WIPO
WORLD
INTELLECTUAL PROPERTY
ORGANIZATION

DOCUMENT MADE AVAILABLE UNDER THE PATENT COOPERATION TREATY (PCT)

International application number:		**PCT/IN2018/050170**
International filing date:		**26 March 2018 (26.03.2018)**
Document type:		**Certified copy of priority document**
Document details:	Country/Office:	**IN**
	Number:	**201741030659**
	Filing date:	**30 August 2017 (30.08.2017)**
Date of receipt at the International Bureau:		**11 June 2018 (11.06.2018)**

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a),(b) or (b-*bis*)

34, chemin des Colombettes
1211 Geneva 20, Switzerland
www.wipo.int

PCT/IN2018/050170

26 MAR 2018

INTELLECTUAL PROPERTY **INDIA**
पेटेंट|डिजाइन| व्यापार
चिह्न|भौगोलिक उपदर्शन

सत्यमेव जयते

भारत सरकार
GOVERNMENT OF INDIA
वाणिज्य एवं उद्योग मंत्रालय
MINISTRY OF COMMERCE & INDUSTRY
पेटेंट कार्यालय
THE PATENT OFFICE

जिस किसी से संबन्धित हो
TO WHOMSOEVER IT MAY CONCERN

मैं, अधोहस्ताक्षरी जो पेटेंट अधिनियम, 1970 की धारा 73(3) के तहत महानियंत्रक एकस्व, अभिकल्प एवं व्यापार चिह्न की ओर से प्रमाणपत्र हस्ताक्षर व जारी करने के लिए प्राधिकृत अधिकारी हूँ, एतदद्वारा यह प्रमाणित करता(ती) हूँ कि निम्नलिखित पेटेंट आवेदन के संबंध मे फाइल दस्तावेज़(जों) की सही प्रतिलिपि इसके साथ संलग्न है:

I, the undersigned, being an officer duly authorized to sign and issue the certificate on behalf of the Controller General of Patents, Designs and Trademarks in accordance with the provisions of Section 73(3) of the Patents Act, 1970, hereby certify that annexed hereto is a True Copy of the document(s) as filed in connection with the following Patent Application:

क) आवेदन संख्या/ a) Application Number: ***201741030659***

ख) फाइल करने की तारीख/ b) Date of Filing: ***30th August, 2017***

ग) अनुरोधित दस्तावेज़(जों) का नाम/ c) Name of the document(s) requested:

1) Application Form-1

2) Complete Specification filed on dated 30th August, 2017 (As per e-filing record)

यह प्रमाणपत्र पेटेंट अधिनियम, 1970 की धारा 147(1) के अधीन मुझमे निहित शक्तियों के तहत जारी किया गया है/This certificate is issued under the powers vested in me U/S 147(1) of The Patents Act, 1970.

दिनांक/ Dated this 17th day of ***May, 2018***

17/5/18

(Bimi G.B.)
नियंत्रक पेटेंट व डिजाइन/ Controller of Patents and Designs
(प्राधिकृत हस्ताक्षरी/ Authorised Signatory)

"**FORM 1** THE PATENTS ACT 1970 (39 of 1970) and THE PATENTS RULES, 2003 **APPLICATION FOR GRANT OF PATENT** (See section 7, 54 and 135 and sub-rule (1) of rule 20)	(FOR OFFICE USE ONLY)

	Application No.	
	Filing date:	
	Amount of Feepaid:	
	CBR No:	
	Signature:	

1. APPLICANT'S REFERENCE / IDENTIFICATION NO. (AS ALLOTTED BY OFFICE)	

2. TYPE OF APPLICATION [Please tick (✓) at the appropriate category]

Ordinary (✓)		Convention ( )		PCT-NP ( )	
Divisional ( )	Patent of Addition ( )	Divisional ( )	Patent of Addition ( )	Divisional ( )	Patent of Addition ( )

3A. APPLICANT(S)

Name in Full	Nationality	Country of Residence	Address of the Applicant	
Etico Life sciences Private Limited	**INDIAN**	**INDIAN**	House No.	**Plot No. 64 & 70, Flat No. 6A**
			Street	**Rohith Residency, A.S.Raju Nagar, Kukatpally**
			City	**Hyderabad**
			State	**Telangana**
			Country	**India**
			Pin code	**500072**

