SUMMARY OF THE INVENTION

It has now been discovered novel ophthalmic compositions for treating dry eye syndrome, which may include a combination of a demulcent or film forming material and a tonicity agent. These compositions may be used to treat dry eye, or to diagnose, cure, mitigate, treat, or prevent dry eye syndrome in man or other animals. These formulations are sterile, buffered, oil and water emulsion artificial tear products formulated for the relief of ocular surface irritation and symptoms of dryness.

In a first aspect there is provided an ophthalmic composition comprising polyoxyethylene (20) sorbitan monooleate, carboxymethylcellulose sodium, glycerin, boric acid, acrylates/C10-30 alkyl acrylate crosspolymer, castor oil, erythritol, levocarnitine, sodium hydroxide, and water.

In a second aspect there is provided a use of an ophthalmic composition as disclosed herein in the manufacture of a medicament for treating, diagnosing, curing, mitigating or preventing dry eye syndrome.

These compositions are typically ophthalmically acceptable liquids. An ophthalmically acceptable liquid includes a liquid formulated that is tolerable to a patient for topical ophthalmic use. Additionally, an ophthalmically acceptable liquid could either be packaged for single use, or for multiple uses containing a preservative to prevent contamination.

For ophthalmic application, solutions or medicaments may be prepared using a physiological saline solution as a major vehicle. Ophthalmic solutions may be maintained at a comfortable pH with an appropriate buffer system. The formulations may also contain conventional, pharmaceutically acceptable preservatives, stabilizers and surfactants.

An ophthalmically acceptable liquid may include demulcents or film forming materials. Examples of demulcents may include, but are not limited to polymers such

as polyvinyl alcohol, povidone, hydroxypropyl methyl cellulose, poloxamers, carboxymethyl cellulose, hydroxyethyl cellulose, acrylates; surfactants such as polyoxyethylene (2080) sorbitan monooleate and glycerin. The amount of demulcent may vary. In some embodiments, the amount of any demulcent such as those listed above may be from about 0.1% w/w to about 2% w/w, or from about 0.3% w/w to about 0.7% w/w, or from about 0.3% w/w to about 0.5% w/w, or about 0.5% w/w.

active agent, dispersing a solid or liquid in a composition, enhancing wetting, modifying drop size, stabilizing an emulsion, or a number of other purposes. Useful surfactants include, but are not limited to, surfactants of the following classes: alcohols; amine oxides; block polymers; carboxylated alcohol or alkylphenol ethoxylates; carboxylic acids/fatty acids; ethoxylated alcohols; ethoxylated alkylphenols; ethoxylated arylphenols; ethoxylated fatty acids; ethoxylated fatty esters or oils (animal and vegetable); fatty esters; fatty acid methyl ester ethoxylates; glycerol esters; glycol esters; lanolin-based derivatives; lecithin and lecithin derivatives; lignin and lignin derivatives; methyl esters; monoglycerides and derivatives; polyethylene glycols; polymeric surfactants; propoxylated and ethoxylated fatty acids, alcohols, or alkyl phenols; protein-based surfactants; sarcosine derivatives; sorbitan derivatives; sucrose and glucose esters and derivatives. In some embodiments, the surfactant may include polyethylene glycol (15)-hydroxystearate (CAS Number 70142-34-6, available as Solutol HS 15® from BASF), polyoxyethylene-polyoxypropylene block copolymer (CAS No. 9003-11-6, available as Pluronic® F-68 from BASF), polyoxyethylene 40 stearate (POE40 stearate), polysorbate 80 or polyoxyethylene (2080) sorbitan monooleate (CAS No. 9005-65-6), sorbitansorbitane monostearate (CAS No. 1338-41-6, available as Span™ 60 from Croda International PLC), polyoxyethylenglyceroltriricinoleat 35 (CAS No. 61791-12-6, available as Cremophor EL® from BASF). The amount of surfactant may vary. In some embodiments, the amount of any surfactant such as those listed above may be from about 0.001% w/w to about 5% w/w, or from about 0.1% w/w to about 2 w/w%, or from about 0.3% to about 0.7%, or from about 0.3% w/w to about 0.5% w/w, or from about 0.1% w/w to about 1% w/w, or about 0.5% w/w.

