properties to be effective for lubricating and protecting the cornea (dry eye patients). Alternatively or additionally, there remains a need for a method or an alternative method to produce an emulsion comprising a fine dispersion of oil droplets that is preserved with an antimicrobial compound, and particularly a process to produce a stable preserved emulsion.

Objects of the ~~Invention~~Embodiments Disclosed

It is an object of ~~at least one aspect of the present invention~~the embodiments disclosed herein to provide a process that is capable producing a stable emulsion having a small mean droplet in the presence of a mucoadhesive polymer.

It is an object of ~~at least one aspect of the present invention~~the embodiments disclosed herein to provide an emulsion which is resistant to phase separation, and particularly offering resistance to phase separation during storage at above standard temperatures and heating/cooling cycling conditions.

~~Summary of the Invention~~

The present ~~invention~~disclosure is directed to an ophthalmic emulsion that includes the following: water forming an aqueous phase; oil forming an oil phase; a hydrophilic surfactant; a hydrophobic surfactant; a charged phospholipid; borate; and a mucoadhesive polymer (e.g., a galactomannan polymer). The oil phase is in droplets within the aqueous phase and the droplets have an average or mean diameter no greater than about 1500 nanometers (nm), more typically no greater than about 1000 nm and still more typically no greater than about 500 nm. These droplets also typically have an average or mean diameter of at least 2 nm, more typically at least 10 nm and still more typically at least 100 nm. The borate and galactomannan polymer cooperatively act to form a gel upon instillation of the emulsion in an eye of an individual.

In an aspect, there is provided an ophthalmic emulsion, the emulsion comprising:

water forming an aqueous phase;

oil forming an oil phase;

a hydrophilic surfactant having an HLB value of at least 8;

a hydrophobic surfactant having an HLB value of below 8;

a charged phospholipid;

borate; and

a mucoadhesive galactomannan polymer;

wherein:

i. the oil phase is in droplets within the aqueous phase and the droplets have an average diameter that is no greater than 1000 nm, but is at least 10 nm, wherein the average diameter is corresponding to 90% of the cumulative undersize distribution by volume measured using a Microtrac S3500 Particle Size Analyzer (Software Version 10.3.1); and

ii. the borate and galactomannan polymer cooperatively act to form a gel upon instillation of the emulsion in an eye of an individual.

In a second aspect, there is provided the use of the emulsion as defined above, for use in the manufacture of a medicament for instilling into an eye of a mammal.

In a third aspect, there is provided a method of forming an emulsion as defined above, comprising

forming a first admixture by mixing the oil and the surfactants at an elevated temperature to form an oil phase admixture;

forming a second admixture by mixing the anionic phospholipid into purified water at an elevated temperature to form a water phase admixture;

mixing the oil phase admixture and the water phase admixture at an elevated temperature and subsequently homogenizing the oil phase mixture with the water phase mixture to form an initial emulsion; and

forming a third admixture by mixing the galactomannan polymer with water and adjusting pH as needed to form a galactomannan polymer slurry; and

mixing the galactomannan polymer slurry with the initial emulsion to form a polymer enhanced emulsion; and

forming a fourth admixture by mixing any combination of the following to form a salt solution: borate, polyol, preservative and any other ingredients; and

mixing the salt solution with the enhanced emulsion followed by the addition of a sufficient quantity (Q.S.) of water and pH adjustment.

Detailed Description of the Invention

The present invention is predicated upon the provision of an ophthalmic oil in water emulsion wherein the emulsion has average oil droplet size that is relatively small. The emulsion will typically be aqueous and include a substantial amount of water. The emulsion will also typically include an anionic phospholipid, a hydrophilic surfactant (high HLB) and a hydrophobic (low HLB) surfactant.