3B. CATEGORY OF APPLICANT [Please tick (✓) at the appropriate category]

Natural Person ()	Other than Natural Person		
	Small Entity ( )	Startup (✓)	Others ( )

4. INVENTOR(S) [Please tick (✓) at the appropriate category]

Are all the inventor(s) Same as the applicant(s) named above?	Yes ( )	No (✓)

If "No", furnish the details of the inventor(s)

Name in Full	Nationality	Country of Residence	Address of the Inventor	
DR. TATHAGATA DUTTA	**INDIAN**	**INDIAN**	House No.	**303, lotus block**
			Street	**Nagarjuna dreamlands dhulapally road, dhulapally, kompally**
			City	**Hyderabad**
			State	**Telangana**
			Country	**India**
			Pin code	**500014**

5. TITLE OF THE INVENTION: EMULSIONS FOR OPHTHALMIC DELIVERY OF ANTIOXIDANTS

6. AUTHORISED REGISTERED PATENT AGENT(S)	IN/PA No.	**975**
	Name	**BHUPATHIRAJU V.S.SR.K.RAJU**
	Mobile No.	
7. ADDRESS FOR SERVICE OF APPLICANT IN INDIA	Name	**BHUPATHIRAJU V.S.SR.K.RAJU**
	Postal Address	**D-50, Madhura Nagar**
	Telephone No.	**4023718069**
	Mobile No.	
	Fax No.	
	E-mail ID	

8. IN CASE OF APPLICATION CLAIMING PRIORITY OF APPLICATION FILED IN CONVENTION COUNTRY, PARTICULARS OF CONVENTION APPLICATION

Country	Application Number	Filing date	Name of the applicant	Title of the invention	IPC (as classified in the convention country)

9. IN CASE OF PCT NATIONAL PHASE APPLICATION, PARTICULARS OF INTERNATIONAL APPLICATION FILED UNDER PATENT CO-OPERATION TREATY (PCT)	
International application number	International filing date

10. IN CASE OF DIVISIONAL APPLICATION FILED UNDER SECTION 16, PARTICULARS OF ORIGINAL (FIRST) APPLICATION	
Original (first) application No.	Date of filing of original (first) app

11. IN CASE OF PATENT OF ADDITION FILED UNDER SECTION 54, PARTICULARS OF MAIN APPLICATION OR PATENT	
Main application/patent No.	Date of filing of main application
12. DECLARATIONS	
(i) Declaration by the inventor(s) **(In case the applicant is an assignee**: the inventor(s) may sign herein below or the applicant may upload the assignment or enclose the assignment with this application for patent or send the assignment by post/electronic transmission duly authenticated within the prescribed period). I/We, the above named inventor(s) is/are the true & first inventor(s) for this Invention and declare that the applicant(s) herein is/are my/our assignee or legal representative. (a) Date (b) Signature(s) (c) Name(s)	

(ii) Declaration by the applicant(s) in the convention country

(In case the applicant in India is different than the applicant in the convention country: the applicant in the convention country may sign herein below or applicant in India may upload the assignment from the applicant in the convention country or enclose the said assignment with this application for patent or send the assignment by post/electronic transmission duly authenticated within the prescribed period)

I/We, the applicant(s) in the convention country declare that the applicant(s) herein is/are my/our assignee or legal representative.

(a) Date

(b) Signature(s)

(c) Name(s) of the signatory

(iii) Declaration by the applicant(s)

I/We the applicant(s) hereby declare(s) that: -

☐✓ I am/ We are in possession of the above-mentioned invention.

☐✓ The provisional/complete specification relating to the invention is filed with this application.

☐ The invention as disclosed in the specification uses the biological material from India and the necessary permission from the competent authority shall be submitted by me/us before the grant of patent to me/us.

☐✓ There is no lawful ground of objection(s) to the grant of the Patent to me/us.

☐ ✓I am/we are the true & first inventor(s).

☐ I am/we are the assignee or legal representative of true & first inventor(s).

☐ The application or each of the applications, particulars of which are given in Paragraph-8, was the first application in convention country/countries in respect of my/our invention(s).

☐ I/We claim the priority from the above mentioned application(s) filed in convention country/countries and state that no application for protection in respect of the invention had been made in a convention country before that date by me/us or by any person from which I/We derive the title.