An ophthalmically acceptable liquid may include a stabilizer. Examples of suitable stabilizers include, but are not limited to, polyvinyl alcohol, povidone, hydroxypropyl methyl cellulose, poloxamers, carboxymethyl cellulose, hydroxyethyl cellulose, and acrylates such as acrylates/C10-30 alkyl acrylate crosspolymer (e.g. Pemule™®, Pemulen™ Pemulen™ TR-2). Acrylates/C10-30 alkyl acrylate

crosspolymer is sold and is known as Pemulen™ ~~TR-2~~ TR-2. In some embodiments, the amount of

some embodiments, the amount of oil such as those listed above may be from about 0.0001% w/w to about 5% w/w, or from about 0.005% w/w to about 1 w/w %, or from about 0.01 % w/w to about 0.2 w/w %, or from about 0.05 % w/w to about 0.5% w/w, or from about 0.2% w/w to about 5% w/w, or from about 0.5% w/w to about 2% w/w, or from about 0.1 to about 0.2%, or about 0.175% w/w, or about 0.075% w/w.

Other excipients may include ~~erthyritol,~~erythritol, a carnitine, including L-carnitine (levocarnitine) or R-carnitine. In some embodiments, the amount of erythritol may be from about 0.05% to about 3 % w/w, or from about 0.1 % w/w to about 0.5 % w/w, or about 0.25% w/w.

In some embodiments, the amount of levocarnitine may be from about 0.05% to about 3 % w/w, or from about 0.1 % w/w to about 0.5 % w/w or about 0.25% ~~w/w~~w/w.

Table 1 includes a list of components that may be used in a dry eye composition.

Table 1

Ingredient	Amount
Polyoxyethylene (~~80~~20) sorbitan monooleate	omitted, or about 0.1-2%, about 0.3%-0.7%, or about 0.5% w/w
Carboxymethylcellulose sodium (low viscosity)	omitted, or about 0.1-2%, about 0.3%-0.7%, or about 0.5% w/w
Glycerin	omitted, or about 0.2-5%, about 0.5-2%, or about 1.0% w/w
Purite®	omitted, or about 0.002%-0.05%, about 0.005%-0.02%, or about 0.01% w/w
Boric Acid	omitted, or about 0.02-2%, about 0.5-0.7%, or about 0.6% w/w

A C10-30 alkyl acrylate crosspolymer	omitted, or about 0.02-0.5%, about 0.05-0.2%, or about 0.1% w/w

Castor Oil	omitted, or about 0.05-0.5%, about 0.1-0.2%, or about 0.175% w/w
Olive Oil, Super Refined (non-preserved)	omitted, or about 0.005-1%, about 0.01-0.2%, or about 0.075% w/w
Erythritol	omitted, or about 0.05-3%, about 0.1-0.5%, or about 0.25% w/w
Levocarnitine	omitted, or about 0.05-3%, about 0.1-0.5%, or about 0.25% w/w
Sodium hydroxide	omitted, or add to pH of about 7-7.5, 7.2-7.4, or about 7.3.
Water	QS 100% w/w

DETAILED DESCRIPTION OF THE INVENTION

Some embodiments of the invention comprise, or consist of, Polyoxyethylene (2080) sorbitan monooleate, carboxymethylcellulose sodium (low viscosity), glycerin, Purite®, boric acid, an acrylates/C10-30 alkyl acrylate crosspolymer (Pemulen™ TR-2), castor oil, olive oil, erythritol, levocarnitine, sodium hydroxide, and water.

Some embodiments of the invention comprise, or consist of, Polyoxyethylene (8020) sorbitan monooleate, carboxymethylcellulose sodium (low viscosity), glycerin, Purite®, boric acid, an acrylates/C10-30 alkyl acrylate crosspolymer (Pemulen™ TR-2), castor oil, erythritol, levocarnitine, sodium hydroxide, and water.

Some embodiments of the invention comprise, or consist of, Polyoxyethylene (8020) sorbitan monooleate, carboxymethylcellulose sodium (low viscosity), glycerin, boric acid, an acrylates/C10-30 alkyl acrylate crosspolymer (Pemulen™ TR-2), castor oil, erythritol, levocarnitine, sodium hydroxide, and water.

Some embodiments of the invention comprise, or consist of polyoxyethylene (2080) sorbitan monooleate, carboxymethylcellulose sodium, glycerin, boric acid,

acrylates/C10-30 alkyl acrylate crosspolymer, castor oil, erythritol, levocarnitine, sodium hydroxide, and water.

Some embodiments of the invention comprise, or consist of polyoxyethylene (2080) sorbitan monooleate, carboxymethylcellulose sodium, glycerin, boric acid, acrylates/C10-30 alkyl acrylate crosspolymer, stabilized oxychloro complexes, castor oil, erythritol, levocarnitine, sodium hydroxide, and water.

