal.

17. The use of claim 16, wherein the amount of the ophthalmic composition is effective to reduce one or more symptoms of *keratoconjunctivitis sicca* or dry eye syndrome.