☐ My/our application in India is based on international application under Patent Cooperation Treaty (PCT) as mentioned in Paragraph-9.
☐ The application is divided out of my /our application particulars of which is given in Paragraph-10 and pray that this application may be treated as deemed to have been filed on DD/MM/YYYY under section 16 of the Act.
☐ The said invention is an improvement in or modification of the invention particulars of which are given in Paragraph-11.

13. FOLLOWING ARE THE ATTACHMENTS WITH THE APPLICATION
(a) Form 2

Item	Details	Fee	Remarks
Complete/ provisional specification)#	No. of pages(16)		
No. of Claim(s)	No. of claims(12) and No. of pages(3)		
Abstract	No. of pages(1)		
No. of Drawing(s)	No. of drawings :0 and No. of pages:0		

In case of a complete specification, if the applicant desires to adopt the drawings filed with his provisional specification as the drawings or part of the drawings for the complete specification under rule 13(4), the number of such pages filed with the provisional specification are required to be mentioned here.
b) Complete specification (in conformation with the international application)/as amended before the International Preliminary Examination Authority (IPEA), as applicable (2 copies). (c) Sequence listing in electronic form (d) Drawings (in conformation with the international application)/as amended before the International Preliminary Examination Authority (IPEA), as applicable (2 copies). (e) Priority document(s) or a request to retrieve the priority document(s) from DAS (Digital Access Service) if the applicant had already requested the office of first filing to make the priority document(s) available to DAS. (f) Translation of priority document/Specification/International Search Report/International Preliminary Report on Patentability. (g) Statement and Undertaking on Form 3 (h) Declaration of Inventorship on Form 5 (i) Power of Authority (j)..... **Total fee ₹.....in Cash/ Banker's Cheque /Bank Draft bearing No..... Date.....on ..... Bank.** I/We hereby declare that to the best of my/our knowledge, information and belief the fact and matters slated herein are correct and I/We request that a patent may be granted to me/us for the said invention. Dated this.....30th.....day of.....August.....2017..... Signature: Name: **BHUPATHIRAJU V.S.SR.K.RAJU** To, The Controller of Patents The Patent Office, at...chennai..... Note: - * Repeat boxes in case of more than one entry. * To be signed by the applicant(s) or by authorized registered patent agent otherwise where mentioned. * Tick (✓)/cross (x) whichever is applicable/not applicable in declaration in paragraph-12. * Name of the inventor and applicant should be given in full, family name in the beginning. * Strike out the portion which is/are not applicable. * For fee: See First Schedule";

FORM 2

THE PATENTS ACT, 1970

(39 of 1970)

&

THE PATENTS RULES, 2003

COMPLETE SPECIFICATION

(Section 10; Rule 13)

EMULSIONS FOR OPHTHALMIC DELIVERY OF ANTIOXIDANTS

ETICO LIFESCIENCES PRIVATE LIMITED,
1st FLOOR, INNOVATION CORRIDOR I, PHASE III,
IKP KNOWLEDGE PARK, TURKAPALLY, SHAMIRPET,
HYDERABAD-500078, TELANGANA, INDIA

AN INDIAN ENTITY

The following specification particularly describes the invention and the manner in which it is to be performed.

FIELD OF THE INVENTION

This invention relates to drug delivery dosage forms and methods to treat medical conditions of the eye. Specifically, this invention relates to emulsion drug delivery dosage forms of antioxidants for drug delivery within the eye.

BACKGROUD

Age related macular degeneration (ARMD) is a severe problem of the eye which accounts for the loss of vision of huge number of elderly population across the globe. The disease which starts as a mild innocent problem of the eye, including occasional floaters and black dots in front of the eye gradually progresses to the loss of peripheral vision to complete loss of vision.

Antioxidants are well known to slow down the progression of the ARMD disease. There are several formulations available in the market containing single or combination of antioxidants like Alpha Tocopherol, Lutein, Zeaxanthin, Beta Carotene, Selenium, etc for oral administration for slowing down the progression of the disease. There are several drawbacks with orally administered drugs or bioactives as the drug does not reach the eye at appropriate concentrations and has either none or very poor pharmacological action in the eye when administered through oral route.

Hence, there is a need for a topical formulation of antioxidants for ocular administrationthat will release the drug in a sustained manner in the eye which on repeated administration will lead to a steady concentration of antioxidants in the aqueous and vitreous humor thereby increasing the macular pigment optical density (MPOD), which will be helpful for better management of Age Related Macular Degeneration.

