LIPOSOMIAL EYE DROPS SOLUTION AND USES THEREOF FOR THE TREATMENT OF DRY EYE SYNDROME.

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DESCRIPTION

Technical Field of the Invention

The present invention relates to ophthalmic formulations, kits and uses thereof, wherein an eye drops solution is composed of Liposomes built with non hydrogenated phospholipids containing Linseed oil, Vitamin A Palmitate, Vitamin E TPGS and in water phase Vitamin B12 and Pycnogenol.

Background of the Invention

Dry eye syndrome is caused by a chronic lack of sufficient lubrication and moisture on the surface of the eye. Consequences of dry eyes range from subtle but constant eye irritation to significant inflammation and even scarring of the front surface of the eye.

Symptoms of dry eyes and dry eye syndrome include:

- Burning sensation Itchy eyes Aching sensations Heavy eyes
- Fatigued eyes
- Sore eyes Dryness sensation
- Red eyes
- Photophobia(light sensitivity)
- Blurred vision
- Another common symptom is something called a foreign body sensation — the feeling that grit or some other object or material is "in" your eye.
- Watery eyes also can be a symptom of dry eye syndrome.

- This is because dryness on the eye's surface sometimes will over-stimulate production of the watery component of your tears as a protective mechanism.

- But this "reflex tearing" does not stay on the eye long enough to correct the underlying dry eye condition.

In addition to these symptoms, dry eyes can cause

steam sterilization (121 C for 15 minutes at 1 atm) destroys all components of liposomes.

- To achieve such result the liposomal eyes drop solution contains liposomes built with **non** hydrogenated phospholipids containing Linseed Oil and Vitamin A Palmitate and also Vitamin E TPGS that for its specific structure improves the filterability of liposomes, but this improvement it is not enough to have a satisfactory filtration procedure, at least at industrial scale, to sterilize liposomal eyes drops. Such drawback is due to Pycnogenols presence in water phase.

- To achieve such result the liposomal eyes drops solution according to the invention contains a specific and peculiar system composed of 2-Amino-2(hydroxymethyl)pro-pane-1,3-diol, that acts as salt forming agent for Pycnogenols (sparkly water soluble), and borate buffer.

- Surprisingly, said liposomal eyes drops solution exerts a shield effect against UVA UVB rays (UVA 315-400 nm - UVB 315 -280). Such unexpected property is linked primarily to liposomes (plus Vitamin E TPGS) and secondarily to Vitamin B12 and Pycnogenols in water phase.

No document of prior art, such as MARTA VICARIO-DE-LA-TORRE ET AL in "Novel Nano-Liposome Formulation for Dry Eyes with Components Similar to the Preocular Tear Film", POLYMERS, vol. 10, no. 4, 11.04.2019, page 425, and CN 1850054 A ,relating to " Vitamin A liposome artificial lacrimal eye drops", disclose an eye drops solution for use in the treatment of dry eye syndrome,

wherein said solution comprises liposomes built with non hydrogenated phospholipids containing Linseed oil, Vitamin A Palmitate, Vitamine E TPGS , and in water phase, Vitamin B12 and pycnogenols.

Summary of the Invention

- The present invention relates to ophthalmic formulations, kits and uses thereof, wherein an eye drops solution is composed of Liposomes built with non hydrogenated phospholipids containing Linseed oil, Vitamin A Palmitate, Vitamin E TPGS and in water phase Vitamin B12 and Pycnogenol.

The presence of Pycnogenols increases the antioxidant capacity in external water phase and the presence of Vitamin E TPGS increases the antioxidant effect on lipophilic phase of liposomes.

The presence of Vitamin E TPGS, inside the liposomes, combined with the presence of Pycnogenol and Vitamin B12 outside the liposomes, have a protective effect (shield) against UV A/UVB rays.

It is further object of the invention, a liposomal eyes drops solution as above described, containing a specific and peculiar system composed of 2-Amino-2(hydroxymethyl) propane-1,3-diol, that act as salt forming agent for Pycnogenol (sparkly water soluble) and borate buffer, in order to improve the filterability of liposomes and have a satisfying filtration procedure to sterilize liposomial eyes drops only by filtration at 0.2 µm, (0,2 micron) avoiding the steam sterilization that would destroy the other components and liposomes structure.

