



# A Review: Preparation Of Eye Drop For Dry Eye Syndrome

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## ABSTRACT

Ophthalmic problem is becoming very common globally over 2 billion people suffer from vision impairment. Eye drop are the most inexpensive ophthalmic formulation. Dry eye syndrome is one of the prevalent cause for irritant feeling in eyes. Dry eye syndrome is an interpalpebral ocular surface problem also called as Keratoconjunctivitis sicca, which cause damage to interpalpebral eye surface due to deficiency of tear or uncontrolled evaporation. Resulting in the damage to the ocular surface which is getting worsen day by day. There are several preparation of eye drop for dry eye condition. There are several studies which are currently being explored with much focus on adjusting the formulation of eye drop to enhance the retention time in the eye. Castor oil is used for its anti inflammatory and lubricant effects, it has been found that it helps in maintaining the lipid layer of tears called as tear film lipid thickness and helps in increasing tear film lipid layer stability. My review objective is the preparation of eye drop containing castor oil as the active ingredient, excipients and preservatives from preventing the microbial growth. the evaluation parameter such as pH, clarity, sterility, viscosity, surface tension were studied to identify the stability of the eye formulation.

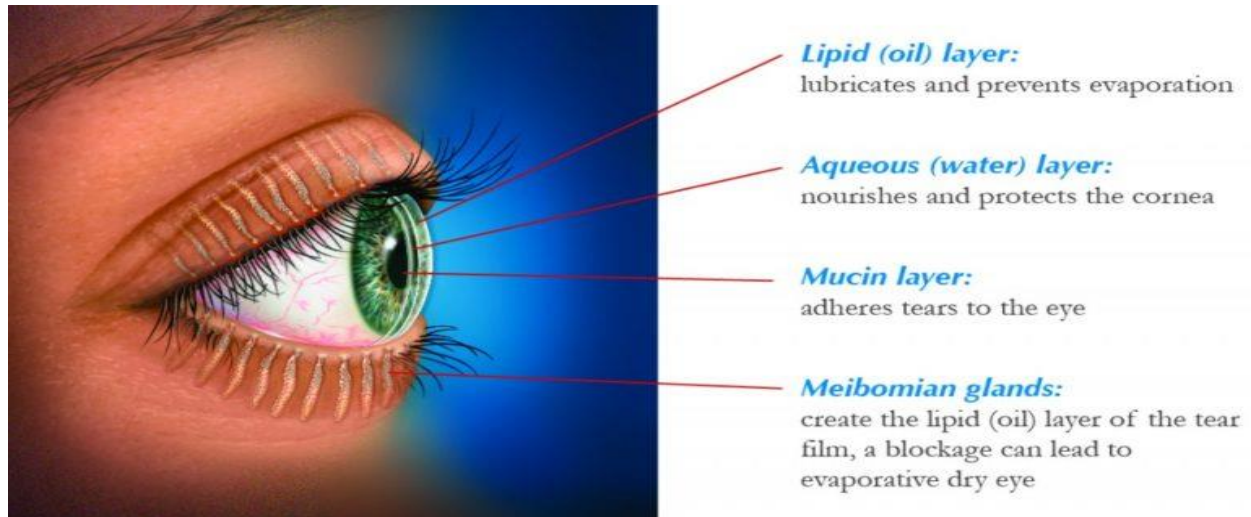
**KEYWORDS :** Keratoconjunctivitis Sicca, Castor Oil, Lubricant, Eye Drop

## INTRODUCTION:

Eye drops are liquid preparation which are applied directly to the ocular surface in few drops.

Eye drop contain saline, lubricant used to treat eye irritation which includes itching, redness, inadequate tear formation as per the diseases. Eye drop generally contain single or multiple medications to treat several eye diseases. eye drops have least side effects than oral medicines and it doesn't interfere with the first pass metabolism. [1]

Eye drop used for the treatment of dry eye helps in protecting the layers of tears that covers the cornea, lacrimal gland helps in the secretion of tears which prevent evaporation of tear by the production of mucus, tears and the use of lubricant. Human tears film has three layers: 1)fatty oils 2)aqueous liquid 3)mucus, all these three layers keep the ocular surface lubricated, clear and smooth, these layers are of semi viscous gel form, the proper integrity of tear film layer act as barrier and help protect the eye from the environment, tear film possess thickness of 3 micro meter and volume of 7-10 micro litre.[2]