SUMMARY

Accordingly, the invention provides new topical drug delivery system that releases the active agent in a sustained manner to provide the desired therapeutic effects, and methods of making such systems. The topical drug delivery system of the invention as disclosed herein is an emulsion. The emulsion composition as disclosed herein provides release of the active agent in sustained manner and repeated administration of the formulation several times a day will lead to a steady concentration of antioxidants in the aqueous &vitreous humor increasing the macular pigment optical density (MPOD), which will be helpful for better management of Age Related Macular Degeneration.

The emulsion composition as disclosed herein is a stable oil-in-water ophthalmic emulsion comprising one or more antioxidants, at least one oil from vegetable, mineral or animal origin, at least one surfactant and at least one pharmaceutically acceptable excipient, wherein the pH range is from about 4 to 8. The concentration of the antioxidant in the emulsion composition as disclosed herein is in the range of about 0.0003%-0.30% w/v and the antioxidant is selected from the group comprising of lutein, zeaxanthin, tocopherol, beta carotene, selenium or a combination thereof.
The oil is a vegetable oil or mineral oil or animal oil or a combination thereof.The vegetable oil is selected from the group comprising of Castor Oil, Cotton seed Oil, Peanut Oil, Coconut oil, Rice bran oil, Sunflower oil, Sesame oil, Soyabeen oil, Flax oil, Canola oil, Olive oil, Mustard Oil, Jojoba oil or a combination thereof.The animal oil is selected from the group comprising of fish oil, shark liver oil, cod liver oil or a combination thereof.The mineral oil is selected from the group comprising of Liquid Paraffin, white mineral oil or a combination thereof.
The surfactant is selected from the group comprising of Polyoxyethylated nonionic surfactants like Polysorbate80, Polysorbate 60, Polysorbate, 40, Polysorbate 20,

Cremophors, Tyloxapols, Poloxamers, Benzalkonium chloride, Benzethoniumchloride, Cetyl alcohol, Carbomer, Cholesterol, Cocamidopropyl betaine, glyceryl monostearate, lanolin alcohols, lauralkonium chlorides, N lauroylsarcosine, Nonoxynol 9, Octoxynol 40, Polyoxyl 35 castor oil, Polyoxyl 40 hydrgenated castor oil. Polyoxyl 40 stearate, Sorbitanmonolaureate, Sorbitan monooleate, Sorbitanmonopalmitate, Polyoxyethylene (2) Steryl Ether, Polyoxyethylene (2) Cetyl Ether, Polyoxyethylene (2) Oleyl Ether, Polyeoxyethyllene (2) Nonylphenylether, Polyoxyethylene (2) isooctylphenyl ether, Polyoxyletheylene (4) lauryl ether, Polyoxylethylene (5) isooctylphenylether or a combination thereof.

The emulsion composition as described herein further comprises at least one pH adjusting agent, at least one buffering agent, at least one osmolarity control agent and at least one antimicrobial preservative.

The pH adjusting agent selected from the group comprising of Hydrochloric Acid, Sodium Hydroxide, Sulphuric Acid, Sodium Sulphate, Acetic Acid, Sodium Citrate, Ammonium Hydroxide, Citric Acid, Diethanolamine, Nitric Acid, Phosphoric Acid or a combination thereof.

The buffering agent selected from the group comprising of Acetic Acid, Boric Acid, Citric Acid, Phosphoric Acid, Potassium Acetate, Potassium Phosphate, Potassium Sulphate, Potassium Sorbate, Sodium Acetate, Sodium borate, Sodium Carbomate, Sodium Citrate, Sodium Phosphate, Sorbic Acid, Tromethamine or a combination thereof.

The osmolarity control agent selected from the group comprising of Sodium Chloride, Sodium Sulphate, Sodium Nitrate, Sorbitol, Mannitol, Calcium Chloride,

Glycerine, Magnesium Chloride, PEG 300, PEG 400, Potassium Chloride, Propylene Glycol or a combination thereof.