Furthermore, the presence of 2-Amino 2(hydroxymethyl) propane-1,3-diol, that acts as salt forming agent of Pycongenols, increases the protective effect of such molecules and the filterability of the solution.

Detailed Description of the Invention

We report below the different steps to reach the final solution according to the present invention.

The qualitative composition of the starting formulation is shown below.

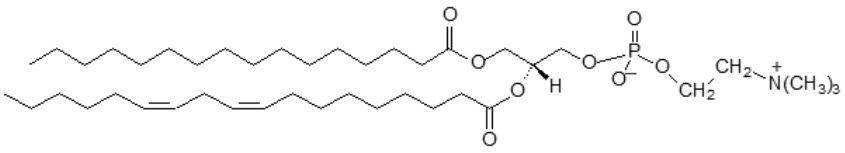
Qualitative Starting Formula

Raw Material	**CAS number**

Phospholipid S80	8030-76-0
Linseed Oil	6217-54-5
Vitamin A palmitate	79-81-2
Hyaluronic sodium salt (1.5-1.7 MDa)	-
Boric Acid	10043-35-3
Sodium Tetraborate Decahydrate	1303-96-4
Sodium Chloride	7647-14-15
Distilled Water	-

- **Description and specific function of each ingredient:**

Phospholipids



1-hexadecanoyl-2-linoleoyl-*sn*-glycero-3-phosphocholine

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- Given that the lipid layer has an important influence on the tear, understanding the structure of this portion of the tear structure is critical. This thin layer of lipid, usually 50nm to 100nm, is not a single homogeneous layer. It is believed that there is a layer of polar lipids overlying the aqueous layer of the tears, and a second layer of non-polar, hydrophobic lipids facing the air.

- It is in this layer that phospholipids play an important role to stabilize the structure

- Phospholipids are the peculiar constituents of liposomes.

Ingredients	%w/w
Phospholipid S80	0.250/**0.750**
Linseed Oil	0.025/**0.075**
Vitamin A palmitate	0.005/**0.015**
Vitamin E TPGS inside liposomes	0.0125/**0.0375**
Pycnogenol	0.0085/**0.0255**
Tris (2-Amino-2(hydroxymethyl)propane-1,3-diol	0.3-0.2/**0.4-0.3**
Vitamin B12	0.00175/**0.00525**
Hyaluronic sodium salt (1.5-1.7 MDa) outside liposomes	0.0750/**0.225**
Boric Acid	0.775
Sodium Tetraborate Decahydrate	0.0600
Sodium Chloride	0.2-0,15
Distilled Water	100
Sterilization by filtration at 0.2 micron	Yes
Ph	7,1-7.4
Osmolality mMOs/kg	275-290

6) The eye drops solution according to claim 5, wherein the composition is as follows:

Ingredients	%w/w
Phospholipid S80	0.500
Linseed Oil	0.050
Vitamin A palmitate	0.010
Pycnogenol	0.017
Tris **(2-Amino-2(hydroxymethyl)propane-1,3-diol**	0.3-0.2
Vitamin B12	0.0035
Hyaluronic sodium salt (1.5-1.7 MDa) out side liposomes	0.150
Vitamin E TPGS outside liposomes	0.025
Boric Acid	0.775
Sodium Tetraborate Decahydrate	0.060
Sodium Chloride	0.2-0,15
Distilled Water	100
Sterilization by filtration at 0.2 micron	Yes

Ph	7,1-7.4
Osmolality mMOs/kg	275 -290

- A clear and red colored solution is obtained;

Third step:

Preparation of Final Sterile Eyes Drops :

An amount "X" of liposomes solution, prepared at first step, is added to a same amount "X" of water colored solution, prepared at second step, obtaining an amount of "2X" of a final standard eyes drop solution of the formula according to claim 5, and

the final standard eye drop solution is sterilized by filtration at 0.2 micron filter.

8) The eye drops solution according to each of claims 4 and 5 for use in the treatment of Dry eye syndrome characterized in that it is used as shield against UVA/UVB rays.

9) The eye drops solution according to each of the preceding claims 1-6 for use in the treatment of Dry eye syndrome characterized in that it is used to reduce the negative effects of dry eyes syndrome.

10) The eye drops solution obtained by the process according to claim 7 for use in the treatment of Dry eye syndrome characterized in that it is used as shield against UVA/UVB rays.