**FIG 1. TEAR FILM LAYER**

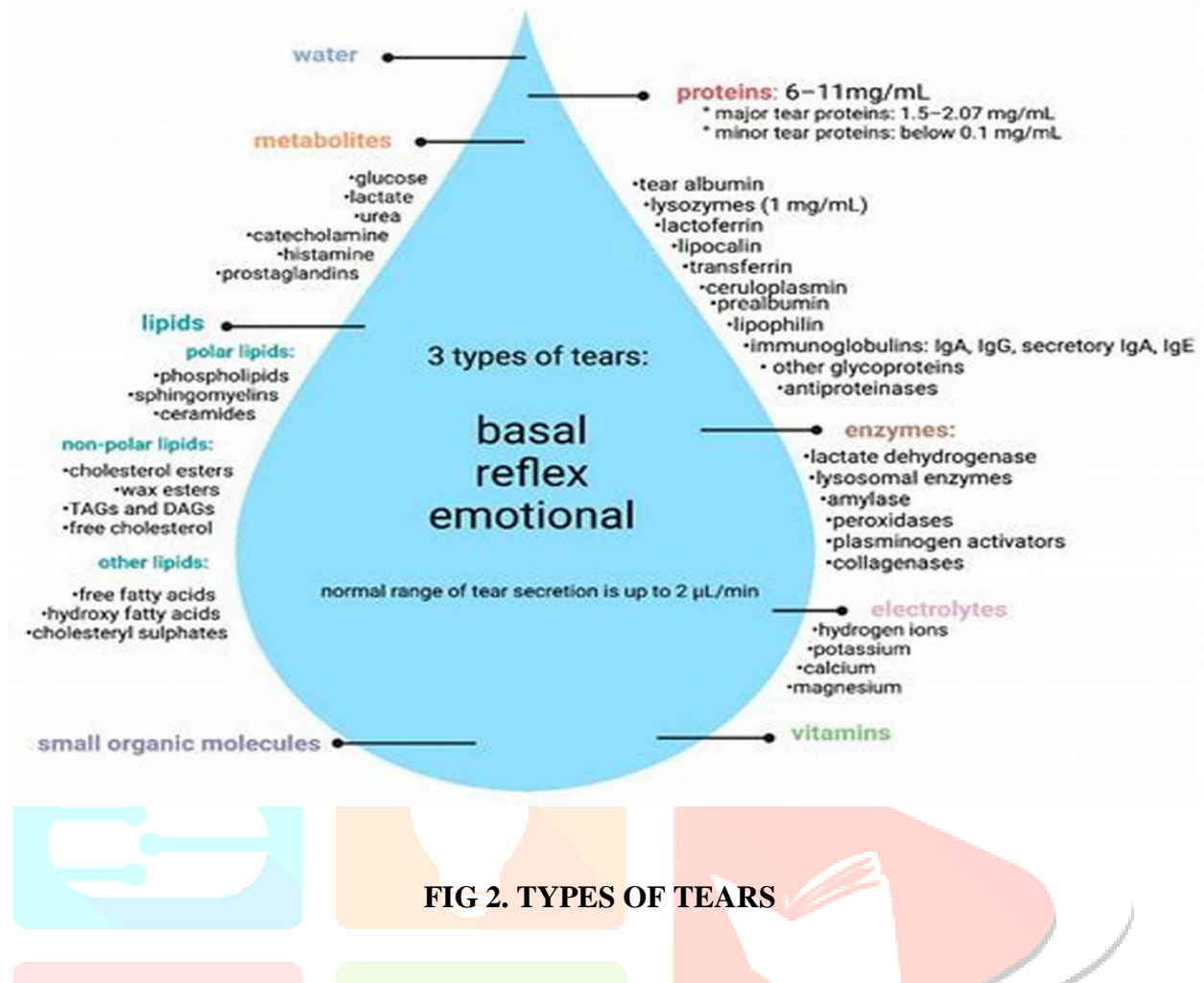
Tears are transparent, clear liquid present in the human eyes and are secreted by lacrimal gland. Tears consist of water, antibodies, electrolytes & enzymes thereby protecting the eye from infection.

Tears are of three type: 1) Basal tears 2) Reflex tears 3) Emotional tears.