The antimicrobial preservative selected from the group comprising of Quaternary ammonium compounds selected from Benzalkonium Chloride, Benzethoniumchloride, Benzododecinium bromide or Polyquatermium-1; or Acid/Base compounds selected from Boric acid, sodium acetate or sodium borate; or Alcohols selected from chlorobutanol or Phenylethyl alcohol; or Organic Mercuric compounds selected from Phenyl mercuric acetate, Phenyl mercuric nitrate or Thimerosal; or Parabens selected from methyl paraben or Propyl Paraben; or Oxidizing agent sodium chlorite; or Metal salt Zinc Chloride or a combination thereof.

DETAILED DESCRIPTION

As described herein, the disclosure provides emulsion compositions for ophthalmic delivery of antioxidants that releases the active agent in sustained manner and repeated administration of the formulation several times a day will lead to a steady concentration of antioxidants in the aqueous and vitreous humor increasing the macular pigment optical density (MPOD), which will be helpful for better management of Age Related Macular Degeneration.

The emulsion composition as disclosed herein is a stable oil-in-water ophthalmic emulsion comprising one or more antioxidants, at least one oil from vegetable, mineral or animal origin, at least one surfactant and at least one pharmaceutically acceptable excipient, wherein the pH range is from about 4 to 8.

The antioxidant is selected from the group comprising of lutein, zeaxanthin, tocopherol, beta carotene, selenium or a combination thereof.The concentration of the antioxidant in the emulsion composition as disclosed herein is in the range of about 0.0003%-0.30% w/v.

The emulsion composition as described herein further comprises at least one pH adjusting agent, at least one buffering agent, at least one osmolarity control agent and at least one antimicrobial preservative.

The oil is a vegetable oil or mineral oil or animal oil or a combination thereof.The vegetable oil is selected from the group comprising of Castor Oil, Cotton seed Oil, Peanut Oil, Coconut oil, Rice bran oil, Sunflower oil, Sesame oil, Soyabeen oil, Flax oil, Canola oil, Olive oil, Mustard Oil, Jojoba oil or a combination thereof.The animal oil is selected from the group comprising of fish oil, shark liver oil, cod liver oil or a combination thereof. The mineral oil is selected from the group comprising of Liquid Paraffin, white mineral oil or a combination thereof.

The surfactant is selected from the group comprising of Polyoxyethylated nonionic surfactants like Polysorbate80, Polysorbate 60, Polysorbate, 40, Polysorbate 20, Cremophors, Tyloxapols, Poloxamers, Benzalkonium chloride, Benzethonium chloride, Cetyl alcohol, Carbomer, Cholesterol, Cocamidopropyl betaine, glyceryl monostearate, lanolin alcohols, lauralkonium chlorides, N lauroylsarcosine, Nonoxynol 9, Octoxynol 40, Polyoxyl 35 castor oil, Polyoxyl 40 hydrgenated castor oil. Polyoxyl 40 stearate, Sorbitanmonolaureate, Sorbitan monooleate, Sorbitanmonopalmitate, Polyoxyethylene (2) Steryl Ether, Polyoxyethylene (2) Cetyl Ether, Polyoxyethylene (2) Oleyl Ether, Polyeoxyethyllene (2) Nonylphenylether, Polyoxyethylene (2) isooctylphenyl ether, Polyoxyletheylene (4) lauryl ether, Polyoxylethylene (5) isooctylphenylether or a combination thereof.

In one embodiment, the topical ocular suspension comprises the antioxidants lutein and zeaxanthin and pharmaceutical excipients.

Example: 1

Lutein + ZeaxanthinOphthalmic Emulsion

S. No	Ingredient	mg/mL
1	Lutein	3 mg
2	Zeaxanthin	3 mg
3	Seasame Oil	36 mg
4	Polysorbate 80	24 mg
5	Hydroxypropyl Methyl Cellulose (HPMC)	10 mg
6	Benzalkonium Chloride	1 mg
7	Water for Injection	q.s
8	Sodium citrate	20 mg
9	Hydrochloric acid/ sodium hydroxide	q.s

Process: Seasame oil was heated to about 70° C and to it was added Lutein & Zeaxanthin and stirred to completely dissolve the same in the oil phase. Sterile purified water was heated to about 70° C,and to it polysorbate 80, Sodium citrate, Benzalkonium Chloride and HPMC was added and mixed to form the aqueous phase. The oil phase was added while stiring the aqueous phase with a high shear mixerto form the emulsion. This crude emulsion was finely divided in a high pressure homogenizer and the volume was made up with sufficient quantity of water for injection and the pH was adjusted using either sodium hydroxide/ hydrochloric

acid and sterilized by filtration through 0.22 µm membrane filter to form the sterile ophthalmic emulsion of antioxidants, which is filled into containers aseptically and sealed.