Example 1

A formulation is prepared for use as an artificial tears product according to Table 2:

Table 2

Ingredient	Amount
Polysorbate 80	0.5% w/w
Carboxymethylcellulose sodium (low viscosity)	0.5% w/w
Glycerin	1.0% w/w
Purite®	0.01% w/w
Boric Acid	0.6% w/w
Pemulen™ TR-2	0.1% w/w
Castor Oil	0.175% w/w
Olive Oil, Super Refined (non-preserved)	0.075% w/w
Erythritol	0.25% w/w
Levocarnitine	0.25% w/w
Sodium hydroxide	Add to pH 7.3
Water	QS 100% w/w

The formulation of Table 2 is administered to a person suffering from dry eye syndrome about 1-10 times per day for relief of dry eye symptoms.

Example 2

A formulation is prepared for use as an artificial tears product according to Table 3:

Table 3

Ingredient	Amount
Polysorbate 80	0.5% w/w
Carboxymethylcellulose sodium (low viscosity)	0.5% w/w
Glycerin	1.0% w/w
Purite®	0.01% w/w
Boric Acid	0.6% w/w
Pemulen™ TR-2	0.1% w/w
Castor Oil	0.25% w/w
Erythritol	0.25% w/w
Levocarnitine	0.25% w/w
Sodium hydroxide	Add to pH 7.3
Water	QS 100% w/w

The formulation of Table 3 is administered to a person suffering from dry eye syndrome about 1-10 times per day for relief of dry eye symptoms.

Some embodiments of the present invention include:

1. An ophthalmic composition comprising polyoxyethylene (20~~80~~) sorbitan monooleate, carboxymethylcellulose sodium, glycerin, boric acid, acrylates/C10-30 alkyl acrylate crosspolymer, castor oil, erythritol, levocarnitine, sodium hydroxide, and water.

2. The composition of paragraph 1, wherein the polyoxyethylene (20~~80~~) sorbitan monooleate is present at a concentration of about 0.1% w/w to about 2% w/w.

3. The composition of paragraph 1 wherein the carboxymethylcellulose sodium is present at a concentration of about ~~0.1~~0.1% w/w to about 2% w/w.

4. The composition of paragraph 1, wherein the glycerin is present at a concentration of about 0.2% w/w to about 5% w/w.

5. The composition of paragraph 1, wherein the boric acid is present at a concentration of about 0.02% to about 2% w/w.

6. The composition of paragraph 1, wherein the acrylates/C10-30 alkyl acrylate crosspolymer is present at a concentration of about 0.02% to about 0.5% w/w.

7. The composition of paragraph 1, wherein the castor oil is present at a concentration of about 0.05% to about 0.5% w/w.

8. The composition of paragraph 1, wherein the erythritol is present at a concentration of about 0.05% or about 3% w/w.

9. The composition of paragraph 1, wherein the levocarnitine is present at a concentration of about 0.05% to about 3% w/w.

10. The composition of paragraph 1, wherein the pH is about 7.3.

11. The composition of paragraph 1, comprising about 0.5% w/w polyoxyethylene (~~80~~20) sorbitan monooleate, about 0.5% w/w carboxymethylcellulose sodium, about 1.0% w/w glycerin, about 0.6% w/w boric acid, about 0.1% w/w acrylates/C10-30 alkyl acrylate crosspolymer , about 0.25% w/w castor oil, about 0.25% w/w erythritol, about 0.25% w/w levocarnitine, sodium hydroxide , a pH of about 7.3 and water.

12. A method of treating, diagnosing, curing, mitigating or preventing dry eye syndrome comprising administering an effective amount of an ophthalmic composition according to paragraph 1 to an eye of a man or other animal in need thereof.

13. The method according to paragraph 12, wherein the ophthalmic composition comprises about 0.5% w/w polyoxyethylene (~~80~~20) sorbitan monooleate, about 0.5% w/w carboxymethylcellulose sodium, about 1.0% w/w glycerin, about 0.6% w/w boric acid, about 0.1% w/w acrylates/C10-30 alkyl acrylate crosspolymer, about 0.25% w/w castor oil, about 0.25% w/w erythritol, about 0.25% w/w levocarnitine, sodium hydroxide , a pH of about 7.3 and water.

14. The composition of paragraph 1, further comprising stabilized oxychloro complexes.

15. The composition of paragraph 14, wherein the stabilized oxychloro ~~complexe~~complex is present at a concentration of about 0.002% or about 0.05% w/w.

16. The ophthalmic composition of paragraph 11, further comprising about 0.01 % w/w of stabilized oxychloro-~~complexe.~~ complex.

17. A method of treating, diagnosing, curing, mitigating or preventing dry eye syndrome comprising administering an effective amount of an ~~opthalmic~~ ophthalmic composition according to paragraph 14 to an eye of a man or other animal in need thereof.