1) Basal tears: these are the basic tears which are present all day in our eye & help fight infection, the oils keep the tears in place & prevent them from evaporation.

2) Reflex tears: these type of tears comes out rapidly out of the lacrimal glands due to dust or allergies and help to flush out irritants.

3) Emotional tears: these type of tears comes out in response to emotions and helps to wash out stress related toxins.[3]

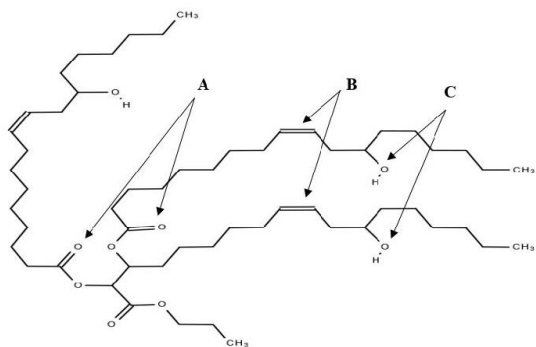


**FIG 2. TYPES OF TEARS**

Castor oil is the active ingredient used in this preparation, also known as *Ricinus communis* which is an annual oil seed crop very often known as castor. Castor oil are extracted from the seed and are mostly in used for pharmaceutical preparation such as cosmetic, perfumes and lubricant.[4] Castor oil is used as lubricant for the dry eye treatment by preventing the tear evaporation and providing the adequate lubrication to enhance the residence time increases the thickness of tear film lipid layer & improving the stability in eye.[3] The chemical profile of castor oil consist of the ricinoleic acid structure, hydroxyl group, carboxylic group structure. Fatty acid composition of castor oil are ricinoleic, stearic acid, palmitic acid, linolenic, linoleic acid and among others. Among these chemical constituent, ricinoleic acid, an unsaturated fatty acid is the prime acid consisting about 90% of the total oil composition. Castor oil found in india contains ricinoleic acid 87.3%, oleic acid 4.69%, linoleic acid 4.92%, stearic acid 1.24%, palmitic acid 1.016%, linolenic 0.63%, this composition of fatty acid which may vary from region to region across globe.[4]

**PHYSIOCHEMICAL PROFILE OF CASTOR OIL**

Physicochemical parameters	Value
Partition coefficient	2.7
Iodine value	83g I <sub>2</sub> /100 g oil.
Acid value	0.14 to 1.97mg/ g oil.
Specific gravity	313 °C
Boilling point	313 °C
Density	0.961 g/cm <sup>3</sup>
Refractive index	1.477
Viscosity	0.413cp
Optical rotation	not more than plus 3.5
Dielectric constant	4.7 [4]

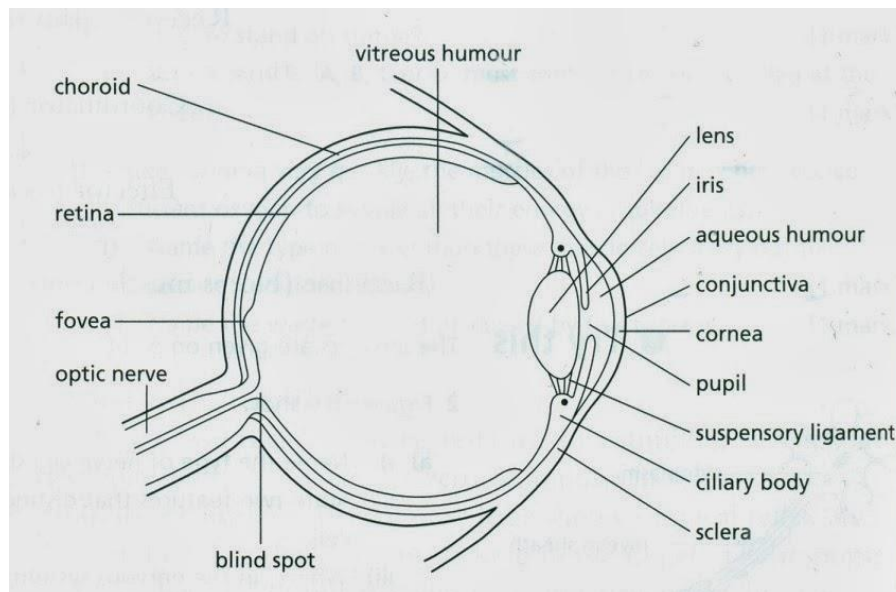
**FIG 3.STRUCTURE OF CASTOROIL****FIG 4. CASTOR OIL**

A indicate carboxyl group, B indicate double bond, C indicate hydroxyl group

**HUMAN EYE-** Eye is an specialized sense organ which is responsible for vision,eye provides vision which located in bony socket called orbit,spherical in shape,diameter about 2.5cm.