In another embodiment, the ophthalmic emulsion comprises of the antioxidants lutein, zeaxanthin, alpha tocopherol, and selenium and pharmaceutical excipients.

Example: 2

Lutein , Zeaxanthin, Alpha Tocopherol & Selenium Ophthalmic Emulsion

S. No	Ingredient	mg/mL
1	Lutein	3mg
2	Zeaxanthin	6mg
3	Alpha Tocopherol	0.5 mg
4	Selenium	0.01 mg
5	Peanut Oil	81 mg
6	Poloxamer 188	56 mg
7	Polyethylene Glycol (PEG) 400	20 mg
8	Sodium chloride	9 mg
9	Phenyl mercuric nitrate	2 mg
10	Water for Injection	q.s
11	Sodium Hydroxide/Hydrochloric Acid	q.s

Process: Peanut oil was heated to about 70° C and to it was added Lutein, Zeaxanthin and alpha tocopherol and stirred to completely dissolve the same in the oil phase. Sterile purified water was heated to about 70° C ,and to it Selenium, Poloxamer 188,

Polyethylene Glycol (PEG) 400, Sodium Chloride, and Phenyl mercuric nitrate was added and mixed to form the aqueous phase. The oil phase was added while stirring the aqueous phase with a high shear mixerto form the emulsion. This crude emulsion was finely divided in a high pressure homogenizer to form a stable emulsion of antioxidants and the volume was made up with sufficient quantity of water for injection and the pH was adjusted using either sodium hydroxide/ hydrochloric acid and sterilized by filtration through 0.22 µm membrane filter to form the sterile ophthalmic emulsion of antioxidants, which is filled into containers aseptically and sealed.

In another embodiment of the invention, the ophthalmic emulsion comprises of the antioxidants lutein and alpha tocopherol and pharmaceutical excipients.

Example: 3

Lutein + AlphaTocopherol Ophthalmic Emulsion

S. No	Ingredient	mg/mL
1	Lutein	2 mg
2	Alpha Tocopherol	0.3mg
3	Medium Chain Triglycerides (MCT)	54 mg
5	Poloxamer 407	39 mg
6	Sodium Citrate	0.2 mg
7	Citric Acid	0.6mg
8	Benzalkonium Chloride	1 mg
9	Hydrochloric Acid/Sodium Hydroxide	q.s
10	Water for Injection	q.s

Process: Medium Chain Triglycerides was heated to about 70° C and to it was added Lutein, and alpha tocopherol and stirred to completely dissolve the same in the oil phase. Sterile purified water was heated to about 70° C,and to it Poloxamer 407, Sodium Citrate, Citric Acid, and Benzalkonium Chloride was added and mixed to form the aqueous phase. The oil phase was added while stirring the aqueous phase with a high shear mixerto form the emulsion. This crude emulsion was finely divided in a high pressure homogenizer to form a stable emulsion of antioxidants and the volume was made up with sufficient quantity of water for injection and the pH was adjusted using either sodium hydroxide/ hydrochloric acid and sterilized by filtration through 0.22 µm membrane filter to form the sterile ophthalmic emulsion of antioxidants, which is filled into containers aseptically and sealed.

In another embodiment of the invention, the ophthalmic emulsion comprises of beta carotene and pharmaceutical excipients.

Example: 4

Beta Carotene Ophthalmic Emulsion

S. No	Ingredient	mg/mL
1	Beta Carotene	9 mg
2	Fish Oil	60 mg
3	Kolliphor EL (Polyethoxylated Castor Oil)	54 mg
4	Sodium Citrate	0.2 mg
5	Citric Acid	0.6mg
6	Benzalkonium Chloride	1 mg

7	Hydrochloric Acid/Sodium Hydroxide	q.s
8	Water for Injection	q.s

Process: Fish Oil was heated to about 70° C and to it was added Beta carotene and stirred to completely dissolve the same in the oil phase. Sterile purified water was heated to about 70° C,and to it Kolliphor EL, Sodium Citrate, Citric Acid, and Benzalkonium Chloride were added and mixed to form the aqueous phase. The oil phase was added while stirring the aqueous phase with a high shear mixerto form the emulsion. This crude emulsion was finely divided in a high pressure homogenizer to form a stable emulsion of antioxidants and the volume was made up with sufficient quantity of water for injection and the pH was adjusted using either sodium hydroxide/ hydrochloric acid and sterilized by filtration through 0.22 µm membrane filter to form the sterile ophthalmic emulsion of antioxidants, which is filled into containers aseptically and sealed.