18. The method according to paragraph 17, wherein the ophthalmic composition comprises about 0.5% w/w polyoxyethylene (~~80~~20) sorbitan monooleate, about 0.5% w/w carboxymethylcellulose sodium , about 1.0% w/w glycerin, about 0.01 % w/w of stabilized oxychloro complexes, about 0.6% w/w boric acid, about 0.1% w/w acrylates/C10-30 alkyl acrylate crosspolymer, about 0.25% w/w Castor Oil, about

What is claimed is:

1. An ophthalmic composition comprising polyoxyethylene (~~80~~20) sorbitan monooleate, carboxymethylcellulose sodium, glycerin, boric acid, acrylates/C10-30 alkyl acrylate crosspolymer, castor oil, erythritol, levocarnitine, sodium hydroxide, and water .

2. The composition of claim 1, wherein the polyoxyethylene (~~80~~20) sorbitan monooleate is present at a concentration of about 0.1% w/w to about 2% w/w.

3. The composition of claim 1 wherein the carboxymethylcellulose sodium is present at a concentration of about 0.1% w/w to about 2% w/w.

4. The composition of claim 1, wherein the glycerin is present at a concentration of about 0.2% w/w to about 5% w/w.

5. The composition of claim 1, wherein the boric acid is present at a concentration of about 0.02% to about 2% w/w.

6. The composition of claim 1, wherein the acrylates/C10-30 alkyl acrylate crosspolymer is present at a concentration of about 0.02% to about 0.5% w/w.

7. The composition of claim 1, wherein the castor oil is present at a concentration of about 0.05% to about 0.5% w/w.

8. The composition of claim 1, wherein the erythritol is present at a concentration of about 0.05% or about 3% w/w.

9. The composition of claim 1, wherein the levocarnitine is present at a concentration of about 0.05% or about 3% w/w.

10. The composition of claim 1, wherein the pH is about 7.3.

11. The composition of claim 1, comprising about 0.5% w/w polyoxyethylene (~~80~~20) sorbitan monooleate, about 0.5% w/w carboxymethylcellulose sodium, about 1.0% w/w glycerin, about 0.6% w/w boric acid, about 0.1% w/w acrylates/C10-30 alkyl acrylate crosspolymer , about 0.25% w/w castor oil, about 0.25% w/w erythritol, about 0.25% w/w levocarnitine, sodium hydroxide , a pH of about 7.3 and water.

12. ~~A method of treating, diagnosing, curing, mitigating or preventing dry eye syndrome comprising administering an effective amount~~ Use of an ophthalmic composition according to claim 1 ~~to an eye of a man or other animal in need thereof~~in the manufacture of a medicament for treating, diagnosing, curing, mitigating or preventing dry eye syndrome.

13. The ~~method~~ use according to claim 12, wherein the ~~ophthalmic composition~~ medicament comprises about 0.5% w/w polyoxyethylene (~~80~~20) sorbitan monooleate, about 0.5% w/w carboxymethylcellulose sodium, about 1.0% w/w glycerin, about 0.6% w/w boric acid, about 0.1% w/w acrylates/C10-30 alkyl acrylate crosspolymer, about 0.25% w/w castor oil, about 0.25% w/w erythritol, about 0.25% w/w levocarnitine, sodium hydroxide , a pH of about 7.3 and water.

14. The composition of claim 1, further comprising stabilized oxychloro complexes.

15. The composition of claim 14, wherein the stabilized oxychloro ~~complexe~~ complex is present at a concentration of about 0.002% or about 0.05% w/w.

16. The ophthalmic composition of claim 11, further comprising about 0.01 % w/w of stabilized oxychloro complexes.

17. ~~A method of treating, diagnosing, curing, mitigating or preventing dry eye syndrome comprising administering an effective amount~~ Use of an opthalmic

composition according to claim 14 ~~to an eye of a man or other animal in need thereof~~ in the manufacture of a medicament for treating, diagnosing, curing, mitigating or preventing dry eye syndrome.

18. The ~~method~~ use according to claim 17, wherein the ~~ophthalmic composition~~ medicament comprises about 0.5% w/w polyoxyethylene (~~80~~20) sorbitan monooleate, about 0.5% w/w carboxymethylcellulose sodium , about 1.0% w/w glycerin, about 0.01 % w/w of stabilized oxychloro complexes, about 0.6% w/w boric acid, about 0.1% w/w acrylates/C10-30 alkyl acrylate crosspolymer, about 0.25% w/w Castor Oil, about 0.25% w/w erythritol, about 0.25% w/w levocarnitine, sodium hydroxide to obtain a pH of about 7.3 and water.