## PARTS OF EYE:

- 1) **SCLERA:** It is white tough thick in nature and protects the inner parts of the eye.
- 2) **CORNEA:** it forms the round swelling portion located on the anterior portion of the eye ball, light comes through transparent bulge and most of the refraction of light rays occur through the cornea.
- 3) **IRIS:** Iris a dark diaphragm muscular in nature present between the lens and the cornea, help in controlling the dimensions of the pupil, depends on how much light enters.
- 4) **PUPIL:** It is the small opening between the iris helps in regulating and controlling the amount of light entering the eye.
- 5) **LENS:** It is the transparent, convex and adjustable part of the eye, lens helps in creating real and inverted images with the help of cornea refracts light focuses on the retina
- 6) **CILIARY MUSCLES:** It carry the lens in place and help in changing the arch of the lens.
- 7) **AQUEOUS HUMOUR:** These are viscous watery fluid that is present in the area between the lens and cornea.
- 8) **VITREOUS HUMOUR:** These are glassy, smooth like substance present between the retina and lens.
- 9) **RETINA:** Retina is the innermost layer of eye where the images are formed. it consist of large number of light sensitive cells called photoreceptor, they are of two types:
  - a) **Rods:** It is responsible for vision at dim light.
  - b) **Cones:** It is responsible for vision at bright light and gives colour vision. [6][7]



**FIG 5. STRUCTURE OF EYE**

**EYE DISEASES:-**

Numerous individual experience challenges with their eyesight, facing various conditions that can cause discomfort within different parts of the eye. Some issues are minor and may resolve spontaneously, while others necessitate the attention of a specialized healthcare professionals.

1. **AGE RELATED MACULAR DEGENERATION:** It affects the retina of human eye due to aging, Macula a part of retina which is light sensitive tissue is damaged that causes vision loss.
2. **CATARACT:** This affects the human eye lens development of cloudy around lens, which result in blurry vision, trouble with color light, difficulty in reading/seeing at night.
3. **DIABETIC RETINOPATHY:** It is caused by diabetes damaging the retina and the blood vessels of the eye, resulting in vision loss and blindness in diabetic person.[8]
4. **GLAUCOMA:** It affects the optic nerve carrying the signal from human eye to brain, by damaging the optic nerve which result in vision loss, if untreated.
5. **BLEPHARITIS:** It is characterized by inflammation, pain, reddening, scalling and swelling of the eye lids.
6. **COLOUR BLINDNESS:** Difficulty distinguishing between colors, such as red and green or blue.[8][12].
7. **CONJUNCTIVITIS :** Also known as “ pink eye”, this is a contagious disease that causes the whites of the eyes to appear pink and may produce a sticky discharge.[9]
8. **KERATOCONUS:** A condition that changes the shape of the cornea, leading to distorted vision
9. **MACULAR DEGENERATION:** A disease that destroys sharp, central vision and can lead to blindness.
10. **REFRACTIVE ERRORS :** Common vision problem that cause eye pain and sudden loss of vision, such as nearsightedness, farsightedness, and astigmatism.[8][12]
11. **DRY EYE :** Human tears is very important for maintaining the normal vision. It consist of tear film layer which provide lubrication to the human eye, any dysfunction in tear film result in unstability of tear film causing insufficient tear formation or tears evaporation resulting in drying, itching, inflammation of the eye. [13]



**FIG 6. DRY EYE**

### **ADVANTAGE OF EYE DROP**

1. It Provide direct ocular application at the site of action & ensure availability of active pharmaceutical ingredients at higher concentration than oral route.
2. Ocular route has fastest drug absorption & show least side effects.
3. It bypasses the first pass metabolism & there is no issue of unpleasant taste & odour.
4. It doesn't provide any type of pain as in parental route administration.
5. It require small amount of drug in formulation