In another embodiment of the invention, the ophthalmic emulsion comprises of zeaxanthin and pharmaceutical excipients.

Example: 5

Zeaxanthin Ophthalmic Emulsion

S. No	Ingredient	mg/mL
1	Zeaxanthin	6 mg
2	Liquid Paraffin	69 mg
3	Polyethylene glycol oleyl ether (Brij® 93)	54 mg
4	Sodium borate	2 mg

5	Boric acid	6 mg
6	Benzalkonium Chloride	1 mg
7	Sorbitol	12 mg
8	Hydrochloric Acid/Sodium Hydroxide	q.s
9	Water for Injection	q.s

Process: Liquid Paraffin was heated to about 70° C and to it was added Zeaxanthin and stirred to completely dissolve the same in the oil phase. Sterile purified water was heated to about 70° C,and to it Polyethylene glycol oleyl ether (Brij® 93), Sodium Borate, Boric Acid, Sorbitol and Benzalkonium Chloride was added and mixed to form the aqueous phase. The oil phase was added to the aqueous phase while stirring the aqueous phase with a high shear mixerto form the emulsion. This crude emulsion was finely divided in a high pressure homogenizer to form a stable emulsion of antioxidants and the volume was made up with sufficient quantity of water for injection and the pH was adjusted using either sodium hydroxide/ hydrochloric acid and sterilized by filtration through 0.22 µm membrane filter to form the sterile ophthalmic emulsion of antioxidants, which is filled into containers aseptically and sealed.

In another embodiment of the invention, the ophthalmic emulsion comprises of lutein and pharmaceutical excipients.

Example: 6

Lutein Ophthalmic Emulsion

S. No	Ingredient	mg/mL

1	Lutein	3 mg
2	Jojoba oil	60 mg
3	Polyethylene glycol oleyl ether (Brij® 93)	45 mg
4	Sodium borate	2 mg
5	Boric acid	6 mg
6	Benzalkonium Chloride	1 mg
7	Sorbitol	12 mg
8	Hydrochloric Acid/Sodium Hydroxide	q.s
9	Water for Injection	q.s

Process: Liquid Paraffin was heated to about 70° C and to it was added Lutein and stirred to completely dissolve the same in the oil phase. Sterile purified water was heated to about 70° C,and to it Polyethylene glycol oleyl ether (Brij® 93), Sodium Borate, Boric Acid, Sorbitol and Benzalkonium Chloride were added and mixed to form the aqueous phase. The oil phase was added to the aqueous phase while stirring the aqueous phase with a high shear mixerto form the emulsion. This crude emulsion was finely divided in a high pressure homogenizer to form a stable emulsion of antioxidants and the volume was made up with sufficient quantity of water for injection and the pH was adjusted using either sodium hydroxide/ hydrochloric acid and sterilized by filtration through 0.22 μm membrane filter to form the sterile ophthalmic emulsion of antioxidants, which is filled into containers aseptically and sealed.

The method for preparing the topical ocular suspension according to the disclosure described herein is not limited to the above methods. The ophthalmic emulsion for

ocular delivery of antioxidants according to the disclosure described herein can be prepared by using various other techniques.

CLAIMS

We claim

1. A stable oil-in-water ophthalmic emulsion for ocular delivery of antioxidants comprising one or more antioxidants as an active agent, at least one oil selected from vegetable, mineral or animal origin, at least one surfactant and at least one pharmaceutically acceptable excipient, wherein the pH is in the range of about 4 to 8.

2. The stable oil-in-water ophthalmic emulsion of claim 1, wherein the antioxidant is selected from the group comprising of lutein, zeaxanthin, tocopherol, beta carotene, selenium or a combination thereof.

3. The stable oil-in-water ophthalmic emulsion of claim 1, wherein theconcentration of antioxidant is in the range of about 0.0003%-0.3% w/v.