### **DISADVANTAGE OF EYE DROP**

1. Through ocular route there is rapid elimination of eye drop, which result in increase loss of drug and thereby causing poor retention of drug at the site of action.
2. The quick elimination of eye drop through tears & eye blink result in short period of therapeutic effect of drug.
3. After application of ocular formulation may temporarily cause blurry eye vision.
4. Limited drug are available for ophthalmic formulation.
5. There are special requirement of pharmaceutical processes for manufacture of eye drop, making it expensive.[14]

**EYE DROPS AVAILABLE IN MARKET-**

S.no	Name of product	Salt name
1)	ECOMOIST ULTRA	Polymethylene glycol400 & propylene glycol
2)	DORZOX-T	Dorzolamide & timolol
3)	CATAREST/ CATAGON	potassium chloride & sodium chloride & calcium chloride
4)	CAFTA	alcaftadine 0.25% w/w
5)	LIQUIFILM	florometholine/hypromellose
6)	BRIVEX	brinzolamide 1% w/v & brimonidine tartarate 0.2% w/v
7)	TEAR DROPS / REFRESH LIQUIGEL	carboxymethyl cellulose
8)	BIMAT-LS	bimatopro 0.01% w/v
9)	BETAFREE	bimatopro 0.01% w/v
10)	T-BET PF	travoprost & timolol
11)	TOBA	tobramycin
12)	DORZOX-T, MONOSOFT	dorzolamide timolol eye drop
13)	PRED-FORTE	prednisolone acetate 0.5%
14)	KIDTRO	atropine sulphate 0.5%
15)	CIPLOX	ciprofloxacin
16)	HYLA	sodium hyaluronate E.D
17)	BRIMOLOL	brimonidine tartarate & timolol maleate
18)	NEPAFLAM	nepafenac 0.5%



19)	MAXMOIST	sodium hyaluronate
20)	NORMO	polyethylene glycol400 & propylene glycol 0.5% w/v
21)	GENTEAL	hydroxy methyl cellulose
22)	SOFT DROP	sodium car boxy methyl cellulose 0.5% & glycerin 0.5%
23)	OLOPAT	olopatadine hydrochloride 0.5% w/v.
24)	REFRESH OPTIVE ADVANCED	CARBOXYMETHYLCELLULOSE(0.5%),GLYCERIN(1% ) ,POLYSORBATE 80(0.5%).[14][15]



**FIG 7. MARKETED PREPARATION OF EYE DROP**

## INGREDIENTS

1. Castor oil- It is obtained from the seeds of *Ricinus Communis*, In pharmaceutical industries castor oil is of great demand.[17][18] Few drops of castor oil on ocular surface has found to increase the tear lipid layer thickness and enhances stability. It has been found from several studies that the castor oil eye drop are found to be safe and effective for the Meibomian gland dysfunction.[19]

2.Sodium chloride - The ph of sodium chloride solution, such as in eye drops, is typically close to neutral,around 7. the eyes natural ph is also close to neutral, so solution with a ph in this range are generally well tolerated. The eye can withstand products over a range of pH from 3.0 to 8.6 , from various study it is found that the efficacy of both hypo tonic and isotonic solution are found to be effective for the symptomatic treatment of dry eye patient. Tear osmolarity is 289mosm/L, In dry eye case there is an hyper tonic state which cause irritation in human eye, thus it is important that the osmolarity of eye drop for dry eye should be below 289mosm/L that is hypotonic or isotonic to treat dry eye syndrome. Sodium chloride is found as as a potent tonicity modifier and are used widely among the eye drop as eye wash,in case of eye drop, it is very important to maintain the hypo tonic or isotonic condition in order to prevent any corneal inflammation due to hyper osmolarity.[20][21]

3.Glycerin (1%) is used as surfactant to maintain the surface tension. It is widely used in combination with other ingredients as surfactant in eye drop. Glycerin are formulated to prolong the non invasive tear film break up time has longer time period of 120 minutes than other marketed formulation thereby it is found that the glycerin 1% are new therapy for dry eye diseases treatment.[22][23]

4.Preservatives are very important to prevent the growth of the microorganism in an ophthalmic formulation,some traditional preservative are found to be very effective against the traditional one. Stabilized oxychloro complex is used as preservative in eye drop formulation to prevent the growth of microorganisms, as it is found from the study that it doesn't show any cytotoxic effect in the cornea area of the eye when examine through in-vitro rabbit eye test.soc caused the least amount of side effects comparative to other preservative[24]

**PREPARATION**

<b>Ingredients</b>	<b>ACTION</b>
<b>Castor OIL(0.25%)</b>	<b>Lubricant</b>
<b>Sodium chloride (0.6%)</b>	<b>Tonicity Modifier</b>
<b>Stabilized oxychloro complex (0.005%)</b>	<b>Preservative</b>
<b>Glycerin (1%)</b>	<b>Surfactant</b>

**Method of preparation :**

1. Weigh and measured all the required ingredients of eye drop properly and keep separately as per required. Take 100 ml beaker and dissolve 0.6 gm of sodium chloride in sterile purified 100ml of water followed by addition of glycerin 1%.
2. Add castor oil (0.25%) and dissolve it with stabilized oxychloro complex (0.005%) by continuous shaking.
3. The prepared eye drop is subjected to evaluation test.

**EVALUATION TEST OF EYE DROP**

1. Ph: Normal tears possess a pH of 7.4 and have some buffer capacity. Ideally an ophthalmic solution should have same pH and isotonicity solution as the lacrimal fluid. So the overall pH of the eye drop is calculated through pH paper around reading 7.4 neutral.
2. Clarity: The clarity test for eye drops assesses the transparency or clearness of the solution. During the clarity test, the eye drop solution is visually inspected against a light background to check for any cloudiness, particulate matter, or discoloration. The solution should appear clear and free of any visible particles.
3. Sterility test: The sterility test is typically conducted using aseptic techniques, it involves taking a sample from the batch of eye drop solution and inoculating it into a suitable culture media. (soybean- casein digest medium or fluid thioglycollate medium) The culture medium is then monitored for the growth of microorganisms over a specified incubation period (7 days), if no microbial growth is detected during the incubation period, the eye drop batch is considered sterile. However, if microbial growth occurs, it indicates contamination and then batch may be rejected.

4. Leakage test: The leakage test for eye drop is performed to ensure the integrity of the container and closure system. Preventing any leakage of the eye drop solution during storage and use. This test is important to maintain the sterility, stability, and proper dosing of the eye drops. There are various methods for conducting a leakage test, and the specific procedure may vary depending on the type of packaging used for the eye drop container.

Dye penetration test is the most common test for eye drop container, in this it is immersed in dye solution, if there is any leakage, dye will penetrate into the container, making it visible this method provides a visual indication of leaks and can be useful in detecting even small defects.

5. Viscosity test: Viscosity is an important parameter to evaluate the ophthalmic preparation, the required viscosity should not exceed 30mpas, measure through brookfield viscometer/Ostwald's viscometer.

6. Sterilization method: The plastic eye drop container is sterillised through physical method that is autoclave at 121 degree Celsius for 15 minutes, and the contamination is observed.

7. Surface tension: Through Stalagmometer the drop of sample and standard is compared by adjusting through dropper, if more will be the surface tension lesser will be the drop fall out and lesser the surface tension more drop will come out[25].

### Observation

Name of the test	Observation
appearance	Clear, colourless
pH	7.4
Clarity test	Free from foreign matter
Sterility test	Free from microbial contamination
Leakage test	Should be free from any leakage
Sterilisation	Should be free from contamination

## CONCLUSION

The eye is a crucial sensory organ that enables us to see our Environment. By enabling us to view and understand visual information, it plays a key part in our daily lives. Our current way of living, which includes a lot of screen time, prolonged close work, and pollution has a huge impact on how well our eye's function. Digital eye strain, dry eye syndrome, myopia, and other visual discomforts are becoming more common due to these lifestyle factors. In this review, we have discussed about the preparation of eye drop for dry eye syndrome. This eye drop including castor oil as antioxidant & lubricant, sodium chloride as tonicity modifier, glycerin as surfactant & stabilized oxychloro complex as preservative. These components can promote eye health and lower the risk of common eye disorders by supporting the health of the retina, lens, and other ocular structures.