4. The stable oil-in-water ophthalmic emulsion of claim 1, wherein the oil is a vegetable oil or mineral oil or animal oil or a combination thereof.

5. The stable oil-in-water ophthalmic emulsion of claim 1, wherein the vegetable oil is selected from the group comprising of Castor Oil, Cotton seed Oil, Peanut Oil, Coconut oil, Rice bran oil, Sunflower oil, Sesame oil, Soyabeen oil, Flax oil, Canola oil, Olive oil, Mustard Oil, Jojoba oil or a combination thereof.

6. The stable oil-in-water ophthalmic emulsion of claim 1, wherein the animal oil is selected from the group comprising of fish oil, shark liver oil, cod liver oil or a combination thereof.

7. The stable oil-in-water ophthalmic emulsion of claim 1, wherein the mineral oil is Liquid Paraffin, white mineral oil or a combination thereof.

8. The stable oil-in-water ophthalmic emulsion of claim 1, wherein the surfactant is selected from the group comprising of Polyoxyethylated nonionic surfactants like Polysorbate80, Polysorbate 60, Polysorbate, 40, Polysorbate 20, Cremophors, Tyloxapols, Poloxamers, Benzalkonium chloride, Benzethonium chloride, Cetyl alcohol, Carbomer, Cholesterol, Cocamidopropyl betaine, glyceryl monostearate, lanolin alcohols, lauralkonium chlorides, N lauroylsarcosine, Nonoxynol 9, Octoxynol 40, Polyoxyl 35 castor oil, Polyoxyl 40 hydrgenated castor oil. Polyoxyl 40 stearate, Sorbitanmonolaureate, Sorbitan monooleate, Sorbitanmonopalmitate, Polyoxyethylene (2) Steryl Ether, Polyoxyethylene (2) Cetyl Ether, Polyoxyethylene (2) Oleyl Ether, Polyeoxyethyllene (2) Nonylphenylether, Polyoxyethylene (2) isooctylphenyl ether, Polyoxyletheylene (4) lauryl ether, Polyoxylethylene (5) isooctylphenylether or a combination thereof.

9. The stable oil-in-water ophthalmic emulsion of claim 1, further comprises at least one pH adjusting agent selected from the group comprising of Hydrochloric Acid, Sodium Hydroxide, Sulphuric Acid, Sodium Sulphate, Acetic Acid, Sodium Citrate, Ammonium Hydroxide, Citric Acid, Diethanolamine, Nitric Acid, Phosphoric Acid or a combination thereof.

10. The stable oil-in-water ophthalmic emulsion of claim 1, further comprises at least one buffering agent selected from the group comprising of Acetic Acid, Boric Acid, Citric Acid, Phosphoric Acid, Potassium Acetate, Potassium Phosphate, Potassium Sulphate, Potassium Sorbate, Sodium Acetate, Sodium borate, Sodium

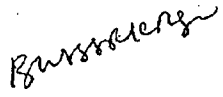
Carbonate, Sodium Citrate, Sodium Phosphate, Sorbic Acid, Tromethamine or a combination thereof.

11. The stable oil-in-water ophthalmic emulsion of claim 1, further comprises at least one osmolarity control agent selected from the group comprising of Sodium Chloride, Sodium Sulphate, Sodium Nitrate, Sorbitol, Mannitol, Calcium Chloride, Glycerine, Magnesium Chloride, PEG 300, PEG 400, Potassium Chloride, Propylene Glycol or a combination thereof.

12. The stable oil-in-water ophthalmic emulsion of claim 1, further comprises at least one antimicrobial preservative selected from the group comprising of Quaternary ammonium compounds selected from Benzalkonium Chloride, Benzethonium chloride, Benzododecinium bromide or Polyquatermium-1;or Acid/Base compounds selected from Boric acid, sodium acetate or sodium borate;or Alcohols selected fromchlorobutanol orPhenylethyl alcohol;or Organic Mercuric compounds selected from Phenyl mercuric acetate, Phenyl mercuric nitrate or Thimerosal; or Parabens selected from methyl paraben or Propyl Paraben;or Oxidizing agent sodium chlorite; or Metal salt Zinc Chloride or a combination thereof.

Dated this 29th day of August 2017

Signature



BHUPATHIRAJU VSSRK RAJU
Patent Agent (IN/PA-975)
Agent for the applicant