## REFERENCES

1. Clotilde Jumella, et al. "Advances and limitation of drug delivery system Formulated as eye drops". Journal of control release. 2021, 0168-3659, vol321.
2. A. J. Bron, et al. "Functional aspects of the tear film lipid layer", experimental eye research. 2004, vol78 (3), pp 347-360.
3. BA (Hons Oxon), "The composition and interfacial properties of tears, tear substitutes and tear models", journal of the British contact lens association, vol6(2), pp57-66
4. Akwasi Yeboah, et al. "Castor oil (*Ricinus communis*): a review on the chemical composition and physicochemical properties". Food science and technology, Campinas. 2020, 0101-2061,
5. M. I. Fitrandi, et al. "Physicochemical Properties and Antibacterial Activity of Castor Oil and Its Derivatives". IOP Conference series: Materials science and Engineering, 2019, 1757-899X, vol833.
6. Collin E Willoughby MD, Anatomy and physiology of the human eye: effects of mucopolysaccharidosis disease on structure and function – a review, Clinical and Experimental Ophthalmology, 2010, vol38, 1442-9071.
7. Herbert Gross, et al. "Human Eye". Handbook Of Optical System, 2008, vol4.
8. Karin Attebo, et al. "Knowledge and beliefs about common eye diseases". Australian and New Zealand Journal of Ophthalmology, 2009, vol25(3).

9. Nicolas.R.Galloway,et all. "Common Diseases of the Conjunctiva and Cornea".Common Eye Diseases and their Management,2016,pp 47-63.
- 10.Nicolas.R.Galloway,et all. "Cataract",Common Eye Diseases and their Management,2016,pp 88-99.
- 11.Nicolas.R.Galloway,et all. "Glaucoma",Common Eye Diseases and their Management,2016,pp 101-114.
- 12.Ning Cheung MBBS,et all. "Obesity and Eye Diseases",Survey of Ophthalmology,2007,vol52(2),pp180-195.
- 13.BY MICHAEL A,et all. "The Definition & Classification of Dry Eye Disease",Guidelines from the 2007 International Dry Eye Workshop,2008,pp 1-6.
- 14.Clotilde Jumelle,et all. "Review article:Advances and limitations of drug delivery systems formulated as eye drops", Journal of Control Release,2020, vol321,pp1-22.
- 15.Arjun Watane ,et all. "The Effect of Market Competition on the Price of Topical Eye Drops",Seminars in Ophthalmology,2022,vol37 ,pp 42-48.
- 16.Miki Uchino,et all. "Adherence to Eye Drops Usage in Dry Eye Patients and Reasons for Non-Compliance: A Web-Based Survey", Journal of Clinical medicine,2022,vol11(2).
- 17.D.S ogunniyi, "Castor oil as vital industrial raw material",bioresoucre technology,vol97(9),pp1086-1091.
- 18.Vinay R. Patel,et all. "Castor Oil: Properties, Uses, and Optimization of Processing Parameters in Commercial Production",Lipid Insights,2016,pp1-12.
- 19.Cecile Maissa, "Effect of castor oil emulsion eye drops on tear film composition and stability",contact lens and anterior eye,vol33(2).
- 20.Ying li,Comparison of 0.3% Hypotonic and Isotonic Sodium Hyaluronate Eye Drops in the Treatment of Experimental Dry Eye",current eye research,2017,vol 42(8),pp1108-1114.
- 21.Johannaes Nepp,et all. "The clinical use of viscoelastic artificial tears and sodium chloride in dry-eye syndrome",Biomaterilas,2001,vol22(24),pp 3305-3310.
- 22.William G Gensheimer,et all, "Novel Formulation of Glycerin 1% Artificial Tears Extends Tear Film Break-Up Time Compared with Systane Lubricant Eye Drops",JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTIC,2012,vol28(8).

23. William.G.Gensheimer,et all, “Novel formulation of glycerin 1% artificial tears extends tear film break -up Time compared with systane lubricant eye drop”,Journal of ocular pharmacology and Therapeutics,2012,vol28(5).

24.A.Oyejide,et all, “comparative ocular histopathological effects of eye drop containing purite or benzalkonium chloride preservatives on Rabbit” investigaitive ophthalmology and visual science,2023,vol44(13).

25.Andjelka Racic,et all. “Formulation of olopatadine hydrochloride viscous eye drops – physicochemical, biopharmaceutical and efficacy assessment using in vitro and in vivo approaches”,European Journal of Pharmaceutical Sciences,2021,vol 166.

